

2. Studies of Cancer in Humans

The available knowledge on the relationship between the consumption of alcoholic beverages and a variety of human cancers is based primarily on epidemiological evidence. The cancers considered to be causally related to alcoholic beverage consumption in the previous *IARC Monographs* on alcohol drinking (IARC, 1988) included those of the upper aerodigestive tract (oral cancer and cancers of the oropharynx, hypopharynx, larynx and oesophagus), liver, colon, rectum and possibly breast. Since 1988, many cohort and case–control studies on the relationship between consumption of alcoholic beverages and these and other cancers have been conducted in many different countries. The most comprehensive evidence has been obtained from several large cohort studies that investigated different cancer sites and, when available, different types of alcoholic beverage consumed. These cohort studies are described briefly in Section 2.1. The case–control studies are described in the sections pertaining to particular cancer sites. Additionally, two meta-analyses (Bagnardi *et al.*, 2001; Corrao *et al.*, 2004) found significantly increased risks for cancer at all of the aforementioned sites associated with alcohol drinking. Meta odds ratios less than 1.00 were found for melanoma, cervical cancer and kidney cancer. A positive dose-response relationship was observed for most of these sites. [The Working Group noted that the Bagnardi *et al.*, 2001 study appears to be more comprehensive than Corrao *et al.*, 2004, although a detailed list of the studies included in both meta-analyses is not given].

In reviewing these epidemiological studies, the Working Group took particular note of those that adequately considered issues related to bias and confounding. In this respect, since much of the evidence relates to cancers known to be caused by tobacco smoking, confounding by the effects of tobacco smoking is critical for many sites. Thus, the few studies that considered the risks from alcoholic beverage consumption in lifelong nonsmokers are particularly important.

The terminology and methods used to characterize the combined effects of two or more agents have been poorly standardized. For the purposes of this monograph, interdependence of effects is called ‘effect modification’, and the terms ‘synergism’ and

'antagonism' are used to describe the consequences of the interdependence of disease when both risk factors are present (Rothman & Greenland, 1998).

The effect of a risk factor for a disease may be estimated on an absolute (additive) scale or a relative (multiplicative) scale. In general, epidemiological studies use the relative risk scale, and present ratio measures (e.g. the relative risk that compares risk in the exposed group to that in a referent, typically unexposed, group). In those studies in which the findings depart (in either direction) from this scale, lack of synergy in the multiplicative scale (i.e. similar relative risks in low and high incidence groups) can imply synergy in the additive scale, and thus have important public health implications.

The Working Group did not evaluate studies of precancerous lesions, e.g. adenomas and polyps of the rectum, precursor lesions of the oral cavity or intraepithelial neoplasia of the cervix uteri for several reasons: firstly, many studies considered invasive cancers, secondly, precancerous lesions do not necessarily progress to cancer during the subjects' lifetime and thirdly, the implications of studies on lesions that have a high propensity not to progress to invasive cancer are uncertain.

In this respect, the pooling of results from many small studies and meta-analyses provide an opportunity to evaluate sites for which relatively few cases accrue. The Working Group placed substantial weight on the findings for cancer sites for which studies had been pooled.

Assessment of alcoholic beverage intake in case-control and cohort studies

In cohort studies, it may be difficult to obtain lifetime estimates of exposure to alcoholic beverages, especially for those studies that only collected data at baseline, since there is a risk that individuals may change their drinking habits during the period of observation. Even in case-control studies, in which, theoretically, there is an opportunity to collect exposure data up to the date of interview, problems of recall, including difficulties in recollection and classical recall bias, may result in complications in the development of reliable estimates of cumulative exposure. In general, the Working Group felt that the classification of subjects as current drinkers (light and heavy), former drinkers and never drinkers is valid and that data on amounts drunk per day (or per week for light or occasional drinkers) are also sufficiently reliable. However, estimates of various patterns of exposure to alcoholic beverages, especially binge drinking, are not available in most studies. Nevertheless, in spite of the differences in the quality and reliability of data on exposure between cohort and case-control studies, when data were available that produce findings that are congruent from both types of study, the Working Group placed much weight upon such evidence.

Alcoholic beverage intake in epidemiological studies has usually been assessed by interviews or questionnaires regarding usual intake over a period of months or years. Two main methods have been used: semiquantitative questionnaires (e.g. how often on average do you consume a bottle of beer?) or frequency-quantity questionnaires (e.g. how many days per week do you drink beer? And, on the days you drink, how many

bottles of beer do you drink?). These questions can refer to consumption of either alcoholic beverages in general or specific beverages (e.g. beer, wine and liquor), which can then be summed to compute total intake of alcohol. Total alcohol intake is calculated by assuming (based on knowledge of the contents in the population studied) a specific amount of alcohol for each type of beverage (e.g. 12 g of alcohol per glass of wine, 13 g per bottle of beer and 15 g for one glass of liquor). Alcoholic beverage consumption can also be assessed by diet diaries or 24-hour recalls, but multiple days of intake are usually required because intake in many populations can vary considerably from day to day or over a year. Because these methods impose a substantial burden on the participant and/or investigator, they have rarely been used in cohort studies and, in case-control studies, they are not appropriate because alcoholic beverage consumption may have changed due to the occurrence of disease. However, these methods provide a quantitative measure of intake that can serve as a criterion of validity in subsamples of a study population.

Multiple sources of error can contribute to imperfect measurement of alcoholic beverage consumption. These include errors in reporting the frequency of intake, which can be influenced by many factors including inaccurate memory, social norms of desirability and subtle indications of judgment by the interviewers. Also, serving size and alcohol content of the same serving size can vary over time for the same person and between people. However, some of these sources of variation are tempered by averaging over time; for example, although serving size may vary from drink to drink over time for an individual, the average intake for one person compared with that of another may vary to a much lesser degree. Also, the differences among individuals in alcoholic beverage intake are large, and errors in serving sizes are usually minor in relation to the overall range of alcoholic beverage intake.

The validity of alcoholic beverage intake as assessed in typical epidemiological studies has been evaluated by comparisons with daily diaries or recalls, by associations with biological variables that reflect alcoholic beverage intake and by their ability to predict well established relationships such as those between alcoholic beverage consumption and risks for cirrhosis. Correlations between alcoholic beverage intake assessed by standardized questionnaire and diaries or 24-hour recalls have been evaluated in many studies and are high, generally ranging from 0.7 to 0.9 (Kaaks *et al.*, 1997; Willett, 1998; Lee *et al.*, 2007). Although the mean reported intakes in these studies are usually well below that of the average population, based on production or sales of alcoholic beverages, these comparisons are misleading because a larger percentage of alcoholic beverages is consumed by a small group of heavy drinkers (Greenfield & Rogers, 1999), who are less likely to participate in epidemiological studies.

The relationship between alcoholic beverage intake assessed by a questionnaire and that assessed by detailed recording can be used to adjust relative risks for measurement error in epidemiological studies (Rosner, 1995; Willett, 1998); several variations of this approach have been used, but they basically consist of two steps: first a regression calibration is conducted by assessing intake using a detailed method in a

sample of the study population; then the true intake (intake assessed by the detailed method) is regressed on the 'surrogate method' (intake assessed by the questionnaire). The relationship between surrogate intake and true intake, expressed by the regression slope, is then used to correct the observed relative risk for error. Refinements of this method allow the calculation of confidence intervals (CIs) and adjustment for errors in covariates (Rosner, 1995). This approach to measurement error has been used in large cohort studies of alcoholic beverages and cancer, and the adjustments have been small (less than 5% change in relative risks) (Smith-Warner *et al.*, 1998; Cho *et al.*, 2004; Lee *et al.*, 2007).

Studies on biomarkers, such as HDL (Giovannucci *et al.*, 1991), provided strong evidence that alcoholic beverage consumption assessed by questionnaire has high validity.

The evidence described above suggests that the questionnaires commonly used in epidemiological studies provide reasonably accurate quantitative assessments of alcoholic beverage intake over the time period considered, typically a few months or a year. In a cohort study with long follow-up, repeated measures of exposure over time may provide a more accurate measure of long-term intake and allow a more detailed examination of temporal relationships (Willett, 1998). In both case-control and cohort studies, it may be useful to ask about alcoholic beverage intake during past periods of life (for example between the ages 20 and 30 years) because, for some cancers, that may be the period of maximal susceptibility. Few data are available of the validity of reported remote intake.

In summary, evidence based on comparisons with detailed assessments of alcoholic beverage intake using diaries or recalls and non-specific biomarkers indicate that recent alcoholic beverage consumption assessed by the questionnaires typically used in epidemiological studies has a high degree of validity within the ranges of consumption in the general population, and that important associations will not be missed. Further, the results of correction analysis of measurement error suggest that estimates of quantitative dose-response relationships for recent intake are reasonably accurate. However, with long follow-up, repeated measures of intake may be useful. The assessment of intake at remote periods of life may be useful, but the validity of these measures has not been well quantified.

2.1 Description of cohort studies

Information on cohort studies of cancer and alcoholic beverage consumption in general populations and special populations is given in Tables 2.1a and 2.1b, respectively.

2.1.1 Studies in general populations (Table 2.1a)

These studies are classified by the country in which the study was conducted.

Table 2.1a. Cohort studies of cancer and alcoholic beverage consumption in general populations

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Asia/Oceania								
<i>Australia</i>								
Melbourne Collaborative Cohort Study	1990–94	Baglietto <i>et al.</i> (2005, 2006)	1990–2003	Cohort of 41 528 men and women, aged 27–75 years	Interview	Cases/deaths	Breast, prostate	
<i>China</i>								
Zoucheng/Shandong Study	1982	Zhang <i>et al.</i> (1997)	1982–94	7809 men and 7994 women from probabilistic sample of general population in three counties, aged ≥ 20 years	Baseline questionnaire		Lung	No dose–response found for frequency, amount or duration of drinking; lung cancer mortality found in crude analyses
Linxian Nutrition Intervention Trial	1986	Guo <i>et al.</i> (1994); Tran <i>et al.</i> (2005)	1986–2001	Nested case–control study; a cohort of 29 584 adults in a randomized intervention trial, aged 40–69 years	Structured interview	Cases	Oesophagus, stomach	Drinking alcoholic beverages was relatively uncommon in Lin Xian residents, but was reported by 22% of the cancer patients.

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Shanghai Men's Study	1986–89	Yuan <i>et al.</i> (1997)	1986–95	18 244 male residents of Shanghai, aged 45–64 years	Structured interviewed	Deaths	Upper aerodigestive tract, stomach, colon, rectum, liver, lung	Joint effects of alcohol and smoking examined
Jiashan County Screening Study	1989–90	Chen <i>et al.</i> (2005a)	1989–2001	31 087 men and 33 256 women screened for colorectal cancer in 1989–90, aged ≥ 30 years	Interviewer-administered standardized questionnaire	Deaths	Colon, rectum	No differences in risk for men and women; among only one case among former drinkers
Yunnan Tin Corporation Miners Cohort	1992	Lu <i>et al.</i> (2000a)	1992–97	7965 miners, aged ≥ 40 years; 10 years of high-risk professional activity	Interviewer-administered questionnaire		Lung	
<i>Japan</i> Japanese Physicians' Study	1965	Kono <i>et al.</i> (1985, 1986, 1987)	1965–83	5130 male Japanese physicians, aged 27–89 years	Self-administered questionnaire	Deaths	Upper aerodigestive tract, oesophagus, stomach, large bowel, liver, lung	Joint effects of alcohol and tobacco examined

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Six Prefecture Study	1965	Hirayama (1989, 1992); Kinjo <i>et al.</i> (1998)	1966–82	122 261 male and 142 857 female, Japanese adults aged 40–69 years at the baseline of 1965, from 29 public health districts in six prefectures of Japan	Interviewer-administered standardized questionnaire	Deaths	Mouth, pharynx, oesophagus, stomach, proximal colon, rectum, sigmoid colon, upper and lower digestive tract, liver, prostate	Joint effect of alcohol and tobacco examined
Life Span Study	1979–81	Goodman <i>et al.</i> (1997a)	1979–89	Analytical cohort of 22 000 residents of Hiroshima and Nagasaki in 1945 [age range not stated]	Self-administered questionnaire	Cases	Breast	No association in women who drank beer, sake or other alcoholic beverages
Chiba Center Association Study	1984	Murata <i>et al.</i> (1996)	1984–93	Nested case–control study; cohort of 17 200 men part of a gastric mass screening survey	Self-administered questionnaire	Cases	Oral cavity, pharynx, oesophagus, stomach, colon, rectum, liver, pancreas, biliary tract, larynx, lung, prostate urinary bladder	The effect of tobacco smoking was examined.

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Aichi Cancer Center Hospital Study	1985	Kato <i>et al.</i> (1992a)	1985–89	3 914 subjects who underwent gastroscopic examination	Self-recorded questionnaire, cancer registry and death certificate	Cases	Stomach	Non-significant increase for risk in stomach cancer among past and daily drinkers
Aichi Prefecture Study	1986	Kato <i>et al.</i> (1992b)	1986–91	9 753 Japanese men and women, aged ≥ 40 and ≥ 30 years, respectively	Baseline survey using a mailed questionnaire; death certificate	Cases	Stomach	Association between alcohol intake and stomach cancer slightly weakened when smoking status, diet and family history of stomach cancer were included in the multivariate analysis.
Japanese Collaborative Cohort Study (JACC)	1988–90	Lin <i>et al.</i> (2002, 2005); Sakata <i>et al.</i> (2005), Wakai <i>et al.</i> (2005); Nishino <i>et al.</i> (2006)	1988–99	110 792 (46 465 men, 64 327 women), aged 40–79 years	Self-administered questionnaire	Cases/deaths	Oesophagus, colon, rectum, breast, pancreas, lung,	Relative risks by smoking status reported

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Hospital-Based Epidemiologic Research Program at the Aichi Chiba Center (HERPACC)	1988–99	Inoue <i>et al.</i> (2003)	1988–2000	Nested case– control study of 78 755 hospital patients, aged 32–85 years	Self- administered questionnaire	Cases	Pancreas	Increased risk in men and women, separately; the increased risk in former drinkers may be due to ill-health
Japan Public Health Center Study Cohort I	1990	Sasazuki <i>et al.</i> (2002)	1990–99	27 063 men, 27 435 women born in 1930–49, aged 40–59 years at baseline	Self- administered questionnaire, death certificates, cancer registry	Cases	Stomach	Data for women collected but not presented
Takayama City Cohort	1992	Shimizu <i>et al.</i> (2003)	1993–2000	Analytic cohort of 13 392 men and 15 695 women, aged ≥35 years	Self- administered standardized questionnaire	Cases	Colon, rectum	Significant dose–response relationship between alcohol consumption and colon cancer in both sexes

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Japan Public Health Center Study Cohort II	1993	Otani <i>et al.</i> (2003)	1993–99	42 540 male and 47 464 female Japanese, aged 40–69 years	Self-administered standardized questionnaire	Cases	Colon, rectum	In men, no interaction of smoking with alcoholic beverage consumption for colon, rectal or colorectal cancer; no associations for colorectal cancer in women
North America								
<i>Canada</i>								
Nutrition Canada Survey Cohort	1970–72	Ellison (2000)	1970–93	12 795 respondents to a population survey, aged 50–84 years	Interviews	Cases	Prostate	
National Breast Screening Study	1980–85	Friedenreich <i>et al.</i> (1993); Jain <i>et al.</i> (2000a,b); Rohan <i>et al.</i> (2000); Navarro Silvera <i>et al.</i> (2005)	1980–93	Total 89 835 women, aged 40–59 years; 56 837 women, aged 40–59 years	Self-administered lifestyle questionnaire	Cases	Breast, endometrium, thyroid	

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
<i>USA</i>								
American Registry of Radiologic Technologists	1926–82	Boice <i>et al.</i> (1995); Freedman <i>et al.</i> (2003)	1926–89	146 022 radiologic technologists, aged 23–90	Self-administered questionnaire	Cases	Melanoma, breast	Nested case–control study
University of Pennsylvania Alumni Study	1931–40	Whittemore <i>et al.</i> (1985)	1931–78	13 356 male and 4 076 female students examined at the University of Pennsylvania in 1931–40	College physical examination, questionnaires	Cases/deaths	Buccal cavity, oesophagus, stomach, small intestine, colon, rectum, liver, biliary tract, pancreas, larynx, trachea, bronchus, lung, melanoma, other skin, breast, urogenital organs, prostate, testis, urinary bladder, kidney, brain, thyroid, Hodgkin disease, non-Hodgkin lymphoma, leukaemia, other cancer	Data on collegiate alcohol consumption limited

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Minnesota Breast Cancer Family Study	1944–52	Vachon <i>et al.</i> (2001)	1944–90	Breast cancer patients from the Tumor Clinic of the University of Minnesota; 544 families representing 4418 family members	Telephone interviews (surrogate and self-reported)	Cases	Breast	Higher risk in first-degree relatives for daily versus never drinkers; validation study verified 136 of 138 breast cancers through medical and pathology records
US Army Veterans Study	1944–45	Robinette <i>et al.</i> (1979)	1946–74	4401 chronic alcoholic male veterans, hospitalized in 1944–45	Death certificates	Deaths	Buccal cavity, pharynx, nasopharyngitis, oesophagus, stomach, large intestine, rectum, pancreas, larynx, trachea, bronchus, lung, prostate, testis, penis, urinary bladder, kidney, malignant lymphoma, lymphatic and haematopoietic leukaemia, ureter	Compared with age-matched male veterans hospitalized for nasopharyngitis; no individual exposure data; no information on potential confounders

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Framingham Study (1948) and Framingham Offspring (1971)	1948, 1971	Gordon & Kannel (1984); Zhang <i>et al.</i> (1999); Djoussé <i>et al.</i> (2002, 2004)	1948–present	In 1948, 5209 subjects, aged 28–62 years at first examination; in 1971, 5124 children of the original cohort participated	Questionnaire, physical examination	Cases	Colon, lung, breast, urinary bladder	
Western Electric Company Cohort Study	1957	Garland <i>et al.</i> (1985)	1957–76	1954 men, aged 40–55 years, employed for at least 2 years at the Western Electric Company	28-day diet history and interview	Cases	Colorectal	Compared alcoholic beverage intake reported at initial examination; no information regarding the exposure or relative risk given

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
American Cancer Society Prevention Study I (CPSI)	1959–60	Garfinkel <i>et al.</i> (1988); Boffetta & Garfinkel (1990)	1960–72	Analytical cohort of 581 321 women across the USA, aged >30 years; 276 802 white men, aged 40–59 years, volunteers for the American Cancer Society in 25 states	Self-administered questionnaire	Deaths	Buccal cavity, oesophagus, larynx, breast,	Based on mortality only
Tecumseh Community Health Study	1959–60	Simon <i>et al.</i> (1991)	1959–87	Analytical cohort of 1954 women, aged >21 years	Interview-administered questionnaire	Cases	Breast	No difference in risk by menopausal status (but low numbers)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Harvard Alumni Study	1962, 1966	Whittemore <i>et al.</i> (1985); Sesso <i>et al.</i> (2001)	1988–93	7612 male Harvard alumni	Questionnaire	Cases/deaths	Buccal cavity, oesophagus, stomach, small intestine, colon, rectum, liver, biliary tract, pancreas, larynx, trachea, bronchus, lung, melanoma, other skin, breast, prostate, testis, urogenital organs, urinary bladder, kidney, thyroid, Hodgkin disease, non-Hodgkin lymphoma, leukaemia, brain, other cancer	Relative risk adjusted for smoking.
Kaiser Permanente Medical Care Program Study	1964	Klatsky <i>et al.</i> (1981, 1988); Hiatt <i>et al.</i> (1988, 1994); Iribarren <i>et al.</i> (2001); Efrid <i>et al.</i> (2004)	1964–88	Original cohort contained 182 357 Kaiser Foundation Health Plan members	Self-administered questionnaire	Deaths/cases	Colon, rectum, pancreas, prostate, brain, thyroid	

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
American Men of Japanese Ancestry Study/ Honolulu Heart Study	1965–68	Pollack <i>et al.</i> (1984); Kato <i>et al.</i> (1992c); Nomura <i>et al.</i> (1990, 1995); Stemmermann <i>et al.</i> (1990); Chyou <i>et al.</i> (1993, 1995, 1996)	1965–93	6701 American men of Japanese ancestry, born from 1900–19, and residing on the Hawaiian island of Oahu, 8 006 subjects for the Honolulu Heart Study	Structured interview	Cases	Oral cavity, pharynx, oesophagus, upper aerodigestive tract, stomach, colon, rectum, liver, biliary tract, pancreas, larynx, lung, prostate, urogenital organs, urinary bladder, renal, lymphoma, leukaemia	SEER Registry used as a reference
Lutheran Brotherhood Insurance Study	1966	Hsing <i>et al.</i> (1990, 1998a); Kneller <i>et al.</i> (1991); Chow <i>et al.</i> (1992); Zheng <i>et al.</i> (1993)	1966–86	17 633 male white policy holders, aged ≥ 35 years, of the Lutheran Brotherhood Insurance Society	Questionnaire	Deaths	Stomach, colorectum, pancreas, lung, prostate	Relative risk for total alcoholic beverage consumption and risk for lung cancer not available

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
[name not given] Hawaiian Cohort Study	1968	Le Marchand <i>et al.</i> (1994)	1968–89	41 400 persons in the State of Hawaii, (20 316 men), aged >18 years	Lifestyle questionnaire	Cases	Prostate	Data recorded on current drinking status, age when drinking started, amount and frequency of intake of beer, wine, saké and hard liquor.
NHANES I Epidemiologic Follow-up Study	1971–75	Schatzkin <i>et al.</i> (1987); Yong <i>et al.</i> (1997); Breslow <i>et al.</i> (1999); Su & Arab (2004)	1971–93	14 407 men and women, aged 25–74 years, who completed a medical examination	Interviewer- administered questionnaire	Cases	Colon, lung, breast, prostate	Joint effects of tobacco and alcohol examined (Yong <i>et al.</i> , 1997)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Nurses' Health Study	1976	Willett <i>et al.</i> (1987a,b); Fuchs <i>et al.</i> (1995); Garland <i>et al.</i> (1999); Colditz & Rosner (2000); Michaud <i>et al.</i> (2001); Chen <i>et al.</i> (2002a); Wei <i>et al.</i> (2004); Lee <i>et al.</i> (2006)	1976–2004	121 700 female nurses aged 30–55; cohort size after exclusions: 80 253	Questionnaire	Cases	Colon, rectum, pancreas, breast, renal	Relative risk adjusted for smoking; joint effects of tobacco and alcohol examined
Breast Cancer Detection and Demonstration Project (BCDDP)	1979–81, 1987–89	Flood <i>et al.</i> (2002)	1993–98	45 264 women, aged 40–93 years, participated in a breast cancer screening programme	Mailed, self-administered standardized questionnaire	Cases	Colon, rectum	Interaction with smoking where the association of alcoholic beverages with colorectal cancer observed only in nonsmokers
New York State Cohort	1980	Bandera <i>et al.</i> (1997)	1980–87	27 544 men and 20 456 women long-term residents of New York State	Mailed questionnaire	Cases	Lung	Relative risk adjusted for smoking

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Leisure World Study	1981–83, 1985	Shibata <i>et al.</i> (1994)	1982–90	Analytical cohort of 13 976 men and women 65–80 years	Self-administered questionnaire	Cases	Pancreas	
	1981–82	Wu <i>et al.</i> (1987)	1981–85	11 888 residents of a retirement community	Mailed, self-administered standardized questionnaire	Cases	Colorectum	For men, results similar for right and left colon, but with lower statistical significance for left colon; for women, association was apparent but not significant for the left colon.
American Cancer Society, Cancer Prevention Study-II (CPS II)	1982	Boffetta <i>et al.</i> (1989); Thun <i>et al.</i> (1997); Coughlin <i>et al.</i> (2000); Feigelson <i>et al.</i> (2003)	1982–96	Analytical cohort of 1.2 million men and women, recruited 1982, aged >30 years	Self-administered questionnaire	Cases/deaths	Mouth, pharynx, oesophagus, colon, rectum, liver, pancreas, larynx, breast, multiple myeloma, lymphatic and/or haematopoietic	Cases not verified, nested case-control design (Boffetta <i>et al.</i> , 1989)
Iowa 65+ Rural Health Study	1982	Cerhan <i>et al.</i> (1997)	1982-93	3673 residents (1420 men), aged >65 years, from two rural counties in Iowa	Interview	Cases	Prostate	

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Second Cancers Following Oral and Pharyngeal Cancers Study	1984–85	Day <i>et al.</i> (1994a)	1984–89	1090 first primary cancers of the oral cavity and pharynx included in a multicentre population-based case–control study from 4 areas of the USA	Interviewer-administered questionnaire	Cases	Oral cavity, pharynx, oesophagus, larynx, lung	Information on alcoholic beverage type and cessation of alcoholic beverage drinking
Iowa Women's Health Study	1985–86	Potter <i>et al.</i> (1992); Gapstur <i>et al.</i> (1993); Harnack <i>et al.</i> (1997, 2002); Chiu <i>et al.</i> (1999); Kushi <i>et al.</i> (1999); Folsom <i>et al.</i> (2003); Kelemen <i>et al.</i> (2004)	1986–2001	99 826 randomly selected women, aged 55–69 years, from Iowa driver's licence list	Mailed questionnaire	Cases	Colon, rectum, pancreas, lung, breast, endometrium, ovary, kidney, non-Hodgkin lymphoma, lymphatic/haematopoietic cancers	Nested case–control study; odds ratio for total alcoholic beverage consumption not available; joint effect of smoking and alcohol examined (Potter <i>et al.</i> , 1992)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Cohort of Iowa Men	1986–89	Cantor <i>et al.</i> (1998) Putnam <i>et al.</i> (2000)	1986–1995	Analytical cohort of 1572 men, aged ≥ 65 years	Mailed, self-administered standardized questionnaire and supplemental telephone interview	Cases	Prostate, urinary bladder	
Health Professionals Follow-up Study (HPFS)	1986	Giovannucci <i>et al.</i> (1995); Michaud <i>et al.</i> (2001); Platz <i>et al.</i> (2004); Wei <i>et al.</i> (2004); Lee <i>et al.</i> (2006)	1986–2000	HPFS: 51 529 men, aged 40–75 years	Self-administered standardized questionnaire	Cases	Colon, rectum, pancreas, prostate, renal,	Combined analysis of NHS and HPFS, performed by Lee <i>et al.</i> (2006), Wei <i>et al.</i> (2004), Michaud <i>et al.</i> (2001), relative risk adjusted for smoking.
Study of Osteoporotic Fractures	1986–88	Lucas <i>et al.</i> (1998)	1986–89	Analytical cohort of 8015 white women, aged ≥ 65 years	Self-administered questionnaire	Cases	Breast	No association in women with a positive family history, but few cases ($n=20$)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
National Health Interview Survey (NHIS)	1987	Breslow <i>et al.</i> (2000)	1987–95	Sub-cohort of 20 195 adults, aged 18 years or older, who completed the Cancer Epidemiology Supplement	Cancer Epidemiology Supplement questionnaire (in-home interview)	Cases	Lung	Deaths arising within the first year of follow-up excluded; relative risk adjusted for smoking
The β -Carotene and Retinol Efficacy Trial (CARET)	1988	Omenn <i>et al.</i> (1996)	1988–1995	4060 male asbestos workers and 14 254 smokers	Questionnaire	Cases	Lung	Intervention trial
Prostate Lung, Colorectal and Ovarian Cancer Screening Trial (PLCOCAST)	1993–2001	Stolzenberg-Solomon <i>et al.</i> (2006)	1993–2003	Analytical cohort of 25 400 women, aged 55–74 years	Self-administered questionnaire	Cases	Breast	
California Teachers Study	1995–96	Horn-Ross <i>et al.</i> (2004); Chang <i>et al.</i> (2007)	1995–2003	Analytical cohort of 103 460 women, aged 21–84 years	Self-administered questionnaire	Cases	Breast, ovary	
Scandinavia								
<i>Denmark</i>								
Copenhagen City Heart Study	1964	Prescott <i>et al.</i> (1999); Petri <i>et al.</i> (2004)	1964–96	Analytical cohort of 13 074 women, aged 20–91 years	Self-administered questionnaire	Cases	Breast, lung	Relative risk adjusted for smoking (Prescott <i>et al.</i> , 1999)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Glostrup Population Study	1964–86	Høyer & Engholm (1992); Petri <i>et al.</i> (2004)	1964–90	Analytical cohort of 5207 women; aged 30–80 years	Self-administered questionnaire	Cases	Breast	
Copenhagen Male Study	1970	Gyntelberg (1973); Hein <i>et al.</i> (1992); Suadicani <i>et al.</i> (1993)	1970–88	Cohort of 5249 men aged 40–59 years	Danish Central Population Register and Questionnaire		Colon, rectum, lung	
Danish Diet, Cancer and Health Study <i>Finland</i>	1993–97	Tjønneland <i>et al.</i> (2003, 2004)	1993–2000	Analytical cohort of 23 778 women; aged 50–64 years	Self-administered questionnaire	Cases	Breast	
α -Tocopherol β Carotene Cancer Prevention (ATBC) Study	1985–88	Glynn <i>et al.</i> (1996); Woodson <i>et al.</i> (1999); Stolzenberg-Solomon <i>et al.</i> (2001); Mahabir <i>et al.</i> (2005); Lim <i>et al.</i> (2006)	1985–93	29 133 white male smokers, aged 50–69 years in southwestern Finland	Self-administered questionnaire	Cases/deaths	Colon, rectum, pancreas, lung, renal, non-Hodgkin lymphoma, Hodgkin lymphoma, multiple myeloma	Relative risk by type of alcoholic beverage and by smoking categories reported (Woodson <i>et al.</i> , 1999; Mahabir <i>et al.</i> , 2005)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
<i>Norway</i>								
Norwegian Cohort of Waitresses	1932–1978	Kjaerheim & Andersen (1994)	1959–91	5314 waitresses organized in the Restaurant Workers Union	Employers lists from Restaurant Workers Union	Cases	Tongue, mouth, pharynx, oesophagus, stomach, colon, rectum, liver, gall bladder, pancreas, larynx, lung, melanoma, breast, cervix uteri, other female genital, urinary bladder, kidney, brain, leukaemia	No individual exposure data. Estimates not adjusted for smoking.
Norwegian Cohort	1960	Heuch <i>et al.</i> (1983)	1960–73	Analytical cohort of 16 713 men and women, aged 45–74 years	Self-administered questionnaire	Cases	Pancreas	Joint effects of tobacco and alcohol examined
	1968	Kjaerheim <i>et al.</i> (1998)	1968–92	10 960 men born in 1893–1929	Mailed survey	Cases	Oral cavity, pharynx, oesophagus, larynx	Relative risk adjusted for smoking
	1984–86	Lund Nilsen <i>et al.</i> (2000)	1984–96	22 895 men (\geq 40 years) with no history of any cancer	Questionnaire	Cases	Prostate	Relative risks adjusted for smoking

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
HUNT-1 Cohort Study	1984– 1986	Sjödahl <i>et al.</i> (2007)	1984–2002	69 962 inhabitants of the country of Nord-Trondelag, at least 20 years of age; follow- up by linkage to the Norwegian Cancer Registry and the Norwegian Central Person Registry	Health survey	Cases	Stomach	
Norwegian Women and Cancer Study (NOWAC) <i>Sweden</i>	1991–97	Dumeaux <i>et al.</i> (2004)	1991–2001	Analytical cohort of 86 948 women, aged 30–70 years	Self- administered questionnaire	Cases	Upperaerodigestive tract, pancreas, breast	Relative risk not adjusted for smoking
Swedish Twin Registry Study	1967	Grönberg <i>et al.</i> (1996); Terry <i>et al.</i> (1998, 1999); Isaksson <i>et al.</i> (2002)	1967–92	Analytical cohort of 21 884 men and women recruited in 1961, aged 36–75 years	Questionnaire	Cases	Stomach, pancreas, endometrium, prostate	No adjustment for smoking (Terry <i>et al.</i> , 1999)

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Swedish Mammography Cohort	1987–90	Holmberg <i>et al.</i> (1995); Rashidkhani <i>et al.</i> (2005); Suzuki <i>et al.</i> (2005); Larsson <i>et al.</i> (2007)	1987–2004	66 651 Swedish women, aged 40– 76 years, living in the counties of Västmanland and Uppsala, who responded to a questionnaire	Self- administered questionnaire	Cases	Stomach, endometrium, breast, renal	Nested case- control design (Holmberg <i>et al.</i> , 1995)
Malmö Diet and Cancer Cohort	1991–96	Mattisson <i>et al.</i> (2004)	1991–2001	Analytical cohort of 11 726 women; aged ≥ 50 years	Interview- administered diet history	Cases	Breast	Relative risk adjusted for smoking
Western Europe								
<i>France</i>								
Supplementation and Vitamins and Minerals Antioxidant Study (SU. VI.MAX)	1994	Hirvonen <i>et al.</i> (2006)	1994–2002	Analytical cohort of 4 396 women, aged 35–60 years	Telephone- administered 24-h recalls	Cases	Breast	

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
<i>Netherlands</i>								
Netherlands Cohort Study	1986	Goldbohm <i>et al.</i> (1994); Schuurman <i>et al.</i> (1999); Zeegers <i>et al.</i> (2001); Schouten <i>et al.</i> (2004); Balder <i>et al.</i> (2005); Loerbroks <i>et al.</i> (2007)	1986–97	58 279 men and 62 573 women from 204 municipal population registries, aged 55–69 years	Mailed self-administered standardized	Cases	Colon, rectum, lung, endometrium, ovary, prostate, urinary bladder	Case–cohort design; for colon cancer, possible limitation: misclassification of alcohol consumption; no adjustment for smoking (Schuurman <i>et al.</i> 1999)
<i>United Kingdom</i>								
British Doctor's Study	1978	Doll <i>et al.</i> (1994, 2005)	1978–2001	Male physicians born between 1900 and 1930	Mailed questionnaire	Deaths	Large bowel, rectum, lung, other cancers,	Relative risk for alcohol use on lung cancer mortality not given; no adjustment for smoking
Oxford Vegetarian Study	1980–84	Sanjoaquin <i>et al.</i> (2004)	1980–99	10 998 vegetarian and non-vegetarians (4162 men, 6836 women), aged 16–89 years; no personal history of cancer	Self-administered standardized questionnaire	Cases	Colorectum	Association between alcohol partially confounded by smoking

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
General Practitioner Research Database Study	1994	Lindblad <i>et al.</i> (2005)	1994–2001	287 oesophageal adenocarcinomas and 10 000 controls, aged 40–84 years	Interview	Cases	Oesophagus, stomach	Nested case–control study
Multi-Country European Prospective Investigation into Cancer and Nutrition (Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, Netherlands, UK)	1992	Boeing (2002); Rohrmann <i>et al.</i> (2006); Tjønneland <i>et al.</i> (2007);	1992–2004	521 457 from 10 European countries; most study centres recruited from the general population; other sources of recruitment included members of insurance plans, blood donors, mammographic screening, employees of enterprises, civil servants	Dietary instruments developed specifically for each country	Cases	Oral cavity, pharynx, oesophagus, lung, breast	Relative risks reported by histological type and by smoking status

Table 2.1a (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Multicentric European Study of Second Primary Tumours Italy, Spain, Switzerland	1979–82	Dikshit <i>et al.</i> (2005)	1979–2000	A cohort of 928 cases of laryngeal cancer from a multicentric population-based case-control study from, Italy, Spain and Switzerland	Interviewer-administered questionnaire	Cases	Oral cavity, pharynx, oesophagus, lung	

HERPACC, Hospital-based Epidemiologic Program at Aichi Cancer Center; HUNT, Helseundersøkelsen i Nord-Trøndelag; NHANES, National Health and Nutrition Examination Survey; NHS, Nurses Health Study; PLCOCST, Prostate Lung, Colorectal and Ovarian Cancer Screening Trial

(a) *Asia/Oceania*

(i) *Australia*

Melbourne Collaborative Cohort Study

This cohort was recruited in 1990–94 from the Melbourne metropolitan area, using the electoral rolls, advertisements and community announcements in the local media. The cohort comprised 41 528 people (17 049 men) aged 27–75 years. A structured interview included alcoholic beverage consumption for those who had ever drunk 12 alcoholic drinks in a year. Cancer cases were ascertained from the Victoria Cancer Register through to 31 December 2003 (Baglietto *et al.*, 2005, 2006).

(ii) *China*

Zoucheng/Shandong Study

A 12.5-year prospective cohort study was carried out in a rural area of Zoucheng city. A probabilistic sample from three townships, aged 20 years and older, was identified in 1982 and consisted of 7809 men and 7994 women. An individual case card was created for each of the villagers and their smoking and drinking habits were recorded. Data concerning their death and change in health were collected annually. Mortality follow-up was to 1994 (Zhang *et al.*, 1997).

Lin Xian Nutrition Intervention Trial Study

In the frame of an intervention trial for micronutrients, approximately 30 000 residents of the Lin Xian region, aged 40–69 years, were interviewed in 1985 to obtain information on usual dietary intake, tobacco use, alcoholic beverage consumption, family history of cancer and other factors. The cohort was followed-up from 1986 through to May 1991, with little loss to follow-up. Information on cause of death and incidence of cancer was collected from local hospitals or a study medical team. Relative risks were adjusted for potential confounders as well as the vitamin/mineral intervention group (Guo *et al.*, 1994; Tran *et al.*, 2005).

Shanghai Men's Study

A cohort of 18 244 male residents of four small geographically defined communities from a wide area of Shanghai, aged 45–64 years, were enrolled between January 1986 and September 1989 (80% of eligible subjects). A structured questionnaire was completed at a face-to-face interview. The information obtained included level of education, history of tobacco use and alcoholic beverage consumption, current diet and medical history. Cancer incidence was ascertained through the population-based Shanghai Cancer Registry and vital status was ascertained by inspection of the Shanghai death-certificate records. Only 108 subjects were lost to follow-up, which continued until February 1993 (Yuan *et al.*, 1997).

Jiashan County Screening Study

Screening for colorectal cancer was initiated in May 1989–April 1990 when all residents, aged 30 years and over, in 10 small towns in Jiashan County, Zhejiang Province, China, were invited for screening and a face-to-face questionnaire was completed

by professional interviewers including information on alcoholic beverage drinking and smoking habits. Of 75 842 eligible individuals, 31 087 men and 33 256 women responded, about 70% of whom were farmers. Subjects were followed through the Cancer Registration System and a rapid reporting system from the Colorectal Registry, that was documented to be 95% complete. Deaths were ascertained through the Jiashan County Death Registration System through to 2001. Out-migration was estimated to be less than 1% annually (Chen *et al.*, 2005a).

Yunnan Tin Corporation Miners Cohort

A cohort of 7965 Yunnan Tin Corporation miners aged 40 years and over was established in 1992. Cumulative radon exposure for each subject was obtained by adding-up the estimated working level months, for each job held at the Yunnan Tin Corporation before baseline screening. A questionnaire was administered by interviewers at baseline which included data on alcoholic beverage consumption. Follow-up continued until 1997 (Lu *et al.*, 2000a).

(iii) *Japan*

Japanese Physicians' Study

A survey of smoking habits and alcoholic beverage consumption among physicians in western Japan was carried out using self-administered questionnaires in 1965. From 6815 male respondents in nine prefectures (51% response rate), a cohort of 5477 male physicians was established. Vital status was followed until 1983 and was confirmed by various medical associations. Copies of death certificates were obtained from the District Legal Affairs Bureau and the cause of death was coded with the ICD-8. After exclusions, the analyses were performed on 5130 men. Statistical analysis was performed using the Cox proportional hazards model (Kono *et al.*, 1985, 1986, 1987).

Six Prefecture Study

In 1965, 122 261 men and 142 857 women, aged 40–69 years (95% of the census population), in 29 health centre districts from six prefectures in Japan were interviewed. The six prefectures were selected as being representative of the entire country. The one-page questionnaire administered at baseline included questions on smoking, alcoholic beverage consumption and dietary habits, occupation and marital status. A record linkage system was established for the annual follow-up. During the 16-year follow-up period, 8% of the cohort migrated from the original health districts. Deaths among cohort members were monitored by linkage to vital statistics kept at each public health centre (Hirayama, 1989; 1992; Kinjo *et al.*, 1998).

Life Span Study

The Life Span Study cohort originally consisted of 100 000 survivors [sex distribution not reported] of the atomic bomb blasts in Hiroshima and Nagasaki. The cohort was expanded in 1968 and 1985 by adding approximately 10 000 survivors each time. The total cohort included approximately 120 000 individuals, of whom approximately 27 000 were non-exposed controls. Information on smoking was obtained from three interview surveys conducted on a subgroup of the entire cohort in 1963–64, 1964–68

and 1968–70, and four postal surveys conducted on various subgroups in 1965, 1969, 1979 and 1980.

The cancer incidence in 61 505 survivors for whom smoking data were available was reported. For 42% of this group, information on smoking was available from at least two surveys. Information on cancer incidence and mortality was obtained from the Radiation Effects Research Foundation tumour registry and mortality database. Poisson regression models were used to fit log-linear relative risk and linear excess relative risk models (Akiba, 1994; Land *et al.*, 1994; Goodman *et al.*, 1995).

Chiba Center Association Study

The Chiba Center Association Study was a nested case–control study based on a cohort population of 17 200 male participants in a mass screening for gastric cancer by the Chiba Cancer Association in Japan in 1984. Cancer cases in cohort members were detected by record linkage to the Chiba Cancer Registry. The participants were followed from 1984 until 1993. For each cancer case, two controls were selected from the cohort population by matching on sex, birth year and area of residence (Murata *et al.*, 1996).

Aichi Cancer Center Hospital Study

The relation of atrophic gastritis, other gastric lesions and lifestyle factors to stomach cancer risk was prospectively studied among 3,914 subjects who underwent gastroscopic examination and responded to a questionnaire survey at the Aichi Cancer Center Hospital. During 4.4 years of follow-up on average, 45 incident cases of stomach cancer were identified at least three months after the initial examination. If the baseline endoscopic findings indicated the presence of atrophic gastritis, the risk of developing stomach cancer was increased 5.73-fold, compared with no indication at the baseline. The risk further increased with advancing degree of atrophy and increasing extension of atrophy on the lesser curvature. These trends in the relative risks were statistically significant ($P = 0.027$ and $P = 0.041$, respectively). The risk for stomach cancer was statistically significantly increased among subjects with gastric polyps, but not among those with gastric ulcer. Stomach cancer cases tended to consume more cigarettes, alcohol, rice, pickles and salted fish gut/cod roe and less fruits and vegetables and to have more family histories of stomach cancer than noncases, although these differences were not statistically significant. The results of the present study provide additional evidence on the relation between atrophic gastritis and stomach cancer and suggest a need for intensive follow-up of patients with atrophic gastritis and gastric polyps (Kato *et al.*, 1992a).

Aichi Prefecture Study

Stomach-cancer mortality was prospectively studied among 9753 Japanese men and women who first responded to a mailed questionnaire in 1985 and were then followed through May 31, 1991. During this follow-up period, 57 stomach-cancer deaths were identified. Current smokers had an increased risk of death from stomach cancer compared with never-smokers (relative risk (RR) = 2.29, 95% confidence interval (CI): 1.15–4.56), but there was no dose-response to number of cigarettes smoked.

Daily alcohol drinkers who consumed 50 ml or more of alcohol per day also had a greater risk than nondrinkers (RR = 3.05, 95% CI: 1.35-6.91). There was no association between stomach-cancer mortality and individual food consumption except a positive association with fruit intake. However, frequent use (greater than or equal to 3-4/week) of meat broiling and traditional style Japanese salad preparation in their cooking procedures were positively associated with stomach-cancer mortality. The RR values compared with infrequent use (less than or equal to 1-2/month) were 2.27 (95% CI: 1.06-4.85) and 3.10 (95% CI: 1.40-6.85), respectively. A positive family history of cancer, especially stomach cancer, significantly increased the risk for stomach-cancer death (RR = 2.01, 95% CI: 1.12-3.63). The effects of these variables remained after adjustment for other variables (Kato *et al.*, 1992b).

Japan Collaborative Cohort (JACC) Study for Evaluation of Cancer Risk

A baseline survey was conducted in 45 areas throughout Japan from 1988 through to 1990 by investigators from 25 centres. At the end of 1990, a total of 127 500 (125 760) inhabitants were enrolled in this cohort. Among them, 110 792 subjects (46 465 men, 64 327 women aged between 40 and 79 years at baseline) were followed-up through to the end of 1997 and subsequently to 1999. The baseline data, which included details on alcoholic beverage consumption and tobacco use were collected using a self-administered questionnaire. Population registers were used to identify subjects who had moved out of a study area. The date and cause of death were confirmed annually or biannually by reviewing death certificates with the approval of the Prime Minister's office. In one analysis of 38 600 women participants in the cohort, follow-up was to 31 December 1997 (Lin *et al.*, 2002; 2005; Sakata *et al.*, 2005; Wakai *et al.*, 2005; Nishino *et al.*, 2006).

The Hospital-based Epidemiological Research Program at the Aichi Cancer Center (HERPACC)

A database was established in 1988 in the Aichi Cancer Center that included all outpatients on a first visit who completed a self-administered questionnaire on lifestyle factors which included information on alcoholic beverage consumption. The database was routinely linked with the hospital cancer-registry to identify cases of cancer. Between January 1988 and December 1999, 78 755 subjects were included. Cases were frequency-matched by age to cancer-free subjects, selected at random from the database, and the study was analysed as a nested case-control study (Inoue *et al.*, 2003).

The Japan Public Health Center Study Cohorts (I and II)

A population-based cohort of 27 063 men and 27 435 women was established in 1990 from subjects who registered their addresses in 14 administrative districts of four Public Health Center areas. All subjects were born between 1930 and 1949 (40-59 years of age at baseline). Subjects were asked to reply to a lifestyle questionnaire, which included information on alcoholic beverage consumption. A total of 43 149 subjects (20 665 men (76%), 22 484 women (82%)) returned their questionnaires. All subjects were followed from 1 January 1990 to 31 December 1999. All deaths of cohort subjects were based on death certificates from each Public Health Center. Newly diagnosed cases of

cancer were reported by hospitals in and around the study areas when the birth date and residence fulfilled the criteria for inclusion into the cohort. (Sasazuki *et al.*, 2002).

A second cohort was established in 1993, and included six Public Health Centers in six prefectures, which comprised all residents aged 40–69 years (except for Osaka, which included other ages and was excluded from this cohort). By combining the first with the second cohort and excluding subjects deemed to be ineligible, a study population of 42 540 men and 47 464 women was defined for analysis. Mortality data were obtained from the Ministry of Health, Labour and Welfare; those who moved to other areas were identified from residential registers; cancer cases were identified through local major hospitals and population-based cancer registries. Follow-up was until 31 December 1999 (Otani *et al.*, 2003).

Takayama City Cohort

A cohort was established in September 1992 among 36 990 residents of Takayama City, aged 35 years or older, who were asked to complete a questionnaire that included data on alcoholic beverage consumption. A total of 34 018 (92%) subjects responded. Details on patients with colon and rectal cancer were obtained from the two major hospitals in Takayama City, which cover about 90% of the colorectal cases in the city. Details of subjects who moved away from the city during the study were obtained from the residential registers. Follow-up was until 31 December 2000. After excluding those with incomplete data and non-melanoma skin cancer, the analysis cohort comprised 13 392 men and 15 659 women (Shimizu *et al.*, 2003).

(b) North America

(i) Canada

Nutrition Canada Survey Cohort

The Nutrition Canada Survey was conducted between September 1970 and December 1972, and incorporated 12 795 people from all 10 provinces in Canada who responded to the invitation to participate (a 47% response rate), together with 3295 unsolicited volunteers who participated. A retrospective cohort study was performed by linking the records for those aged 50–84 years to the Canadian Cancer Registry and the Canadian National Mortality Data Base to the end of 1993. Data on alcoholic beverage consumption had been collected at baseline by a 24-hour diet recall and a 1-month food-frequency questionnaire (Ellison, 2000).

National Breast Screening Study

The National Breast Screening Study is a multicentre, randomized controlled trial of mammography screening for breast cancer. Between 1980 and 1985, 89 835 women aged 40–59 years were randomized. In 1982, a semiquantitative diet questionnaire, which included data on alcoholic beverage consumption, was distributed to new attendees and previously enrolled women returning to the screening centres for further screening. A total of 56 837 women returned the dietary questionnaires. Reports on the diet cohort are based mainly on a case-cohort analysis, with a 10% subsample selected

at random from the cohort as controls. The National Breast Screening Study diet cohort is included in the Pooling Project (Friedenreich *et al.*, 1993; Jain *et al.*, 2000a,b; Rohan *et al.*, 2000; Navarro Silvera *et al.*, 2005).

(ii) *USA*

American Registry of Radiologic Technologists

The cohort was based upon 143 517 radiological technologists certified by the American Registry of Radiologic Technologists for at least 2 years during 1926–1982. A questionnaire was mailed to 132 519 who were known to be alive and data on cancers diagnosed were obtained from that questionnaire, with 79 016 female respondents. Thus, this study was essentially of factors associated with the prevalence of breast cancer among those still alive at the time of the questionnaire, and was analysed as a nested case–control study (Boice *et al.*, 1995; Freedman *et al.*, 2003).

University of Pennsylvania Alumni Study

Physical and social characteristics recorded at college physical examination and reported in subsequent questionnaires to alumni in 1962 or 1966 by 50,000 former students from Harvard University and the University of Pennsylvania were reviewed for their relationship to major site-specific cancer occurrence. The records of 1,359 subjects who died with a major site-specific cancer in a 16- to 50-year follow-up period and of 672 subjects who reported such a cancer by mail questionnaire in 1976 or 1977 were compared with those of 8,084 matched classmates who were known to be alive and free of cancer at the time subjects with cancer had died or had been diagnosed. Cigarette smoking, as reported both in student years and years as alumni, predicted increased risk for cancers of the respiratory tract, pancreas, and bladder. Student coffee consumption was associated with elevated risk for leukemia, but it was unrelated to cancers of the pancreas and bladder. Male students with a record of proteinuria at college physical examination experienced increased risk for kidney cancer, and those with a history of tonsillectomy experienced increased risk for prostate cancer. Students who at college entrance reported occasional vague abdominal pain were at elevated risk for pancreatic and colorectal cancers in later years. Increased body weight during college was associated with increased risks for kidney and bladder cancers, whereas for alumni this index was associated only with kidney cancer. Increased weight-for-height during college (but not in 1962 or 1966) predicted increased occurrence of female breast cancer. Jewish students experienced elevated risk for subsequent cancers of the female breast, colon, and combined colorectum. These and other findings are presented as clues deserving further exploration for any etiologic significance that they may hold for the cancer sites studied (Whittemore *et al.*, 1985).

Minnesota Breast Cancer Family Study

A family study on breast cancer was initiated between 1944 and 1952, including a total of 544 families and data on 4418 family members. Information was obtained from interviews, medical history questionnaires and death certificates. Follow-up of this cohort was initiated in 1990; families in which the proband was diagnosed with breast

cancer before 1940 were excluded. Telephone interviews were completed with 6194 living women and 2974 surrogates from 426 multigeneration families; after excluding those with missing data, data on 9032 women were available for analysis (Vachon *et al.*, 2001).

US Army Veterans Study

A cohort of 4401 US Army service men hospitalized for chronic alcoholism in 1944-45 was drawn as a sample from records of the US Department of Defense and the Veterans' Administration. Of these, 98% were <40 years of age at the time of hospitalization. They were matched for age with an equal number of enlisted men hospitalized for acute nasopharyngitis during the same period. Deaths in these groups were ascertained through the Veterans' Administration Beneficiary Identification and Records Locator Subsystem, and death certificates were obtained to code for cause of death. Follow-up for death was estimated to be 90-98% complete. No information was available on the drinking habits of individual members of the cohort or on average consumption by the cohort members. It was noted that only 7.5% of the chronic alcoholics had been discharged from military service for medical disability, including alcoholism. The mortality experience of the cohort was compared with that of the matched cohort of nasopharyngitis patients, and the mortality of both cohorts was compared with that of US males for selected causes of death. Overall mortality was approximately 80% higher in the alcoholics group than in the nasopharyngitis group (SMR, 1.9) (Robinette *et al.*, 1979).

Framingham Study and Framingham Offspring Study

The Framingham Study began in 1948. The original cohort included 5209 persons (2873 women) aged 28-62 years at the first examination, who were examined biennially thereafter. In 1971, examination was begun on many of the children of the original cohort and their spouses. Of 5124 subjects aged 12-60 years enrolled in the Framingham Offspring Study, 2641 were women, and have been followed at 4-year cycles. Information on alcoholic beverage consumption was obtained at the examinations. Cancer cases have been identified by self reports and, for non-respondents, by linkage with the National Death Index and a cancer registry, with confirmation of diagnosis by searching for medical records. The median follow-up was 34.3 years (range, 0.2-42.5 years) for the original cohort and 19.3 years (range, 0.2-22.6 years) for the offspring cohort (average for the total cohort of 9821 subjects, 27.3 years) (Gordon & Kannel, 1984; Zhang *et al.*, 1999; Djoussé *et al.*, 2002, 2004).

Western Electric Company Cohort Study

In 1957, 3102 men were randomly selected from the population of 5397 men aged 40-55 years who had been employed for at least 2 years at the Western Electric Company's Hawthorne Works in Chicago; 2080 (67.1%) agreed to participate in a long-term, prospective, epidemiological study (Western Electric Health Study). Another 27 men served as a pilot group, bringing to 2107 the total number initially examined from October, 1957 to December, 1958. Approximately 65% were first and second generation Americans, predominantly of German, Polish, or Bohemian ancestry; most of the

others were descendants of earlier emigrants from the British Isles. The men worked at various occupations associated with the manufacture of telephones and related products (Garland *et al.*, 1985).

American Cancer Society Cancer Prevention Study I (CPS-I)

Between October 1959 and February 1960, volunteers for the American Cancer Society in 25 states recruited more than one million subjects, aged 30 years and over, from among their friends, neighbours and acquaintances. Families were enrolled, with the condition that there be at least one person aged over 45 years in the family. All family members over 30 years of age were requested to fill out a detailed four-page questionnaire. Vital status was checked yearly to 1965 and again in 1971 and 1975. Death certificates of deceased participants were obtained from state health departments. For 581 321 women, deaths were ascertained for 12 years (Garfinkel *et al.*, 1988). For 276 802 white men in the cohort aged 40–59 years, enrolled in 1959 and followed for 12 years, 9293 deaths from all cancers were observed and related to alcoholic beverage consumption obtained at baseline (Boffetta & Garfinkel, 1990).

Tecumseh Community Health Study

A community health study was initiated in the town of Tecumseh, MI, through interviews and medical examinations in 1959–60. Information on alcoholic beverage consumption was obtained by trained interviewers. Follow-up was for up to 28 years by mailed questionnaires, with review of death certificates to confirm cause of death. The cohort included in the analysis totalled 1954 women (Simon *et al.*, 1991).

Harvard Alumni Study

A cohort of undergraduates who had entered the University of Harvard between the years of 1916 and 1950 was identified when they responded to a health questionnaire sent out in 1962 or 1966. Updated information was obtained from 13 905 cohort members from periodic surveys that assessed lifestyle habits and medical history. The questions asked for information on daily amount of cigarette smoking, age at start and cessation of cigarette smoking, weight, height and physical activity. In surveys conducted in 1988 and 1993, participants were asked whether a cancer had been diagnosed by a physician. Deaths that occurred up to 1992 were traced using information from the alumni office to obtain death certificates. The authors claimed that mortality follow-up was virtually complete (Whittemore *et al.*, 1985; Sesso *et al.*, 2001).

Kaiser Permanente Medical Care Program Study

The first cohort for this study was selected from 87 926 white or black men and women who underwent at least one multi-phasic health check-up within the Kaiser Permanente Medical Care Program from July 1964 and August 1968 and who were followed through to 1976. From data in the baseline questionnaire, four groups were extracted, each of 2015 persons, matched for age, race and cigarette smoking, according to the usual number of alcohol-containing drinks/day (0, ≤ 2 , 3.5 and ≥ 6). Mortality was ascertained by a search of California death indexes (Klatsky *et al.*, 1981).

An expansion of this cohort comprised 94 549 men and 110 425 women, aged 10–89 years at baseline in 1964–73, who underwent at least one multi-phasic health

check-up within the Kaiser Permanente Medical Care Program and were followed through to 1997 (Iribarren *et al.*, 2001). Cancer incidence was ascertained from the first health examination through the San Francisco–Oakland Surveillance, Epidemiology and End Result (SEER) programme and the Northern California Kaiser Permanente Medical Care Program. Attrition due to termination of health plan coverage and death was of the order of 2% per year; the median follow-up time was 19.9 years (range, <1–33 years) (Klatsky *et al.*, 1981; Iribarren *et al.*, 2001).

Between 1978 and 1985, a similar cohort was established, which included 122 894 (for one study 106 203) men and women who received a multi-phasic health examination during 1978–84. Cancer cases were ascertained as for the first cohort (see above). Follow-up was eventually to 31 March 1999 (Klatsky *et al.*, 1988; Hiatt *et al.*, 1988, 1994; Efrid *et al.*, 2004).

American Men of Japanese Ancestry Study and Honolulu Heart Study

A cohort of 8006 American men of Japanese ancestry, born during the years 1900–19 and who resided on the Hawaiian island of Oahu, were interviewed and examined clinically from 1965 to 1968. Information obtained at the interview included age, smoking history, usual occupation, type of housing, education and religion. A food-frequency questionnaire and a 24-hour dietary recall was also administered. Newly diagnosed cases of cancer were identified through continuous surveillance of Oahu hospitals and linkage with the Hawaii Tumor Registry through to 1994 (Pollack *et al.*, 1984; Nomura *et al.*, 1990, 1995; Stemmermann *et al.*, 1990; Kato *et al.*, 1992c; Chyou *et al.*, 1993, 1995, 1996).

Lutheran Brotherhood Insurance Study

A cohort of 26 030 white male life insurance policy holders of the Lutheran Brotherhood Insurance Society was identified in 1966, of whom 17 633 responded to a mailed food-frequency questionnaire and were followed for 20 years. Little difference was observed between responders and non-responders with regard to age, urban or rural residence, policy status and cancer mortality at 11.5 years of follow-up. The questionnaire included questions on tobacco use and the longest held occupation, frequency of consumption of 35 food items and the consumption of coffee, beer and spirits. Death certificates were coded for underlying and contributory causes of death. Person-years were accumulated up to death, loss to follow-up or the end of the study in 1986. The age-adjusted relative risks for cancer mortality resulting from exposure to alcoholic beverages were computed using Poisson regression. Statistical interaction between smoking and other risk factors was also examined. About 23% of the cohort members were lost to follow-up due to maturation or lapse of their policies (Hsing *et al.*, 1990, 1998a; Kneller *et al.*, 1991; Chow *et al.*, 1992; Zheng *et al.*, 1993).

Hawaiian Cohort Study

In this study, the consumption of high-fat animal products, raw vegetables, and fresh fruits, as well as obesity, smoking, and drinking was evaluated in relation to subsequent occurrence of prostate cancer. Data from a cohort of 20,316 men of various ethnicities were collected between 1968–1989 in Hawaii. A total of 198 incident

cases with invasive prostate cancer were identified by computer-assisted linkage of this cohort to the statewide Surveillance, Epidemiology, and End Results registry. Weight was not consistently associated with prostate cancer, but there was an association with height. These associations were stronger in men diagnosed before age 72.5 years. The risk estimates for raw vegetable and fresh fruit intakes were close to 1.0. Smoking and alcohol drinking appeared to be unrelated to risk (Le Marchand *et al.*, 1994)

The National Health and Nutrition Examination Survey (NHANES) I Epidemiological Follow-up Study

The first NHANES was performed in 1971–75, based on a probability sample of the civilian non-institutionalized population of the USA. Follow-up surveys were conducted and, by the end of 1992, 96% of the cohort was traced, and death certificates were traced for 98% of decedents. The analytical cohort comprised 3968 men and 6100 women aged 25–74 years at baseline (Schatzkin *et al.*, 1987; Yong *et al.*, 1997; Breslow *et al.*, 1999; Su & Arab, 2004).

Nurses' Health Study

In 1976, a cohort of 121 700 female registered nurses was assembled in the USA. At enrolment, the nurses completed a mailed questionnaire on risk factors for cancer and heart disease. Responses to food-frequency questionnaires were also collected in 1980, when 98 462 nurses responded, and in 1984, 1986 and 1990. The response rate to follow-up questionnaires was almost 96% through to 1990. Family members were the main source of information on vital status for non-respondents but the National Death Index was also used. Multiple logistic regression models were used to compute odds ratios, after controlling for age, total energy intake and other potentially confounding variables. A subset of 89 538 women who reported alcoholic beverage consumption in 1980 were assessed by follow-up questionnaires in 1982 and 1984, and cases of cancer were identified (Willett *et al.*, 1987a). A subsequent report on 85 709 women who reported alcoholic beverage consumption in 1980 and were followed for 12 years considered mortality related to alcoholic beverage consumption (Fuchs *et al.*, 1995). A second cohort of 116 671 women was established from women who completed a more detailed dietary questionnaire in 1989, and were followed by questionnaires every 2 years to 1995 (Garland *et al.*, 1999). This study is included as two cohorts (those initially assembled and followed to 1986, and those who completed a more detailed dietary questionnaire in 1986 and were followed subsequently) in the Pooling Project (Willett *et al.*, 1987b; Fuchs *et al.*, 1995; Garland *et al.*, 1999; Colditz & Rosner, 2000; Michaud *et al.*, 2001; Chen WY *et al.*, 2002a; Wei *et al.*, 2004; Lee *et al.*, 2006).

Breast Cancer Detection Demonstration Project (BCDDP)

A cohort was established based upon the participants in the US Breast Cancer Detection Demonstration Project, which was established between 1973 and 1980 at 29 screening centres in 27 cities and involved 283 222 women. A follow-up cohort was established in 1979 from a subset of the participants, which included 4275 women who had been diagnosed with breast cancer, 25 114 women who had biopsies indicating benign breast disease, 9628 women who were recommended for biopsy but did not have

the procedure and an additional 25 165 women not recommended for biopsy, matched with the other subjects on age, time of entry into the programme, ethnicity, screening centre and length of participation in the Project and comprised a total of 64 182 women. Between 1979 and 1981, 61 433 of the women completed a baseline food-frequency questionnaire, which included questions related to alcoholic beverage consumption. A follow-up questionnaire was sent between 1993 and 1995 in which self-reports of cancer occurrence were made. Medical records confirmed the diagnosis for 80% of these. Non-respondents were contacted by telephone. Women with prevalent colorectal cancers (reported at baseline) were excluded. The final analytical cohort comprised 45 264 women, of whom 40 865 had complete follow-up through to 1995–98. This cohort is included in the Pooling Project (Flood *et al.*, 2002).

The New York State Cohort

A 45-item food-frequency questionnaire was sent to 265 000 residentially stable subjects selected from a private sampling frame in New York State in 1980 and was returned by 57 968 (32 689 men, 25 279 women). Follow-up was passive through to December 1987 from the records of the New York State Department of Health's vital statistics section and cancer registry. A second questionnaire was sent to the subjects who responded in 1980 who were not listed as dead or diagnosed with cancer. Assessment of the validity of follow-up was conducted in a nested case–control study, with each case matched by age, race, gender and country of residence to one control subject randomly selected from a pool of controls alive at the time of diagnosis of the case. The analytical cohort comprised 27 544 men and 20 456 women (Bandera *et al.*, 1997).

Leisure World Study

A detailed health questionnaire was mailed to all residents of a retirement community in California in 1981, and to new residents in 1982, 1983 and 1985. A response rate of 62% was achieved overall (11 888 participants initially, and 13 979 later). Almost all of the residents were Caucasians of the upper-middle class, about two-thirds were women, and 80% were aged 65–86 years. Histological diagnosis of cancer was obtained from local hospitals. All participants were sent a follow-up questionnaire every 2 years. The latest follow-up reported (Shibata *et al.*, 1994) was to 30 June 1990 (Wu *et al.*, 1987; Shibata *et al.*, 1994).

American Cancer Society Cancer Prevention Study II (CPS-II)

The CPS-II is a nationwide prospective mortality cohort study of nearly 1.2 million adults, aged 30 years or more, enrolled by volunteers of the American Cancer Society in 1982. As in CPS-I, enrolment was based on families and excluded persons in institutions and military service and others who would be difficult to trace. Each participant completed a four-page postal questionnaire on tobacco and alcoholic beverage use and diet. Deaths were ascertained from the month of enrolment until 31 December 1996 through personal enquiries made by the volunteers in 1984, 1986 and 1988 and later through linkage with the National Death Index. In one analysis (Thun *et al.*, 1997), 490 000 men and women were followed from 1982 through to 1991, after

excluding those with unquantified smoking and alcoholic beverage use, those missing all data on wine, beer and spirit consumption, and former drinkers who were non-drinkers. In another analysis, 66 561 postmenopausal women were followed for mortality from 1992 to 1997–98 (Boffetta *et al.*, 1989; Thun *et al.*, 1997; Coughlin *et al.*, 2000; Feigelson *et al.*, 2003).

Iowa 65+ Rural Health Study

In late 1981 and 1982, 80 percent of the non-institutionalized residents aged 65 years and older who lived in Iowa and Washington counties, Iowa (US), were enrolled into the Iowa 65+ Rural Health Study ($n = 3,673$), which was one of the four Established Populations for Epidemiologic Studies of the Elderly (EPESE) sites. These two counties are primarily rural, with several small towns. Of the 1,420 men enrolled into the cohort, only the 1,155 men completing the full-form baseline interview were eligible for inclusion into this report. The full-form baseline interview was conducted in the respondent's home by a trained interviewer, and included data on a variety of demographic, health, and social characteristics (Cerhan *et al.*, 1997).

Second Cancers Following Oral and Pharyngeal Cancers Study

The cohort comprised 1090 first primary cancers of the oral cavity and pharynx included in a multicentre population-based case–control study in four areas of the USA in 1984–85, and followed to 1989. Information on alcoholic beverage consumption and tobacco use was obtained at the time the subjects were originally enrolled, and was updated for 80 cases with second cancers and 189 sex-, study area- and survival-matched cancer patients free of second cancers, with analysis as a nested case–control study (Day *et al.*, 1994a).

Iowa Women's Health Study

The Iowa Women's Health Study was conducted on a cohort of women selected randomly from the Iowa Department of Transportation Driver's License list of whom 41 837 completed a postal questionnaire (response rate, 42.7%) sent in 1986. The questionnaire covered information on age, smoking history, physical activity and level of education. The Harvard semiquantitative food-frequency questionnaire was used to assess diet and alcoholic beverage consumption. Incident cases of cancer were ascertained through the Health Registry of Iowa, which is a population-based cancer registry in the SEER Program of the National Cancer Institute. The Iowa Women's Health Study is included in the Pooling Project (Gapstur *et al.*, 1992, 1993; Potter *et al.*, 1992; Harnack *et al.*, 1997, 2002; Chiu *et al.*, 1999; Kushi *et al.*, 1999; Folsom *et al.*, 2003; Kelemen *et al.*, 2004).

Cohort of Iowa men

A retrospective cohort was formed from the controls in a population-based case–control study of six cancer sites conducted 1986–89 in Iowa (Cantor *et al.*, 1998). These controls were randomly selected from the Iowa population using driver's licence records for men aged 40–64 years and from the files of the US Health Care Financing administration for men aged 65 years and older. Of 1989 men invited, 1601 (81%)

agreed to participate. Follow-up was through to 1995. Incident cases of cancer were identified by linkage with the Iowa State Cancer Registry (Putnam *et al.*, 2000).

Health Professionals' Follow-up Study (HPFS)

In 1986, a cohort of 51 529 male dentists, optometrists, osteopaths, podiatrists, pharmacists and veterinarians in the USA were asked to respond to a mailed semi-quantitative food questionnaire. The questionnaire included questions on age, current and past tobacco use, marital status, height and weight, ancestry, medications, disease history, physical activity and diet. Only men who completed the diet questionnaire adequately at baseline and who reported no cancer other than non-melanoma skin cancer were included in the analysis. After all baseline exclusions, 47 931 men, 40–75 years old in 1986 and followed for 6 years comprised the first analysis cohort (Giovannucci *et al.*, 1995); subsequently, follow-up was extended to 31 January 1998 (Platz *et al.*, 2004). Follow-up questionnaires were sent in 1988, 1990 and 1992 to ascertain new cancer cases. Family members and the National Death Index were the main source of information on vital status of non-respondents. This study is included in the Pooling Project (Giovannucci *et al.*, 1995; Michaud *et al.*, 2001; Platz *et al.*, 2004; Wei *et al.*, 2004; Lee *et al.*, 2006).

Study of Osteoporotic Fractures

This cohort was based upon a multicentric prospective study of white women aged 65 years and over who were recruited from population-based listings and followed for the occurrence of osteoporotic fractures. One year after the baseline examination, participants completed a questionnaire. Incident cancers were identified by follow-up at year 3, and verified by perusal of medical records. Those who had died were excluded, leaving 8 015 for analysis (Lucas *et al.*, 1998).

National Health Interview Survey (NHIS)

The 1987 National Health Interview Survey included a core questionnaire completed by 47 240 households containing 122 859 persons. One adult, aged 18 years and over, from each household who completed the core questionnaire was randomly selected to complete a cancer-control or cancer-epidemiology supplement, the latter comprising 22 080 individuals. The response rate for the core questionnaire was 95% and that for the cancer epidemiology supplement was 86%. Records from this cohort were linked to the National Death Index to provide a mortality follow-up through to 31 December 1995. Usable data were available for 20 195 participants (Breslow *et al.*, 2000).

The β -Carotene and Retinol Efficacy Trial (CARET)

This trial of the potential chemopreventive effects of β -carotene and retinol began as a pilot study of 816 asbestos-exposed male workers and 1029 male and female heavy smokers and became a full-blown efficacy trial in 1988, with a total of 4060 male asbestos-exposed workers and 14 254 smokers (44% women) after 3 years of randomization. The trial was stopped 21 months before the planned cessation of the intervention; detailed results of associations with risk factors ascertained at baseline

(including alcoholic beverage consumption) considered cancers ascertained through to 15 December 1995 (Omenn *et al.*, 1996).

Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

A cohort of 25 400 women participated in a study that investigated the association between dietary folate, alcohol consumption, and postmenopausal breast cancer. Dietary data were collected at study enrollment between 1993 and 2001. Folate content was assigned on the basis of pre-fortification (i.e., pre-1998) databases. Of the 25 400 women participants with a baseline age of 55-74 years and with complete dietary and multivitamin information, 691 developed breast cancer between September 1993 and May 2003. Cox proportional hazard models with age as the underlying time metric were used to generate hazard ratios (HRs) and 95% CIs (Stolzenberg-Solomon *et al.*, 2006).

California Teachers Study

This cohort was established in 1995–96 when 133 479 active and retired female teachers and administrators participating in the California State Retirement System returned a 16-page questionnaire that included data on alcoholic beverage consumption. Women who moved out of state or who died contributed person–months to the analysis up to the date of these events. Incident cancer cases are identified by annual linkage to the California Cancer Registry. Follow up was to January 2001 (Horn-Ross *et al.*, 2004; Chang *et al.*, 2007).

(c) Scandinavia

(i) Denmark

Pooled Copenhagen cohort studies

The data from three cohort studies—the Copenhagen City Heart Study, the Glostrup Population Study and the Copenhagen Male Study—were pooled. The Copenhagen City Heart study was initiated in 1976; participants were selected from 90 000 persons living in a defined area around the University Hospital of Copenhagen. An age-stratified sample of subjects aged 20 years or more was selected at random. Seventy-four per cent of those invited to participate (14 223 subjects) attended, and the subjects were followed-up until 1989. The Glostrup Population Studies Cohort (see above) comprised a total of 10 162 subjects (including men and women). The Copenhagen Male Study followed 5246 men, aged 40–59 years, from 14 large workplaces who were examined four times between 1970 and 1985. The combined study cohort included 18 602 men and 14 662 women. Information on smoking and intake of wine, beer and spirits was collected using self-administered questionnaires. Cancer cases were identified by record linkage to the Danish Cancer Register. Vital status was determined from the national Central Person Register. Cox regression was used to adjust for confounding by cigarette smoking, in a model that included six categories of current smoking and eight 10-year bands of duration of smoking. The cohort was eventually followed through to 1998, when 15 491 men and 13 641 women were included (Grønbaek *et al.*, 1998;

Prescott *et al.*, 1999; Albertsen & Grønbaek, 2002; Pedersen *et al.*, 2003). Details concerning the pooled results from these studies are not provided in the Table.

Glostrup Population Study

The Glostrup Population Study was established primarily to investigate cardiovascular disease, and comprised subjects from several birth cohorts (1897–1962) examined between 1964 and 1992, drawn from a study area Southwest of Copenhagen. A study population of 5207 women aged 30–80 years at baseline was considered for the analysis of breast cancer risk factors. Cases of cancer were identified by linkage to the Danish Cancer Register (Høyer & Engholm, 1992; Petri *et al.*, 2004).

Danish Diet, Cancer and Health Study

Between December 1993 and May 1997, 79 729 women aged 50–64 years, who were born in Denmark and living in the greater Copenhagen and Aarhus area, were selected from the Central Population Register and invited to participate in this study. Participants completed a detailed 192-item food-frequency questionnaire that they received by mail before a visit to one of the two study clinics. Information was obtained on alcoholic beverage consumption from the food-frequency questionnaire and on drinking patterns from a lifestyle questionnaire completed at the clinic visit. The study cohort comprised 23 778 women whose records were linked to the Central Population Register for information on vital status and migration and to the Danish Cancer Register for diagnostic details of cancer. Follow-up was to 31 December 2000. This cohort was also included in the EPIC study (Tjønneland *et al.*, 2003, 2004).

(ii) *Finland*

α -Tocopherol β -Carotene (ATBC) Cancer Prevention Study

A cohort of 29 133 white Finnish men, aged 50–69 years, who smoked five or more cigarettes per day and who participated in the ATBC randomized trial, were recruited between 1985 and 1988 and followed for 5–8 years; 27 101 completed the baseline questionnaire. Incident cancers were identified by linkage with the Finnish Cancer Register. Alcoholic beverage consumption was ascertained through a food-use questionnaire administered before randomization in the trial. Deaths were identified from the Register of Causes of Death in Finland. Trial assignment was available [but does not seem to have been incorporated into the analysis] (Glynn *et al.*, 1996; Woodson *et al.*, 1999; Stolzenberg-Solomon *et al.*, 2001; Mahabir *et al.*, 2005; Lim *et al.*, 2006).

(iii) *Norway*

Norwegian Cohort of Waitresses

The cohort consisted of 5,314 waitresses organized in the Restaurant Workers' Union between 1932 and 1978. The follow-up period was from 1959 to 1991. The standardized incidence ratio (SIR) for all causes of cancer was 1.0 (95 percent confidence interval [CI] = 0.9-1.1), based on 430 observed cases. Cancers of the tongue, mouth, pharynx, larynx, esophagus, and liver were grouped together as alcohol-associated cancers. SIR for these cancers combined was 1.1 (CI = 0.5-2.2). For lung cancer, SIR

was 2.3 (CI = 1.6-3.1). Cervical cancer was also more frequent than expected, and breast cancer less frequent than expected. The larger excess of lung cancer and cervical cancer appeared in the sub-cohort working in restaurants with a license to serve alcohol. No excess risk of alcohol-associated cancers could be detected in this cohort of Norwegian waitresses (Kjaerheim & Andersen, 1994)

Norwegian Cohort Study

A cohort of Norwegian men born between 1883 and 1929, who completed a self-administered dietary questionnaire in 1967, was followed from 1968 (Heuch *et al.*, 1983) through to 1992. The target population was initially drawn from three sources: approximately 19 000 persons randomly drawn from lists of residents of Norway from the 1960 population census, approximately 5200 drawn from four selected counties and approximately 13 000 from a cohort of Norwegians living in Norway who had siblings living in the USA (Kjaerheim *et al.*, 1998). The study population for the Heuch *et al.* (1983) analysis comprised 16 713 men and women aged 45–74 years who responded to a questionnaire on dietary habits (which included alcoholic beverage consumption) and were followed to 31 December 1968. The study population for the Kjaerheim *et al.* (1998) analysis comprised 10 960 men who were alive and living in Norway on 1 January 1968, and who had no diagnosis of cancer before that date. Information on cancer incidence in both analyses was obtained through the population-based Norwegian Cancer Register (Heuch *et al.*, 1983; Kjaerheim *et al.*, 1998; Lund Nilsen *et al.*, 2000).

HUNT-1 Cohort Study

All inhabitants of the county of Nord-Trondelag who were at least 20 years of age were invited by mail to participate in a health survey, 'Helseundersøkelsen i Nord-Trondelag 1' (HUNT-1), in 1984. Of 85 100 adults invited, 75 043 attended and were subsequently followed. Those who attended were examined and completed detailed questionnaires including information on alcoholic beverage consumption and tobacco smoking. After exclusions of persons followed for less than 3 years, 69 962 persons were included in the study. Follow-up to 2002 was by linkage to the Norwegian Cancer Register and the Norwegian Central Person Register (Sjödahl *et al.*, 2007).

Norwegian Women and Cancer Study (NOWAC)

Between January 1991 and January 1997, 179 388 women aged 30–70 years, sampled according to birth years from the national population register at Statistics Norway, were invited to participate in a study. Mailing was conducted in 24 sets over 7 years; 102 443 women responded. The questionnaire included detailed information on alcoholic beverage consumption and diet. Cancer incidence was determined by linkage to the Norwegian Cancer Register (Dumeaux *et al.*, 2004).

(iv) *Sweden*

Swedish Twin Register Study

A cohort of 12 889 twin pairs of the same sex, identified from the Swedish Twin Register, was asked to complete a questionnaire in 1961; 10 942 responded initially. Zygosity was based on questions of childhood similarity. In 1967, a 107-item

questionnaire regarding lifestyle factors including alcoholic beverage consumption was mailed to registrees. Mortality in twins was followed-up by record linkage to the Swedish Cancer and Death Registers through to 1997. Information from death certificates and hospital records and other data were collected for the period up to 1981; the underlying cause of death was determined according to the ICD 8th revision. For the period after 1981, the underlying cause of death as stated on the death certificate was used (Grönberg *et al.*, 1996; Terry *et al.*, 1998, 1999; Isaksson *et al.*, 2002).

Swedish Mammography Cohort

The Swedish Mammography Cohort was established between 1987 and 1990, when all women who were born between 1914 and 1948 and resided in Uppsala and Vastmanland counties in central Sweden were invited to undergo a mammography and complete a mailed questionnaire on diet (67 items), including alcoholic beverage consumption, weight, height and education. A total of 66 651 women (74% of those approached) who returned the questionnaire formed the cohort. A second 96-item questionnaire was mailed in 1997 and was returned by 39 227 women. Follow-up was by record linkage to the National Swedish Cancer Register, the Regional Cancer Register and the Swedish Death and Population registers at Statistics Sweden. An initial report was conducted as a nested case-control study and included cases detected at the first screen (Holmberg *et al.*, 1995). After various exclusions, the final cohort for analysis comprised 61 433 women for the first questionnaire and 36 664 for the second. This cohort was included in the Pooling Project (Holmberg *et al.*, 1995; Rashidkhani *et al.*, 2005; Suzuki *et al.*, 2005; Larsson *et al.*, 2007).

Malmö Diet and Cancer Cohort

The population for this cohort was defined in 1991 as all persons who lived in the city of Malmö and were born during 1926–45, and was expanded in May 1995 to include all women born during 1923–50 and all men born during 1923–45. On completion of the baseline examinations in October 1996, 28 098 persons were regarded as the base cohort, with a subsample of 11 726 postmenopausal women. Exposure data on alcoholic beverage consumption were collected by an interview-based modified diet history, including a 7-day menu book that recorded details of alcoholic beverage consumption. Cancer cases were identified by linkage to the National Swedish Cancer Register and the Southern Swedish Tumour Register (Mattisson *et al.*, 2004).

(d) *Western Europe*

(i) *France*

Supplémentation en Vitamines et Minéraux Antioxydants Study

The objective of the study was to evaluate the relation between antioxidant-rich beverages and the incidence of breast cancer. This prospective study consisted of 4396 women without a history of cancer who were participants in the French Supplémentation en Vitamines et Minéraux Antioxydants Study. Beverage consumption was estimated by using three nonconsecutive 24-hour recalls. Incident cancer cases were identified

through clinical examinations performed every other year, including, e.g., a screening mammogram, and through a monthly health questionnaire. Participants were followed for a median 6.6 years (Hirvonen *et al.*, 2006).

(ii) *Netherlands*

Netherlands Cohort Study

This cohort was based on 204 municipal population registries throughout the Netherlands, and comprised 58 279 men and 62 573 women, aged 55–69 years in 1986, who completed a self-administered questionnaire at baseline. Follow-up was by record linkage to cancer registries and the Dutch database of pathology reports, initially to 1989, and subsequently to 1992. The cohort was analysed as a case–cohort; a subcohort of 3500 subjects randomly sampled from the cohort after baseline exposure measurement was followed to 1992 to obtain information on vital status and was used as control (Goldbohm *et al.*, 1994; Schuurman *et al.*, 1999; Zeegers *et al.*, 2001; Schouten *et al.*, 2004; Balder *et al.*, 2005; Loerbroks *et al.*, 2007).

(iii) *United Kingdom*

British Doctors' Study

In 1951, a questionnaire was sent to all British doctors included in the Medical Registry; 34 440 men and 6194 women responded, representing 69% and 60%, respectively, of those doctors not known to have died at the time of the inquiry. Further questionnaires were sent in 1957, 1966, 1972, 1978 and 1990 to men and in 1961 and 1973 to women; on each occasion, at least 94% of those alive responded. Reports were published on cause-specific deaths after 10, 20 and 40 years for men and after 10 and 22 years for women; more than 99% of the subjects had been traced. Information on causes of death was obtained principally from the Registrars General of the United Kingdom or from the records of the general Medical Council, the British Medical Association, relatives or friends. Because the subjects in the study were themselves physicians, they were a reasonably uniform socioeconomic group and the causes of death were certified more accurately than might have been the case among a sample of the general population. Data on alcoholic beverage consumption were available for the last 23 years of the study (1978–2001) and, for this period, data by drinking habit, adjusted for smoking (adjusted for 5-year calendar periods), were available, and were considered for 12 321 male doctors who were alive in 1978 (Doll *et al.*, 1994, 2005).

Oxford Vegetarian Study

This cohort included 11 140 vegetarians and non-vegetarians recruited in the United Kingdom between 1980 and 1984, who were contacted through the Vegetarian Society of the United Kingdom, media publicity and through other participants. Non-vegetarian participants were nominated by vegetarian participants from among their friends and relatives. Upon entry into the study, participants completed a food-frequency questionnaire and answered questions on other lifestyle factors including information on alcoholic beverage consumption. Participants were followed for information on cancer and

death through the National Health Service central registry to 31 December 1999. The analysis cohort comprised 10 998 participants aged 16–89 years at entry (Sanjoaquin *et al.*, 2004). This cohort is included in the European Prospective Investigation of Nutrition and Cancer (EPIC).

General Practitioner Research Database Study

The general practitioner research database contains longitudinal patient records, and totals >35 million patient–years of data on British primary care. The information was recorded by general practitioners during standard medical care, including patients' demographics, medical disorders, diagnoses from hospital referrals and drug prescriptions. Information on alcoholic beverage consumption was included when present in the records, but appears not to have been collected specifically; only information recorded at least 2 years before the index date was considered. The study period was from 1 January 1994 to 31 December 2001. The study was analysed as a nested case–control study; the index date was the date of diagnosis for cases, and was randomly selected for the 10 000 controls who were frequency-matched to the cases (Lindblad *et al.*, 2005).

(iv) *Multiple countries in Europe*

Multicentric European Study of Second Primary Tumours

A cohort of 928 (876 male, 52 female) cases of laryngeal and hypopharyngeal cancer was identified between 1979 and 1982 from a multicentric population-based case–control study in Italy, Spain and Switzerland that was conducted to study the effects of tobacco, alcoholic beverage consumption, diet and occupation on the development of cancers. The cohort was followed until 2000 for the occurrence of second primary tumours using population, mortality and cancer-registry files. Exposure information was obtained through interviews. Approximately 7% of the cohort was lost to follow-up. Of the 876 men and 52 women, 145 men and six women developed second primary tumours during the follow-up period. The Cox proportional hazard model, adjusted for age, centre, occupation, smoking and site of first cancer, was used to estimate hazard ratios (Dikshit *et al.*, 2005).

European Prospective Investigation into Cancer and Nutrition (EPIC)

A cohort of healthy adults was recruited from Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, the Netherlands and the United Kingdom to study multiple exposures, including cigarette smoking, vegetable/fruit intake and alcoholic beverage consumption, on risks for various cancers. Recruitment was initiated in 1992, and active and passive follow-up is ongoing. Exposure information was obtained from mailed questionnaires. Relative risks were obtained using the proportional hazard model adjusting for follow-up time, sex, education, body mass index, vegetable and fruit consumption, tobacco smoking and energy intake (Boeing, 2002; Rohrmann *et al.*, 2006; Tjønneland *et al.*, 2007).

Table 2.1b Cohort studies of cancer and alcoholic beverage consumption in special populations

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
North America								
<i>Canada</i>								
Canadian Alcoholics Study	1951	Schmidt & Popham (1981)	1951–70	9 889 alcoholic men, aged ≥ 15 years, admitted to the clinical service of the Addiction Research Foundation of Ontario between	Death records	Deaths	Buccal cavity, pharynx, oesophagus, stomach, large intestine, rectum, liver, pancreas, larynx, bronchus, lung, prostate, lymphoma, leukaemia	Local reference population, US veterans used as a reference population, no individual exposure data, no information on potential confounders
<i>United States</i>								
Massachusetts Cohort of Chronic Alcoholics	1930, 1935, 1940	Monson & Lyon (1975)	1930–71	1139 men and 243 women admitted in 1930, 1935 or 1940 to a mental hospital with a diagnosis of chronic alcoholism	Death certificates	Deaths	Buccal cavity, oesophagus, stomach, colon, rectum, large intestine, liver, biliary tract, pancreas, larynx, lung, breast, urogenital organs, prostate, urinary bladder, kidney, brain, leukaemia, other cancer	Compared with US population; half of group lost to follow-up; no individual exposure data; no information on confounders.

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Seventh-day Adventists study	1976	Mills <i>et al.</i> (1994); Singh & Fraser (1998)	1976–82	60 000 Seventh-day Adventists in California identified by census questionnaire, aged >25 years	Lifestyle questionnaire	Cases	Buccal cavity, oesophagus, stomach, large intestine, colon, rectum, biliary passages and liver, pancreas, bronchus, lung, melanoma, breast, cervix, corpus uteri, ovary, urinary bladder, kidney, brain, Hodgkin disease, leukaemias	Study population had a low prevalence of alcohol consumption; joint effect of alcohol and tobacco examined.
Scandinavia								
<i>Denmark</i>								
Danish Brewery Workers Cohort	1939–63	Jensen (1979); Thygesen <i>et al.</i> (2005)	1943–99	14 313 Danish brewery workers employed at least 6 months in 1939–63; age not given	Cancer registry database	Case/deaths	Buccal cavity, pharynx, oesophagus, stomach, colon, rectum, liver, pancreas, nasal cavities, larynx, lung, melanoma, other skin, prostate, testis, penis, urinary bladder, kidney, ureter, brain, nervous system, lymphatic and haematopoietic leukaemia	Local male population; national mortality rates used for comparison; no individual exposure data; no information on potential confounders

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Danish Alcohol Abusers Study	1954–87	Tønnesen <i>et al.</i> (1994)	1954–87	18 307 (15 214 men, 3 093 women) alcoholics from a public outpatient clinic for free treatment	Interview	Cases/deaths	Lip, tongue, salivary glands, mouth, pharynx, oesophagus, stomach, kidney, colon, rectum, liver, gall bladder, urinary bladder, pancreas, larynx, lung, pleura, melanoma, non-melanoma skin, breast, cervix uteri, corpus uteri, ovary, prostate, testis, brain, endocrine, non-Hodgkin lymphoma, multiple myeloma, haematopoietic and lymphatic leukaemia	Cohort cancer incidence compared with total Danish population; no information on potential confounders; estimates not adjusted for smoking.
Nationwide Study of Patients with Cirrhosis	1977–89	Sørensen <i>et al.</i> (1998)	1977–93	11 605 1-year survivors of cirrhosis from the Danish National Registry of Patients	Registry database	Cases	Oral cavity, pharynx, oesophagus, stomach, colon, rectum, liver, gall bladder, biliary tract, pancreas, larynx, lung, melanoma, other skin, breast, cervix uteri, endometrium, ovary, prostate, testis, kidney, urinary bladder, brain, nervous system, thyroid, non-Hodgkin lymphoma, leukaemia	Expected rates from national incidences; estimates not adjusted for smoking

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
<i>Finland</i>								
Finnish Alcoholics	1967–70	Hakulinen <i>et al.</i> (1974)	1967–70	Approximately 205 000 male alcohol misusers and mean of 4 370 male chronic alcoholics, aged >30 years	Finnish Cancer Registry	Cases	Salivary glands, pharynx, oesophagus, stomach, colon, liver, pancreas, larynx, lung, bone, skin, prostate, urinary organs, eye, nervous system, thyroid, lymphoma, Hodgkin disease, leukaemia	Local reference; no individual exposure data; no data on potential confounders
<i>Norway</i>								
Norwegian Alcoholics Study	1925–39	Sundby (1967)	1925–62	Alcoholics from Oslo psychiatric department, 1722 males, aged 15–70 years	Death certificate	Deaths	Oral cavity, pharynx, oesophagus, stomach, colon, rectum, liver, pancreas, larynx, lung, prostate, testis, penis, urinary bladder, kidney, brain, Hodgkin disease, multiple myeloma, leukaemia	Local reference; Oslo urban mortality data

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
International Organization of Good Templars Cohort	1980	Kjaerheim <i>et al.</i> (1993)	1980–89	5332 members of the International Organization of Good Templars, aged ≥ 10 years	Hospital and laboratory reports	Cases	Oral cavity, pharynx, oesophagus, stomach, colon, rectum, gall bladder, liver, pancreas, larynx, lung, breast, female genital, prostate, male genital, urinary bladder, kidney, brain, haematopoietic cancers	Expected rates from national incidence

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
<i>Sweden</i>								
Temperance Boards Study	1947	Sigvardsson <i>et al.</i> (1996)	1947–77	15 508 alcoholic women ascertained through the Temperance Boards and 15 508 non- alcoholic women from population, born 1870–1961	Temperance Boards records	Cases	Lip, tongue, salivary glands, mouth, hypopharynx, pharynx, tonsil, oesophagus, stomach, small intestine, duodenum, colon, rectum, liver, gallbladder, bile ducts, pancreas, nose, larynx, bronchus, lung, bone, connective tissue, muscle, breast, malignant melanoma, other skin, uterus, cervix uteri, corpus uteri, ovary, vulva, vagina, other female genital, urinary bladder, kidney, eye, nervous system, thyroid, endocrine glands, non- Hodgkin lymphoma, Hodgkin disease, multiple myeloma, leukaemia, unspecified sites	No adjustment for smoking

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Swedish Brewery Workers Study	1960	Carstensen <i>et al.</i> (1990)	1961–79	6230 men employed in the Swedish brewery, aged 20–69 years	Swedish Cancer Registry	Cases	Buccal cavity, pharynx, oesophagus, stomach, colon, rectum, liver, pancreas, larynx, bronchus, lung, melanoma, prostate, male genital organs, urinary bladder, kidney, urinary system, brain, nervous system, leukaemia, lymphatic and haematopoietic cancers	Swedish male population used as a reference group
Swedish Inpatient Register/ Study of Patients with Chronic Pancreatitis	1964–83	Karlson <i>et al.</i> (1997); Ye <i>et al.</i> (2002)	1964–95	Karlson <i>et al.</i> (1997) Analytical cohort of 4043 patients discharged with pancreatitis in association with alcoholism Ye <i>et al.</i> (2002) 178 688 male and female patients with hospital discharge of alcoholism, 1964–95	Medical and cancer registry records	Cases	Pancreas	Incidence rates compared with national rates; no individual exposure data; no information on potential confounders; risks not adjusted for smoking

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
National Board of Health and Welfare Hospital Discharge study of Alcoholism	1965	Kuper <i>et al.</i> (2000c)	1965–95	Analytical cohort of 36 856 women diagnosed with alcoholism from hospital discharge data	Hospital-discharge records	Cases	Breast	Compared with national incidence rates; no individual exposure information; no adjustment for potential confounders
National Board of Health and Welfare Study of Alcoholic Women	1965–94	Lagiou <i>et al.</i> (2001); Weiderpass <i>et al.</i> (2001a,b),	1964–95	36 856 women hospitalized for alcoholism	Registry-based linkages		Trachea, bronchus, lung, cervix uteri, endometrium, ovary, vagina, vulva	No adjustment for smoking

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Swedish In-patient Register and National Cancer Register Study	1965–94	Boffetta <i>et al.</i> (2001)	1965–95	173 665 patients (138 195 men, 35 470 women) with a hospital discharge diagnosis of alcoholism, aged >20 years	National Cancer Registry	Cases	Lip, tongue, salivary gland, mouth, oral cavity, pharynx, mesopharynx, nasopharynx, hypopharynx, oesophagus, stomach, colon, rectum, liver, biliary tract, pancreas, larynx, lung, melanoma, breast, cervix, corpus uteri, ovary, prostate, testis, urinary bladder, kidney, brain, thyroid, lymphatic, haematopoietic cancers	Compared with incidence in the national population

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Uppsala Alcoholics Study	1965–83	Adami <i>et al.</i> (1992a,b)	1964–84	10 350 individuals from Swedish Uppsala Inpatients Register, with discharge diagnosis for alcoholism	Cancer registry	Cases	Lip, tongue, salivary gland, mouth, oral cavity, pharynx, mesopharynx, nasopharynx, hypopharynx, oesophagus, stomach, colon, rectum, liver, biliary tract, pancreas, larynx, lung, melanoma, breast, cervix, corpus uteri, ovary, prostate, testis, urinary bladder, kidney, brain, thyroid, lymphatic, haematopoietic cancers	

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/deaths	Neoplasms analysed	Comments
Western Europe								
<i>Republic of Ireland</i>								
Dublin Brewers Study	1954–73	Dean <i>et al.</i> (1979)	1954–73	Deaths between 1954 and 1973 among male blue-collar brewery workers	Death certificates	Deaths	Oesophagus, stomach, colon, rectum, liver, gall bladder, pancreas, lung	Compared with Dublin skilled and unskilled manual workers; no individual exposure data; no information on confounders
<i>United Kingdom</i>								
Study of Patients Hospitalized for Alcohol-related Diseases	1948–1971	Prior (1988)	1948–81	1 110 patients/hospitalized in the Birmingham region for alcohol-related conditions	Hospital-discharge records	Cases	Mouth, buccal cavity, pharynx, throat, oesophagus, liver, gall bladder, pancreas, digestive system, larynx, lung, respiratory system, skin, breast, cervix uteri, reproductive system, urinary system, lymphatic and haematopoietic systems	Compared with the West Midlands region

Table 2.1b (continued)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
England and Wales, UK Alcoholics Study	1953–57, 1964	Adelstein & White (1976); Nicholls <i>et al.</i> (1974)	1953–74	1 595 male and 475 female alcoholics aged 15–90 years	Hospital- discharge records	Deaths	Pharynx, oesophagus, stomach, intestine, rectum, liver, pancreas, larynx, lung, breast, cervix uteri, prostate	Reference death rates were sex- specific rates of England and Wales for 1972.

2.1.2 *Studies in special populations (Table 2.1b)*

This group of studies is characterized by the assumption that the study subjects have a pattern of consumption of alcoholic beverages that is different from that of the general population, e.g. alcoholics, brewery workers, members of a temperance organization. Because of the availability of national registries of populations, inpatients and cancer, most of these studies were performed in Scandinavian countries. The estimation of risk in these individuals is not based upon a comparison of exposed and unexposed subjects within the cohort, but with the expected rates of cancer in the general population.

(a) *North America*

(i) *Canada*

Canadian Alcoholics Study

The cohort consisted of 9889 men (79% middle-class; <1% nonwhite) who had been admitted to the main clinical services for alcoholics in Ontario between 1951 and 1970. No information on individual drinking or smoking habits was available, but investigations of samples of the cohort indicated an average daily consumption of 254 mL [\sim 200 g] ethanol and that >92% were still drinking ten years after admission. A total of 94% of cohort members were current smokers, who smoked an average of 28 cigarettes per day. Altogether, 1823 deaths occurred before 1972; 960.9 were expected. Vital status could not be determined for 3.5% of cohort members. Cause-specific mortality was compared with that of the Ontario male population. A further comparison was made with US veterans who smoked 21-39 cigarettes per day, in an indirect attempt to control for the effect of tobacco on the risk of alcohol-related cancers. Results were also reported for 1119 women followed up for 14 years, but only a few cancer deaths were observed (Schmidt & Popham, 1981).

(ii) *United States*

Massachusetts Cohort of Chronic Alcoholics

To test the hypothesis that there is a positive association between chronic alcoholism and carcinoma of the pancreas, the mortality experience of 1382 chronic alcoholics was studied. Analysis was limited to a comparison of observed and expected proportional mortality of different causes of death in the 894 whites who were known to have died. For carcinoma of the pancreas, 3 deaths were observed and 5.2 were expected. The observed/expected ratios for other causes of death, including other sites of cancer, were in accordance with prior studies (Monson & Lyon, 1975).

Seventh-day Adventist Study

The study population was identified in 1973 from 437 California Seventh-day Adventists churches. Adventists are a religious group who do not consume tobacco, alcoholic beverages or pork, and half adhere to a lacto-ovo-vegetarian lifestyle. The list of households was computerized in 1974: 63 530 were identified to which a census

questionnaire was sent; 36 850 households returned a questionnaire listing 95 196 persons. Persons under 25 years of age were excluded from all analyses, and the study population analysed comprised 59 090 subjects. In 1976, a lifestyle questionnaire was sent to all living members (57 841); 40 398 participants returned the questionnaire; non-Hispanic whites had a response rate of 75%. Participant data was linked with data from two cancer registries, which were in operation in California. SIRs were calculated. The group of non-Hispanic members of the cohort was compared with an external population of Connecticut (93% whites) (Mills *et al.*, 1994; Singh & Fraser, 1998).

(b) *Scandinavia*

(i) *Denmark*

Danish Brewery Workers Cohort

A total of 14 313 male members of the Danish Brewery Workers' Union who had been employed for six or more months in a brewery during the period 1939-63 were enrolled in this retrospective cohort study. The brewery workers had the right to consume six bottles (2.1 L) of light pilsener (lager) beer (alcohol content, 3.7 g [\sim 78 g ethanol] per 100 mL) on the premises of the brewery per working day; 1063 members of the cohort worked in a mineral-water factory, with no free ration of beer. No information was available on alcohol consumption or smoking habits of individual members of the cohort; but, on the basis of comparisons with alcohol statistics and population surveys, it was estimated that cohort members with employment in a brewery had a four times higher average beer consumption than the general population. Vital status was ascertained for 99.4% of the cohort members. There were 3550 deaths (SMR, 1.1) in the cohort, and 1303 incident cases of cancer were identified during the period 1943-72 by record linkage with the Danish Cancer Registry. Expected numbers of cancer cases and deaths were computed on the basis of age-, sex-, residence- and time-specific rates (Jensen 1979, 1980).

Danish Alcohol Abusers Study

The study was based on 18 307 alcoholics from Copenhagen who entered a public outpatient clinic for free treatment for alcoholism from 1954 to 1987. From 1968, cohort members had population identification numbers. Prior to that date, the 5969 cohort members without a number were sought by computer linkages with municipal and Danish population registries. The resultant cohort consisted of 15 214 men who were observed for 12.9 years on average and 3093 women who were observed for an average of 9.4 years. The records of these cohort members were linked to the Danish Cancer Register to obtain information on cancer morbidity through to December 1987. The observed cancer incidence was compared with that expected in the Danish population (Tønnesen *et al.*, 1994).

Nationwide Study of Patients with Cirrhosis

In a study based upon the Danish National Register of Patients, persons who were registered between 1977 and 1989 were enrolled if they had been discharged with

alcoholic cirrhosis (ICD-8 571.09), primary biliary cirrhosis (571.90), non-specified cirrhosis (571.92), chronic hepatitis (571.93) or 'other types of cirrhosis, alcoholism not indicated' (571.99). Cirrhosis was considered as a whole, but also as four separate types, largely following the ICD-8 codes given above, except that 'non-specified cirrhosis' and 'cirrhosis, alcoholism not indicated', were merged into one group termed 'nonspecified cirrhosis' (571.92 and 571.99). All members of the study cohort were linked through their personal identification number to the nationwide Danish Cancer Register and followed-up through to 1993. The cohort for this analysis consisted of 11 605 subjects (5079 men and 2086 women with alcoholic cirrhosis) who had survived for 1 year after registration. Expected numbers were computed from the rates in the Danish Cancer Register and compared with those observed (Sørensen *et al.*, 1998).

(ii) *Finland*

Finnish Alcoholics

Between 1944 and 1959, male 'alcohol misusers' were registered by the Finnish State Alcohol Monopoly on the basis of conviction for drunkenness, sanctions imposed by the municipal social welfare boards, and various breaches against the regulations governing alcohol usage. No information was available on the amount of alcohol consumed by the cohort members, nor on types of beverage or smoking habits. The numbers of incident cases of cancer of the oesophagus, of the liver and of the colon among an estimated 205 000 men born 1881-1932 and alive in 1965-68 were obtained by a manual match between the files of the Finnish Cancer Register for these years and the files of the Alcohol Misusers Registry. Person-years at risk during the period 1965-68 were estimated from samples, and these formed the basis for computing expected numbers of cases. Lung cancer risk was determined in a similar fashion, but for only one-third of the group in 1968.

A second group of men more than 30 years of age, who in 1967-70 had been listed as chronic alcoholics by the Social Welfare Office of Helsinki, were also studied. The mean annual number of such men was estimated to be 4370. No information was available on type or amount of alcoholic beverages drunk or on tobacco smoking, but the persons in the group of chronic alcoholics were heavy alcohol drinkers, most of whom drank cheap, strong beverages, wines and denatured alcohols. Incident cases of cancer occurring during 1967-70 were identified by record linkage with the Finnish Cancer Register, and expected numbers were derived on the basis of national incidence rates and computed person-years (Hakulinen *et al.*, 1974).

(iii) *Norway*

Norwegian Alcoholics Study

A total of 1 722 men discharged during 1925-39 from the Psychiatric Department of an Oslo hospital with a diagnosis of alcoholism were enrolled in the study and observed until the end of 1962. No information was available on drinking and smoking habits of individual cohort members or of the cohort as a whole, 408 were considered

to be vagrant alcoholics. Evidence of persistent alcoholism was available for about 75% of the vagrants and for 50% of the remaining group. Follow-up was virtually complete, with 1 061 deaths. Death certificates were located for 1 028 of these, and information on cause of death was available for another 28 persons. The observed numbers of deaths were compared with expected numbers based on causes of deaths for all of Norway (496.9) and for Oslo (629.0). (Sundby, 1967).

International Organization of Good Templars Cohort

A cohort of 5332 members, aged 10 years and over, from the 200 larger and active lodges of the International Organization of Good Templars was followed for 10 years from 1980. Members of the Organization sign a statement that they will not drink alcoholic beverages. Cancer incidence and cause-specific mortality of the cohort was determined by linkage to the Cancer Register of Norway and was compared with that of the total Norwegian population (Kjaerheim *et al.*, 1993).

(iv) *Sweden*

Temperance Boards Study

This cohort study comprised 15 508 Swedish women with a history of heavy alcoholic beverage consumption and 15 508 matched comparison subjects. The excessive alcoholic beverage users were ascertained through a review of the records of all Temperance Boards of Sweden, which operated between 1917 and 1977. During this time, 21 757 women were registered. Before 1947, personal identification numbers did not exist, so the cohort was limited to records after 1947. Linkages were made with the Swedish Cancer Register, which started in 1958 (Sigvardsson *et al.*, 1996).

The Swedish Brewery Workers Study

This study was based upon the Cancer–Environment Register that links cancer incidence data from the Swedish Cancer Register for the period 1961–1979 with information on occupation, occupational status, industry and residence obtained in the 1960 population census. A group of 6230 men who were, according to the census, employed in the Swedish brewery industry in 1960, aged 20–69 years, was followed-up in 1961–79 by linkage to the Swedish Cancer Register. Person–years were computed by linkage with the Swedish Population Register. Relative risks were computed using all Swedish men as the reference group (Carstensen *et al.*, 1990).

Swedish In-patient Register Study of Patients with Chronic Pancreatitis

This cohort was also based on the Swedish In-patient Register, and a very similar methodology to that of Boffetta *et al.* (2001) was used. Records of all patients with a diagnosis of acute, chronic or unspecified pancreatitis were identified, and linked to the Registries of Population, Death and Emigration held by Statistics Sweden. After exclusions of those who could not be identified in these registers and those with pancreatic or other cancers diagnosed at the index hospitalization, 29 530 subjects were included in the cohort. Incident cancers were identified by linkage with the [Swedish] National Cancer Register up to 31 December 1989 (Karlson *et al.*, 1997). In a more recent report using the same database as above (Karlson *et al.*, 1997; Boffetta *et al.*, 2001),

five cohorts were considered: 178 688 subjects admitted to hospital for alcoholism, 3500 admitted for chronic alcoholic pancreatitis, 4952 admitted for chronic non-alcoholic pancreatitis, 13 553 admitted for alcoholic liver cirrhosis and 7057 admitted for non-alcoholic liver cirrhosis. Follow-up was through to 1995 by linkage with national registers. Standardized incidence ratios (SIRs) were computed taking the Swedish population as a reference (Ye *et al.*, 2002).

National Board of Health and Welfare Hospital Discharge Study of Alcoholism

From 1965 onwards, the National Board of Health and Welfare started collecting data on individual hospital discharges in the Inpatient Register. From 1987, the register attained complete nationwide coverage. All patients recorded in the Inpatient Register with a discharge diagnosis of alcoholism were initially selected for inclusion in the study. A total of 196 803 individually unique national registration numbers, assigned to all Swedish residents, were registered at least once with a diagnosis of alcoholism between 1965 and 1994. December 31, 1995 was the end of the observation period. Record linkage of the study cohort to the nationwide Registers of Causes of Death, Emigration and Cancer allowed the calculation of follow-up time, in person-years, of eligible persons at risk as described previously in detail (Adami *et al.*, 1992a, b). From the total cohort 7790 records were excluded because of erroneous or incomplete national registration numbers, a further 3405 patients were excluded because they had prevalent cancers at the time observation began and another 2941 patients because of inconsistencies uncovered during record linkage. Thus a total of 182 667 patients with alcoholism remained eligible, and of these 36 856 were women (Kuper *et al.*, 2000c).

National Board of Health and Welfare Study of Alcoholic Women

This study was essentially on the same female cohort as that considered by Boffetta *et al.* (2001). A total of 36 856 Swedish women (mean age, 42.7 years), who were hospitalized at least once in 1965–94 with a diagnosis of alcoholism and were residents in Sweden, were included in the study. SIRs were calculated by multiplying the number of person–years within 5-year age groups and calendar-year strata by the cancer incidence rates in Swedish women. Exclusions from observed and expected groups were secondary cancers and cancers found incidentally at autopsy. The person–time and events during the first year of follow-up were excluded to avoid increased likelihood of diagnosis of one disease following hospitalization for alcoholism in the presence of a yet undetected malignancy. The authors took co-morbidities into account (i.e. factors in the hospitalization record other than alcohol dependence) and assessed person–time within each co-morbidity stratum (Lagiou *et al.*, 2001; Weiderpass *et al.*, 2001a,b).

Swedish In-patient Register and the National Cancer Register Study

This cohort was based on the Swedish In-patient Register, a database provided by the National Board of Health and Welfare since 1964 that contains complete nationwide records since 1987, and is an expansion of the study of Adami *et al.* (1992a,b). Using the national identification number, which is a unique identifier for each citizen, the cohort was linked to the Registers of Population, Death and Emigration, and the National Cancer Register. The 196 803 persons aged ≥ 20 years who were identified had

a hospital discharge-diagnosis of alcoholism during 1965–94 and a unique national registration number. After exclusions for various reasons, 173 665 persons were included in the analytical cohort (138 195 men, 35 470 women). Incident cancers after discharge were identified by linkage with the National Cancer Register up to 31 December 1995 (Boffetta *et al.*, 2001).

Uppsala Alcoholics Study

A cohort of 10 350 individuals was selected from the Uppsala Inpatient Register (Sweden), with a discharge diagnosis that contained a diagnostic code for alcoholism (International Classification of Diseases [ICD] 7: 307, 322; ICD 8: 291, 303) during 1965–83. After exclusion of those who had an inconsistent registry number, 9353 (8340 men, 1013 women) patients were entered into the study. Follow-up was by record linkage to the nationwide Register of Causes of Death and the National Swedish Cancer Register through to 1984. Expected numbers of cancers were computed from cancer incidence in the Uppsala health-care region to compare with the observed cases (Adami *et al.*, 1992a).

The Uppsala Alcoholics cohort, identified at the same time and followed for the same period, was also analysed as three population-based cohorts with mutually exclusive hospital discharge-diagnoses of alcoholism, cirrhosis or both. It comprised 8517 patients with a diagnosis of alcoholism, 3589 subjects with cirrhosis and 836 subjects with both diagnoses (Adami *et al.*, 1992b).

(c) *Western Europe*

(i) *Republic of Ireland*

Dublin Brewers Study

A list of 1628 deaths during the period 1954–73 was provided by a large brewery in Dublin, Ireland. On the basis of death certificates for all but two of these men and of statistics for the population of employees and pensioners in 1957, 1960, 1967 and 1970, relative risks for specific causes of death were estimated employing both national and regional rates. The expected number of deaths was 1675.8 (regional rates). It was estimated from previous research that ethanol intake among the brewery workers was 58 g per day, compared with 16–33 g per day for other groups of the Irish population. Beer (stout) was consumed on the premises. No information was available on individual consumption of alcohol or tobacco; smoking was forbidden at the brewery for many years. [The Working Group noted that the cohort at risk was estimated indirectly as 2000–3000 men at any one time during follow-up, and no individual follow-up of cohort members was performed.] (Dean *et al.*, 1979)

(ii) *United Kingdom*

Study of Patients Hospitalized for Alcohol-related Diseases

A series of 1110 patients seen at hospitals in the Birmingham Region between 1948 and 1971 for alcohol-related conditions were followed to 1981. By means of cohort analysis, the incidence of cancer in the series was compared with that in the West

Midlands Region. In men the cancer risk was increased 1.7-fold: individual sites at risk were liver (8-fold), buccal cavity and throat (27-fold), respiratory system (2.4-fold), and oesophagus (4-fold). No excess of colorectal cancers was observed. Although in women there was no overall excess of cancers, the risk was high in the biliary system (15-fold) and was moderately increased for *cervix uteri* (4-fold) (Prior, 1988).

A total of 935 patients who had been discharged from four mental hospitals in or near London, UK, during the years 1953-57, or who had died during the key hospitalization and who had been given a primary or secondary diagnosis implicating abnormal drinking, were followed for 10-15 years. Of the total sample, 70 (7.5%) remained untraced and 233 men (34.4%) and 76 women (29.6%) had died; a total of 112.7 deaths was expected. The study was extended to all of England and Wales 1953-64 by Adelstein and White (1976), who covered a total of 1595 men and 475 women (Nicholls et al., 1974)

2.2 Cancer of the oral cavity and pharynx

The evidence for carcinogenic effects of alcoholic beverage consumption on the risk for cancers of the oral cavity and pharynx in humans was considered to be *sufficient* by a previous IARC Working Group (IARC, 1988). This section evaluates the evidence related to the risk for oral and pharyngeal cancer in humans based on relevant cohort and case-control studies published after 1988.

Exposure to alcoholic beverages is given in many different measurements. For comparability between studies, one drink is equivalent to 14 g, 18 mL or 0.49 oz of alcohol, which generally corresponds to 330 mL of beer, 150 mL of wine and 36 mL of hard liquor. Cancers of the oral cavity and pharynx are predominantly squamous-cell carcinomas. The histology of the tumours is given when available. Generally, studies on pharyngeal cancers are predominantly oropharyngeal and hypopharyngeal cancers, rather than nasopharyngeal cancer. Two case-control studies are, however, specifically focused on nasopharyngeal cancer, as noted in the Tables.

The risks for cancer of the oral cavity and pharynx in relation to total alcoholic beverage consumption are summarized in Tables 2.2-2.5. The effect of alcohol types are presented in Table 2.6, the combined or joint effects of alcohol drinking and tobacco smoking are shown in Table 2.7, and the effect of alcohol cessation and the association between alcoholic beverage consumption and risk for oral and pharyngeal cancers among nonsmokers are presented in Tables 2.8 and 2.9, respectively.

2.2.1 Cohort studies (Table 2.2)

Five cohort studies of the general population have been published since 1988 on the relationship between alcoholic beverage consumption and oral or pharyngeal cancer (Boffetta & Garfinkel, 1990; Chyou *et al.*, 1995; Murata *et al.*, 1996; Kjaerheim

Table 2.2 Cohort studies of cancers of the oral cavity and pharynx combined

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Boffetta & Garfinkel (1990), USA, American Cancer Society Prospective Study	Cohort of 276 802 white men from over 25 states; aged 40–59 years; enrolment in 1959; mortality follow-up until 1971; 3% of cohort lost to follow-up	Questionnaire	Oral cavity (ICD 140–145)	<i>Total alcohol</i>			Age, smoking	
				Non-drinker	55	1.0 (reference)		
				Occasional drinker	10	1.2 (0.6–2.4)		
				1 drink/day	6	0.4 (0.2–1.0)		
				2 drinks/day	12	1.0 (0.5–1.9)		
				3 drinks/day	13	2.2 (1.2–4.0)		
				4 drinks/day	13	3.2 (1.7–6.1)		
				5 drinks/day	5	2.7 (1.0–6.8)		
				≥6 drinks/day	26	6.2 (3.7–10.1)		
Irregular drinker	15	2.0 (1.1–3.5)						
Adami <i>et al.</i> (1992a,b) Uppsala, Sweden,	Cohort of 9353 patients (8340 men, 1013 women) diagnosed with alcoholism in the Inpatient Register; incidence follow-up 1965–83	Inpatient Register records	Oral cavity, pharynx (ICD7 140–148)	Overall	36	SIR 4.1 (2.9–5.6)	No information on potential confounders	Age-standardized expected rates from local population; confounding by smoking likely
				<i>Age at follow-up</i>				
				<50 years	NG	9.4 (1.9–27.3)		
				50–64 years	NG	10.1 (6.6–14.7)		
				≥65 years	NG	1.0 (0.4–2.2)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Kjaerheim <i>et al.</i> (1993), Norway	Cohort of 5332 members of the International Organization of Good Templars (signed statement that they will not drink alcoholic beverages), aged ≥ 10 years; enrolment in 1980; incidence follow-up until 1989		Oral cavity, pharynx (ICD7 141–148)	Non-drinkers	<i>Men</i>	SIR [0.11] [0.01–0.40]	None	Age- and sex-specific expected rates from national incidence
					<i>Women</i>	1 [0.38] [0.01–2.12]		
					<i>Both sexes</i>	3 0.44 (0.09–1.27)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Day <i>et al.</i> (1994a), USA	Nested case-control study of second primary cancers; cohort of 1090 first primary cancers of oral cavity and pharynx; enrolment of first primary cancers in 1984-85; follow-up until 1989; 80 (56 men, 24 women) developed second primary cancers during follow-up; 189 (132 men, 57 women) randomly selected from cohort, matched on sex, study area and survival, free of second primary cancer at the end of follow-up	Interviewer-administered questionnaire	Oral cavity, pharynx, oesophagus (ICD9 141, 143-146, 148-149)	<i>Total alcohol</i>		Odds ratio	Age, stage of disease, lifetime smoking	Nested case-control study of second primary cancers among cases of Blot <i>et al.</i> (1988) study; looked at type of alcoholic beverage and cessation of alcoholic beverage consumption
				<5 drinks/week	9	1.0 (reference)		
				5-14 drinks/week	10	1.6 (0.5-5.1)		
				15-29 drinks/week	14	2.1 (0.7-6.6)		
				≥30 drinks/week	24	1.5 (0.5-4.5)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Tønnesen <i>et al.</i> (1994), Copenhagen, Denmark	Cohort of 18 307 (15 214 men, 3093 women) alcoholics from a public outpatient clinic for free treatment; incidence follow-up 1954–87	Interview with a social worker and psychiatrist	Oral cavity, pharynx	Alcoholic	<i>Men</i> 112 <i>Women</i> 22	3.6 (3.0–4.3) 17.2 (10.8–26.0)	None	Age-, sex- and calendar period-specific cohort cancer incidence compared with total Danish population
Chyou <i>et al.</i> (1995), Hawaii, USA, American men of Japanese Ancestry	Cohort of 7995 men of Japanese ancestry identified by the Honolulu Heart Program, aged 45–68 years; recruitment in 1965–68, incidence follow-up until 1993; 1–2% lost to follow-up	Interviewer-administered questionnaire	Oral cavity, pharynx, oesophagus, larynx (ICD8 140–150, 161)	<i>Total alcohol</i> Non-drinker <4 oz/month 4–24.9 oz/month ≥25 oz/month <i>p</i> for trend	16 5 18 52	Hazard ratio 1.0 (reference) 0.6 (0.2–1.6) 1.7 (0.9–3.4) 4.7 (2.6–8.3) <0.0001	Age, number of cigarettes/day, years smoked	Study population from Kato <i>et al.</i> (1992c); looked at type of alcoholic beverage and joint effects with smoking

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Murata <i>et al.</i> (1996), Japan	Nested case-control study among cohort of 17 200 men part of a gastric mass screening survey in 1984; incidence follow-up until 1993; 887 cases and 1774 controls matched on sex, birth year, city/county	Self-administered questionnaire	Oral cavity, pharynx, oesophagus, larynx (ICD9 140-150, 161)	<i>Total alcohol</i> *			None	*Unit is cup of 180 mL of sake: corresponds to 27 mL ethanol
				0 cups/day	17	1.0 (reference)		
				0.1–1.0 cups/day	13	1.0 ($p>0.05$)		
				1.1–2.0 cups/day	11	1.9 ($p>0.05$)		
				≥ 2.1 cups/day	10	9.0 ($p<0.01$) 9.6 ($p<0.01$)		
				χ^2 for trend				
				<i>Nonsmoker</i> *				
				0 cups/day	7	1.0 (reference)		
				0.1–1.0 cups/day	6	1.2 ($p>0.05$)		
				≥ 1.1 cups/day	5	2.1 ($p>0.05$)		
<i>Smoker</i> *								
0 cups/day	10	1.9 ($p>0.05$)						
0.1–1.0 cups/day	7	1.4 ($p>0.05$)						
≥ 1.1 cups/day	16	5.9 ($p<0.01$)						

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden	Cohort of 15 508 alcoholic women ascertained through the Temperance Boards and 15 508 non-alcoholic women from population matched individually on region and date of birth; enrolled in 1947–77; follow-up for incidence	Temperance Boards records	Tongue (ICD7 141), mouth (143, 144), tonsil (145), hypopharynx (147), Pharynx (148)	<i>Tongue</i>	Comparisons	2	1.0 (reference)	None
				Alcoholics	17	8.5 (2.0–37)		
				<i>Mouth</i>	Comparisons	1	1.0 (reference)	
				Alcoholics	12	12.0 (1.6–92)		
				<i>Tonsil</i>	Comparisons	1	1.0 (reference)	
				Alcoholics	11	11.0 (1.4–85)		
				<i>Hypopharynx</i>	Comparisons	1	1.0 (reference)	
				Alcoholics	9	9.0 (1.1–71)		
				<i>Pharynx</i>	Comparisons	0	1.0 (reference)	
				Alcoholics	1	NG		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments	
Kjaerheim <i>et al.</i> (1998), Norway	Cohort of 10 960 men born in 1893–1929 who completed two questionnaires sent to a probability sample of the Norwegian population; incidence follow-up 1968–92; mean age at start of follow-up, 59 years	Mailed survey	Oral cavity, pharynx, larynx, oesophagus (ICD7 141, 143–145, 147, 148, 150, 161)	<i>Total alcohol</i>				Age, smoking	
				Never or <1 time/week	26	1.0 (reference)			
				Previously	4	0.9 (0.3–2.7)			
				1–3 times/week	18	1.1 (0.6–1.9)			
				4–7 times/week	19	3.9 (2.1–7.1)			
				<i>p</i> for trend		0.003			
				<i>Beer</i>					
				Never or <1 time/week	37	1.0 (reference)			
				Previously	11	1.0 (0.5–1.9)			
				1–3 times/week	8	1.4 (0.7–3.1)			
				4–7 times/week	14	4.4 (2.4–8.3)			
				<i>p</i> for trend		<0.001			
				<i>Spirits</i>					
				Never or <1 time/week	42	1.0 (reference)			
Previously	15	1.3 (0.7–2.3)							
1–3 times/week	5	1.4 (0.6–3.6)							
4–7 times/week	5	2.7 (1.1–7.0)							
<i>p</i> for trend		0.06							
Sørensen <i>et al.</i> (1998), Denmark	Cohort of 11 605 1-year survivors of cirrhosis from the Danish National Registry of Patients; recruitment in 1977–89; incidence follow-up until 1993	Admission records of Danish National Registry of Patients	Oral cavity, pharynx	Overall		SIR	None	Expected rates from age-, sex- and site-specific national incidence rates	
				All cirrhosis	143	9.2 (7.8–10.8)			
				Alcoholic cirrhosis	115	11.6 (9.6–14.0)			
				Chronic hepatitis cirrhosis	8	4.2 (1.8–8.2)			

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI) ^a	Adjustment factors	Comments
Boeing (2002), Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, Netherlands, UK, European Prospective Investigation into Cancer and Nutrition	Cohort of 417 752 healthy adults; recruitment initiated in 1992; follow-up ongoing	Mailed questionnaire	Oral cavity, pharynx, oesophagus (ICDO C00.0–C10.9, C13.0–13.9, C15.0–15.9)	<i>Lifelong alcohol</i>		Hazard ratio	Follow-up time, sex, education, body mass index, vegetable and fruit consumption, tobacco smoking, energy intake	Looked at joint effects with smoking and observed a synergistic effect
				No alcohol	4	1.0 (reference)		
Dikshit <i>et al.</i> (2005), Italy, Spain, Switzerland	Occurrence of second primary tumours among a cohort of 876 male cases of laryngeal/hypo-pharyngeal cancer from a multicentric population-based case-control study (1979–82); follow-up until 2000	Interviewer-administered questionnaire	Oral cavity, pharynx, oesophagus (ICD9 140–150)	<i>Total alcohol</i>		Hazard ratio	Age, centre, occupation, smoking, site of first cancer	
				0–40 g/day	4	1.0 (reference)		
				41–80 g/day	4	0.8 (0.2–3.3)		
				81–120 g/day	12	3.0 (0.9–9.5)		
				≥21 g/day	17	3.5 (1.1–11.2)		
						<i>p</i> =0.003		

CI, confidence interval; ICD, International Classification of Diseases; NG, not given; SIR, standardized incidence ratio; ^a p-value indicated when CI not presented

et al., 1998; Boeing, 2002), four of which reported smoking-adjusted relative risks but one did not (Murata *et al.*, 1996). Increases in risk with consumption of alcoholic beverages were observed in all five cohort studies of populations from the USA, Europe and Asia, and heavy consumption was associated with a significantly increased risk. The adjusted relative risks were 9.22 (95% CI, 2.75–30.93) for more than 60 g (or more than four drinks) per day (Boeing, 2002), 6.2 (95% CI, 3.7–10.1) for more than 60 g (or more than four drinks per day) in the American Cancer Society Prospective Study (Boffetta & Garfinkel, 1990) and 3.9 (95% CI, 2.1–7.1) for consumption of alcoholic beverages four to seven times per week in a study in Norway (Kjaerheim *et al.*, 1998). A strong dose–response relationship was reported in three studies (Murata *et al.*, 1996; Kjaerheim *et al.*, 1998; Boeing, 2002); however, two studies found a J-shaped relationship with an inverse association with low levels of alcoholic beverage consumption (Boffetta & Garfinkel, 1990; Chyou *et al.*, 1995). In both studies, an increase in risk was observed with increasing levels of alcoholic beverage consumption thereafter.

Separating the effects of alcoholic beverages and tobacco smoking is generally very difficult. In most of these studies, however, smoking was controlled for in the analyses (Boffetta & Garfinkel, 1990; Chyou *et al.*, 1995; Kjaerheim *et al.*, 1998; Boeing, 2002). The increases in risk with consumption of alcoholic beverages were consistently seen in situations where smoking was controlled for as well as where smoking was not taken into account.

Five cohort studies were based on special populations (Adami *et al.*, 1992a; Kjaerheim *et al.*, 1993; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Sørensen *et al.*, 1998). This type of study usually does not consider individual exposure levels. The point estimates were either the SIRs or standardized mortality ratios (SMRs) without adjusting for tobacco smoking. Among special cohorts of alcoholics, an increase in risk for cancers of the oral cavity and pharynx compared either with the local population rates (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sørensen *et al.*, 1998) or with a population control group (Sigvardsson *et al.*, 1996) has also been shown. Among Swedish alcoholics, Adami *et al.* (1992a) found a fourfold increase in risk (95% CI, 2.9–5.6) for oral cavity and pharyngeal cancers. Tønnesen *et al.* (1994) also found more than a 3.5-fold increase in risk (95% CI, 3.0–4.3) among men and a 17-fold increase (95% CI, 10.8–26.0) among women. In Danish 1-year survivors of cirrhosis, Sørensen *et al.* (1998) found a ninefold increase in risk (95% CI, 7.8–10.8) compared with national incidence rates. Furthermore, among alcoholic cirrhosis patients, the risk was increased more than 11.5-fold (95% CI, 9.6–14.0) compared with fourfold (95% CI, 1.8–8.2) among chronic hepatitis cirrhosis patients. By cancer site, Sigvardsson *et al.* (1996) found 8.5-fold (95% CI, 2.0–37), 12-fold (95% CI, 1.6–92), 11-fold (95% CI, 1.4–85) and ninefold (95% CI, 1.1–71) increases in risk for cancers of the tongue, mouth, tonsil and hypopharynx, respectively, in a Swedish population. Conversely, a cohort study among members of the International Organization of Good Templars in Norway, an organization for which members sign a statement that they will abstain from the consumption of alcoholic beverages, showed a 56% decrease in risk (SIR 0.44; 95% CI,

0.09–1.27) compared with the national incidence rates (Kjaerheim *et al.*, 1993). Data on individual alcoholic beverage and tobacco consumption, however, were not obtained, which makes the separation of the protective effects of abstaining from either factor very difficult, especially since the two habits are usually correlated.

Alcoholic beverages have also been shown to be a risk factor for second primary cancers of the oral cavity and pharynx in two prospective studies of patients with a first primary cancer (Day *et al.*, 1994a; Dikshit *et al.*, 2005). Day *et al.* (1994a) and Dikshit *et al.* (2005) studied the risks for second primary cancers of the upper aerodigestive tract in relation to alcoholic beverage consumption among North Americans and Europeans (from Italy, Spain and Switzerland), respectively. In both studies, an increase in risk was found, although a more dramatic increase was found among Europeans (3–3.5-fold increase in risk among those who drank ≥ 81 g per day) than among North Americans (1.5–2-fold increase in risk among those who drank ≥ 15 drinks [≥ 210 g] per week or ≥ 30 g per day), which may be attributed to differences in categorization.

Results from prospective cohort studies of the general population provide *sufficient* evidence for the important role of alcoholic beverage consumption in the development of oral and pharyngeal cancer. The strength of the association is demonstrated by significantly increased relative risks that range from 3.5 to 9.2. A strong dose–response relationship was observed in almost all of the studies. Alcoholic beverage consumption was associated with an increase in risk for oral and pharyngeal cancer across different geographic regions and populations, which further supports the evidence.

2.2.2 Case–control studies

(a) Cancer of the oral cavity (Table 2.3)

All of the studies listed in Table 2.3 were hospital-based case–control studies (Franceschi *et al.*, 1990; Zheng *et al.*, 1990; Choi & Kahyo, 1991a; Zheng *et al.*, 1997; Rao & Desai, 1998; Balaram *et al.*, 2002; Znaor *et al.*, 2003; De Stefani *et al.*, 2007) and all but one (Rao & Desai, 1998) adjusted for tobacco smoking when evaluating the effect of alcoholic beverage consumption. All six studies of cancer of the oral cavity reported a positive association, with a dose–response relationship with alcoholic beverage consumption in different geographical areas of the world. A study of cancer of the tongue with a relatively large sample size reported increased risks for 20–30 years of alcoholic beverage consumption (odds ratio, 3.3; 95% CI, 1.4–8.9 for men; 2.0; 95% CI, 1.0–4.6 for women) (Rao & Desai, 1998). No obvious association was found in a study of cancer of the tongue with a limited sample size (Zheng *et al.*, 1997).

Overall, the increase in risk for oral cancer associated with alcoholic beverage consumption is consistent, even after controlling for smoking. The strength of the association was shown by elevated adjusted odds ratios for heavy consumption that ranged from 3.0 to 14.8. Furthermore, a dose–response relationship was observed with elevated alcoholic beverage consumption and increased risk in most studies with multiple exposure levels when adjusted for tobacco smoking. The association has been observed

Table 2.3 Case-control studies of cancer of the oral cavity and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–89	157 men identified from hospitals in Milan and Pordenone; under 75 years of age; histologically confirmed; response rate, 98% overall for cases	1272 hospital-based, male non-cancer patients from same hospitals as cases matched on age, area of residence; excluded patients with alcohol- and tobacco-related conditions; response rate, 97%	Interviewer-administered questionnaire	Oral cavity (ICD9 140, 141, 143–145)	<i>Total drinks/week</i> ≤19 20–34 35–59 ≥60 <i>p</i> for trend	15 14 63 65	1.0 (reference) 1.1 (0.5–2.5) 3.2 (1.6–6.2) 3.4 (1.7–7.1) <0.01	Age, area of residence, education, smoking habits	Also looked at pharyngeal cancers; looked at type of alcoholic beverage and joint effects with smoking
Zheng <i>et al.</i> (1990), Beijing, China, 1988–89	404 cases (248 men, 156 women) diagnosed at seven participating hospitals in the Beijing area; histologically confirmed; response rate, 100%	404 randomly selected non-cancer, hospital-based controls individually matched on age, sex, hospital; response rate, 100%	Interviewer-administered standardized questionnaire	Oral cavity (ICD9 141, 143–145)	Men only <i>Total alcohol in spirit equivalent</i> Never drinker <26 g/day 26–49 g/day 50–99 g/day >99 g/day		1.0 (reference) 1.3 (0.7–2.3) 1.1 (0.6–2.1) 1.4 (0.7–2.6) 2.8 (1.2–6.3)	Age, education, smoking	Assessed type of alcoholic beverage and joint effects with smoking

Table 2.3 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Choi & Kahyo (1991a), Seoul, Republic of Korea, 1986–89	157 cases (113 men, 44 women) from the Korea Cancer Center Hospital; cytological and/or histopathological confirmation	471 (339 men, 132 women) hospital-based, non-cancer controls matched (3:1 controls:cases) on age, sex, admission date; excluded patients with alcohol- and tobacco-related conditions	Interviewer-administered standardized questionnaire in hospital	Oral cavity (ICDO 140, 141, 143–145)	Men only			Smoking	Also looked at pharynx and larynx; *1 hop = 90 mL of soju [generally 20% alcohol, 14 g ethanol]; soju is most frequent alcoholic beverage type
					<i>Total alcohol^a</i>	16	1.0 (reference)		
					Non-drinker	9	0.6 (0.3–1.4)		
					<1 hop/day	45	3.6 (1.8–7.2)		
					1–2 hops/day	45	3.6 (1.8–7.2)		
					2–4 hops/day	32	4.2 (2.1–8.4)		
					>4 hops/day	11	14.8 (5.0–43.7)		
Zheng <i>et al.</i> (1997), Beijing, China, 1988–89	111 cases (65 men, 46 women) diagnosed at seven participating hospitals in the Beijing area; aged 20–80 years; histologically confirmed	111 randomly selected non-cancer, hospital-based controls individually matched on age, sex, hospital; excluded patients with alcohol- and tobacco-related conditions	Interviewer-administered standardized questionnaire	Tongue	<i>Total alcohol in spirit equivalent</i>			Education, smoking (matched on age, sex)	Same population as Zheng <i>et al.</i> (1990); looked at type of alcoholic beverage and joint effects with smoking
					Never drinker	64	1.0 (reference)		
					<50 g/day	20	1.2 (0.5–3.2)		
					50 g/day	8	0.7 (0.2–2.3)		
					>50 g/day	19	1.6 (0.6–4.4)		
					<i>Spirits frequency</i>				
<5 days/week	18	0.70 (0.28–1.70)							
≥5 days/week	27	2.34 (0.90–6.06)							

Table 2.3 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments	
Rao & Desai (1998), Bombay, India, 1980–84	637 men from the hospital	635 hospital-based, unmatched controls; free from cancer, infectious disease, benign lesion	Interviewer-administered questionnaire before clinical examination	Tongue (ICD 140–144)	<i>Total duration of alcoholic beverage consumption</i>			Age, residence		
					Anterior tongue	Non-user	102			1.0 (reference)
						1–10 years	11			1.2 (0.6–2.6)
						11–20 years	12			2.0 (0.9–4.4)
						21–30 years	12			3.3 (1.4–8.9)
				≥31 years	4	1.3 (0.3–4.8)				
				Base tongue	Non-user	382	1.0 (reference)			
					1–10 years	38	1.5 (0.9–2.5)			
					11–20 years	35	1.6 (0.9–2.9)			
					21–30 years	32	2.0 (1.0–4.6)			
≥31 years	8	0.5 (0.2–1.4)								
Balaram <i>et al.</i> (2002), southern India, 1996–99	591 cases (309 men, median age 56 years; 282 women, median age 58 years) from three centres in Bangalore, Madras, Trivandrum; response rate, 97%	582 (292 men, 290 women) hospital-based controls from the same hospitals as cases frequency matched by centre, age, sex; response rate, 90%	Interviewer (social worker)-administered questionnaire	Oral cavity	<i>Men only</i>			Centre, age, education, paan chewing, smoking	Looked at cessation of alcoholic beverage consumption and joint effects with paan chewing; former drinkers abstained ≥12 months	
					Abstainers	102	1.0 (reference)			
					Former drinkers	65	1.78 (0.97–3.28)			
					Current drinkers					
					<3 drinks/week	29	2.17 (1.00–4.69)			
					3–13 drinks/week	22	2.14 (0.89–5.19)			
					≥14 drinks/week	29	1.97 (0.85–4.57)			
					<i>p</i> for trend		0.01			

Table 2.3 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Znaor <i>et al.</i> (2003), Chennai, Trivandrum, India, 1993–99	1563 men from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	1711 male patients with non-tobacco-related cancers from same centres as cases and 1927 healthy male hospital visitors from Chennai only	Interviewer-administered questionnaire	Oral cavity (ICD9 140, 141, 143–5)	<i>Total alcohol; average amount of ethanol</i> ^a Never drinker <20 mL/day 20–50 mL/day >50 mL/day	780 213 256 308	1.0 (reference) 1.2 (1.0–1.5) 2.4 (1.9–3.1) 3.0 (2.3–3.8)	Age, centre, education, smoking	Looked at pharynx also ^a Reference was new drinkers
De Stefani <i>et al.</i> (2007), Montevideo, Uruguay, 1988–2000	335 men identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97%	1501 male hospital-based non-cancer controls; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; response rate, 97%	Interviewer-administered questionnaire in hospital	Oral cavity (excluding lip)	<i>Total alcohol</i> Never drinkers 1–60 mL 61–120 mL 121–240 mL ≥241 mL <i>p</i> for trend	34 47 91 86 77	1.0 (reference) 1.2 (0.8–2.0) 4.3 (2.7–6.8) 4.9 (3.1–7.9) 7.0 (4.2–11.5) <0.0001	Age, residence, urban/rural status, hospital, year of diagnosis, education, family history of cancer, occupation, vegetable and fruit consumption, maté intake, smoking	Looked at pharynx also; looked at type of alcoholic beverage and joint effects with smoking

CI, confidence interval; ICD, International Classification of Diseases

across different geographical regions and populations, which further supports the key role of alcoholic beverage consumption in oral and pharyngeal carcinogenesis.

(b) *Cancer of the pharynx (Table 2.4)*

Among nine case–control studies of cancer of the pharynx, three were population-based (Tuyns *et al.*, 1988; Nam *et al.*, 1992; Cheng *et al.*, 1999) and six were hospital-based (Franceschi *et al.*, 1990; Choi & Kahyo, 1991a; Maier *et al.*, 1994; Znaor *et al.*, 2003; De Stefani *et al.*, 2004, 2007). All studies adjusted for or were stratified by tobacco smoking. Results from all of the studies showed a strong association with alcoholic beverage consumption, except for one study of nasopharyngeal cancer in Taiwan, China (Cheng *et al.*, 1999).

Alcoholic beverage consumption was associated with an increase in risk for cancers of the oropharynx and hypopharynx across different geographical regions and populations and the point estimates of adjusted odds ratios ranged from 3.6 to 125.2. Furthermore, all studies but one (Cheng *et al.*, 1999) observed a strong dose–response trend between alcoholic beverage consumption and risk for oro- and hypopharyngeal cancer. A possible explanation for the lack of association in the study from Taiwan may be the categorization of exposure: the highest exposure group contained people who consumed ≥ 15 g (equivalent to just over one drink) per day, which may be too low a level to detect an association.

(c) *Cancer of the oral cavity and pharynx combined (Table 2.5)*

A total of 19 studies of cancer of the oral cavity and pharyngeal cancer combined were identified (Blot *et al.*, 1988; Merletti *et al.*, 1989; Barra *et al.*, 1990, 1991; Maier *et al.*, 1992a; Marshall *et al.*, 1992; Mashberg *et al.*, 1993; Kabat *et al.*, 1994; Sanderson *et al.*, 1997; Hayes *et al.*, 1999; Franceschi *et al.*, 2000; Garrote *et al.*, 2001; Schwartz *et al.*, 2001; Altieri *et al.*, 2004; Castellsagué *et al.*, 2004; Llewellyn *et al.*, 2004a,b; Rodriguez *et al.*, 2004; Shiu & Chen, 2004). Six were population-based (Blot *et al.*, 1988; Merletti *et al.*, 1989; Marshall *et al.*, 1992; Sanderson *et al.*, 1997; Hayes *et al.*, 1999; Schwartz *et al.*, 2001) and the rest were hospital-based. Tobacco smoking was considered as a potential confounding factor in almost all of the studies. Seventeen studies reported a strong association, with a dose–response trend, between alcoholic beverage consumption and cancers of the oral cavity and pharynx and two reported an increased risk, but the 95% CIs included a null value (Merletti *et al.*, 1989; Llewellyn *et al.*, 2004b).

An increase in risk for cancers of the oral cavity and pharynx has been observed in most studies across different geographical regions and populations and the point estimates of adjusted odds ratios ranged from 4.1 to 8.8 for heavy consumption of alcoholic beverages when adjusted for tobacco smoking and other confounding factors. The lack of significant associations in two studies (Merletti *et al.*, 1989; Llewellyn *et al.*, 2004b) may be explained by small sample size (86 male and 36 female cases in the former and

Table 2.4 Case-control studies of pharyngeal cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR (95% CI)	Adjustment factors	Comments
Tuyns <i>et al.</i> (1988), France, Italy, Spain, Switzerland, 1980–83	281 men from Calvados (France), Turin and Varese (Italy), Navarra and Zaragoza (Spain), Geneva (Switzerland); histologically confirmed; response rate, 75% (Spain, Italy), 92% (Geneva)	3057 men stratified by age from census lists, electoral lists, or population registries; response rate, 75% (64% in Geneva, 56% in Turin)	Interviewer-administered questionnaire	Hypopharynx (ICD9 148.0, 148.1, 148.3, 149.8)	<i>Total alcohol</i>			Age, place, age/place interaction, cigarettes/day	Looked at joint effects with smoking
					0–20 g/day	NG	1.0 (reference)		
					21–40 g/day	NG	1.6 (0.7–3.4)		
					41–80 g/day	NG	3.2 (1.6–6.2)		
					81–120 g/day	NG	5.6 (2.8–11.2)		
					≥121 g/day	NG	12.5 (6.3–25.0)		
Franceschi <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–89	134 men, under age 75 years; histologically confirmed; response rate, 98% overall	1272 male hospital-based non-cancer patients from same hospitals as cases matched on age, area of residence; excluded patients with alcohol- and tobacco-related conditions; response rate, 97%	Interviewer-administered questionnaire	Pharynx, hypopharynx/larynx junction included (ICD9 146, 148, 161.1)	<i>Total alcohol</i>			Age, area of residence, education, occupation, smoking habits	Also looked at oral cancers; looked at type of alcoholic beverage and joint effects with smoking
					≤19 drinks/week	13	1.0 (reference)		
					20–34 drinks/week	14	0.9 (0.4–2.0)		
					35–59 drinks/week	34	1.5 (0.8–3.1)		
					≥60 drinks/week	73	3.6 (1.8–7.2)		
	<i>p</i> for trend		0.01						

Table 2.4 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR (95% CI)	Adjustment factors	Comments
Choi & Kahyo (1991a), Seoul, Republic of Korea, 1986–89	152 cases (133 men, 19 women) from the Korea Cancer Centre Hospital; cytological and/or histopathological confirmation	456 (399 men, 57 women) hospital-based non-cancer patients from same hospital matched (3 controls per case) on age, sex, admission date; excluded patients with alcohol- and tobacco-related conditions	Interviewer-administered questionnaire	Pharynx (ICDO 146–149)	Men only <i>Total alcohol^a</i> Non-drinker <1 hop/day 1–2 hops/day 2–4 hops/day >4 hops/day	16 20 44 40 13	1.0 (reference) 1.2 (0.6–2.5) 2.2 (1.1–4.2) 4.1 (2.1–7.9) 11.2 (4.2–29.8)	Smoking	Looked at oral cavity also; ^a 1 hop = 90 mL of soju [generally 20% alcohol, 14 g ethanol]; soju is most frequent alcoholic beverage type

Table 2.4 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR (95% CI)	Adjustment factors	Comments					
Nam <i>et al.</i> (1992), USA, 1986	204 (141 men, 63 women) whites from the National Mortality Followback Survey who died of NPC, age <65 years; overall response rate, 89% for whole study population	408 (282 men, 126 women) randomly selected whites from the same survey matched on age, sex; died from causes unrelated to smoking or alcoholic beverage use	Questionnaire from next of kin	Nasopharynx	<i>Total alcohol</i>									
					0–3 drinks/week	107	1.0 (reference)	Smoking, sex	Looked at joint effects with smoking					
					4–23 drinks/week	40	0.9 (0.5–1.4)	None						
					≥24 drinks/week	57	1.8 (1.1–3.1)	None						
					Men only									
					<i>Total alcohol</i>									
					0–3 drinks/week	64	1.0 (reference)							
					4–23 drinks/week	32	1.1 (0.6–1.8)							
					≥24 drinks/week	45	1.9 (1.1–3.2)							
					<i>p</i> for trend		0.007							
					Women only									
					<i>Total alcohol</i>									
0–3 drinks/week	43	1.0 (reference)												
4–23 drinks/week	8	1.2 (0.4–3.1)												
≥24 drinks/week	12	7.3 (2.1–32.5)												
<i>p</i> for trend		<0.001												

Table 2.4 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR (95% CI)	Adjustment factors	Comments
Maier <i>et al.</i> (1994), Heidelberg, Germany, 1990–91	105 men from the Otorhinolaryngology-Head and Neck Surgery Department of the University of Heidelberg; histologically confirmed	420 male outpatients without known cancer from the same centre as cases matched (4:1 controls:cases) on age, residential area	Interviewer-administered standardized questionnaire	Oropharynx, hypopharynx	<i>Total alcohol</i> <25 g/day 25–50 g/day 50–75 g/day 75–100 g/day >100 g/day <i>p</i> for trend	11 17 22 20 35	1.0 (reference) 3.5 (1.4–8.6) 12.9 (4.7–35.6) 54.7 (13.5–221.0) 125.2 (28.4–551.6) 0.0001	Tobacco smoking	Beer preferred alcoholic beverage in this area
Cheng <i>et al.</i> (1999), Taipei, Taiwan, China, 1991–94	375 cases (260 men, 115 women) from two teaching hospitals in Taipei; histologically confirmed; response rate, 99%	327 (223 men, 104 women) population controls with no history of NPC using the National Household Registration System individually matched on age, sex, residence; response rate, 88%	Interviewer-administered structured questionnaire	Nasopharynx	<i>Total alcohol (in g ethanol/day)</i> 0 <15 ≥15 <i>p</i> for trend	270 47 57	1.0 (reference) 0.7 (0.5–1.2) 1.1 (0.7–1.7) 0.9	Age, sex, race, education, family history of NPC, smoking	
Znaor <i>et al.</i> (2003), Chennai, Trivandrum, India, 1993–99	636 men from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	1711 male patients with non-tobacco-related cancers from same centres as cases and 1927 healthy male hospital visitors from Chennai only	Interviewer-administered questionnaire	Pharynx (ICD9 146, 148, 149)	<i>Total alcohol, average amount of ethanol^a</i> Never drinker <20 mL/day 20–50 mL/day >50 mL/day	297 70 106 162	1.0 (reference) 1.1 (0.8–1.5) 2.3 (1.7–3.2) 3.6 (2.7–4.8)	Age, centre, education, smoking	Looked at oral cavity also ^a Reference category was new drinkers

Table 2.4 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2004), Montevideo, Uruguay, 1997–2003	85 men identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97.5%	640 hospital-based men from the same hospitals as cases; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; frequency matched (2:1 controls:cases) on age, residence; response rate, 97%	Interviewer-administered questionnaire	Hypopharynx	<i>Total alcohol (in mL ethanol/day)</i>			Age, residence, urban/rural status, education, smoking, body mass index	Looked at cessation of alcoholic beverages, type of alcoholic beverages and joint effects with smoking
					Never drinkers	191	1.0 (reference)		
					1–60	175	2.3 (0.7–8.1)		
					61–120	116	7.6 (2.3–24.4)		
					121–240	88	5.6 (1.7–18.6)		
≥241	70	12.8 (4.0–41.2)							
		<i>p</i> for trend		<0.0001					
De Stefani <i>et al.</i> (2007), Montevideo, Uruguay, 1988–2000	441 men identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97%	1501 male hospital-based non-cancer controls; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; response rate, 97%	Interviewer-administered questionnaire in hospital	Pharynx (excluding nasopharynx)	<i>Total alcohol (in mL ethanol/day)</i>			Age, residence, urban/rural status, hospital, year of diagnosis, education, family history of cancer, occupation, vegetable and fruit consumption, maté intake, smoking	Looked at oral cavity also; looked at type of alcoholic beverages and joint effects with smoking
					Never drinkers	33	1.0 (reference)		
					1–60	53	1.4 (0.9–2.2)		
					61–120	97	4.4 (2.8–7.0)		
					121–240	136	7.9 (5.0–12.3)		
≥241	122	11.7 (7.2–18.9)							
		<i>p</i> for trend		<0.0001					

CI, confidence interval; ICD, International Classification of Diseases; NPC, nasopharyngeal carcinoma

Table 2.5 Case-control studies of cancers of the oral cavity and pharynx combined and alcoholic beverage consumption

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Blot <i>et al.</i> (1988), USA, 1984–85	1114 (762 men, 352 women) cases; identified from the population-based registries covering metropolitan Atlanta (GA), Los Angeles, Santa Clara, San Mateo counties (CA), New Jersey; aged 18–79 years; pathologically confirmed; response rate, 75%; 1268 population controls	Interviewer-administered standardized questionnaire	Oral cavity, pharynx (ICD9 141, 143–146, 148, 149), excluding salivary gland, nasopharynx	Men				Age, race, study location, respondent status (self versus proxy), tobacco smoking, other two types of alcoholic beverages
				<i>Hard liquor</i>	<1 drink/week	40	1 (reference)	
					1–4 drinks/week	71	1.0 (0.7–1.3)	
					5–14 drinks/week	99	1.3 (0.9–1.8)	
					15–29 drinks/week	154	2.6 (1.7–3.9)	
					≥30 drinks/week	389	5.5 (3.4–9.1)	
				<i>Beer</i>	<1 drink/week	146	1 (reference)	
					1–4 drinks/week	130	1.2 (0.8–1.7)	
					5–14 drinks/week	141	1.7 (1.2–2.4)	
					15–29 drinks/week	134	3.4 (2.7–5.1)	
					≥30 drinks/week	195	4.7 (3.0–7.3)	
				<i>Wine</i>	<1 drink/week	497	1 (reference)	
					1–4 drinks/week	114	0.7 (0.5–1.0)	
					5–14 drinks/week	70	0.7 (0.4–1.0)	
	15–29 drinks/week	31	0.9 (0.5–1.8)					
	≥30 drinks/week	35	2.5 (0.9–6.5)					

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Blot <i>et al.</i> (1988) (contd)	1268 population controls from random-digit dialling; aged 18–64 years, frequency-matched on age, sex, race (black, white); response rate, 79% (under 65 years) and 76% (≥ 65 years)			Women				
				<i>Hard liquor</i>			1 (reference)	
				<1 drink/week	135	1.3 (0.9–2.1)		
				1–4 drinks/week	78	1.5 (0.9–2.5)		
				5–14 drinks/week	65	4.9 (1.6–14.3)		
				15–29 drinks/week	32	7.8 (2.1–29.2)		
				≥30 drinks/week		1 (reference)		
				<i>Beer</i>		2.2 (1.4–3.6)		
				<1 drink/week	180	2.9 (1.5–5.6)		
				1–4 drinks/week	73	2.3(0.9–6.5)		
				5–14 drinks/week	48	18.0 (2.1–159)		
				15–29 drinks/week	24	1 (reference)		
				≥30 drinks/week	27	0.6 (0.4–1.0)		
				<i>Wine</i>		0.8 (0.4–1.4)		
				<1 drink/week	230	0.5 (0.1–2.3)		
				1–4 drinks/week	60	1.6 (0.2–13.6)		
5–14 drinks/week	41							
15–29 drinks/week	1							
≥30 drinks/week	7							

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments	
Merletti <i>et al.</i> (1989) Torino, Italy, 1982–84	122 cases (86 men, 36 women); histologically confirmed; response rate, 85% 606 (385 men, 221 women) population-based controls, randomly selected from files of residents, stratified by age, sex; response rate, 55%	Interviewer-administered standardized questionnaire	Oral cavity, oropharynx (ICD9 140.3–140.5, 141, 143–146)	Total alcohol				Age, education, area of birth, tobacco habits	Looked at type of alcoholic beverage and joint effect of smoking
				<i>Men</i>					
				1–20 g/day	8	1.0 (reference)			
				21–40 g/day	9	0.7 (0.2–2.6)			
				41–80 g/day	29	1.3 (0.4–3.8)			
				81–120 g/day	14	0.6 (0.2–2.1)			
				>120 g/day	22	2.1 (0.6–6.8)			
				<i>Women</i>					
1–20 g/day	6	1.0 (reference)							
21–40 g/day	13	3.0 (0.9–10.5)							
>40 g/day	12	3.4 (0.9–12.9)							
Barra <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–90	305 men from hospitals in Pordenone and Milan; median age, 58 years; histologically confirmed; refusal rate, 2% 1621 men, hospital-based non-cancer patients; median age, 57 years; matched by area of residence, age; excluded patients with alcohol- and tobacco-related conditions; refusal rate, 3%	Interviewer-administered questionnaire in hospital	Oral cavity, pharynx	<i>Total alcohol</i>			Age, area of residence, occupation, tobacco smoking	Includes study population from Franceschi <i>et al.</i> (1990); looked at types of alcoholic beverage	
				≤20 drinks/week	17	1 (reference)			
				21–55 drinks/week	5	0.8 (0.3–2.3)			
				56–83 drinks/week	12	1.8 (0.8–4.4)			
≥84 drinks/week	41	4.1 (2.0–8.2)							

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Barra <i>et al.</i> (1991), Pordenone, Italy, 1985–90	272 (236 men, 36 women) cases from hospitals in Pordenone; median age, 60 years; histologically confirmed; refusal rate, 3% 1884 (1122 men, 762 women) non-cancer, hospital-based patients; median age, 58 years; matched by area of residence, age; excluded patients with alcohol- and tobacco-related conditions; refusal rate, 3%	Interviewer-administered questionnaire in hospital	Oral cavity, pharynx	<i>Total alcohol</i> ≤20 drinks/week 21–34 drinks/week 35–55 drinks/week 56–83 drinks/week ≥84 drinks/week <i>p</i> for trend	24 28 21 31 83 106	Non-cancer controls 1.0 (reference) 2.2 (1.2–4.0) 2.4 (1.2–4.7) 6.6 (3.5–12.5) 11.4 (6.0–21.4) ≤ 0.01	Age, sex, education, occupation, tobacco	Includes study population from Barra <i>et al.</i> (1990) study; also compared results with cancer control group with similar results; looked at types of alcoholic beverage

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Maier <i>et al.</i> (1992a), Giessen & Heidelberg, Germany	200 male patients selected from ENT departments from University of Heidelberg and Giessen with squamous cells cancer of the head and neck; 800 male subjects without known cancer served as controls selected from out patients clinics	Interviewer-administered questionnaire	Head and neck	Total alcohol <25 g/day 25–50 g/day 50–75g/day 75–100 g/day >100 g/day		1.0 (reference) 1.7 (1.0–2.7) 6.7 (3.9–11.3) 16.2 (7.1–36.8) 21.4 (11.2–40.6)	Tobacco	Females excluded due to low number of cases

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Marshall <i>et al.</i> (1992), New York, USA, 1975–83	290 (201 men, 89 women) identified from pathology records of 20 major hospitals in Erie, Niagara, Monroe (New York); aged 45 years or younger; pathologically confirmed; response rate of those contacted, 60%	Interviewer-administered standardized questionnaire	Oral cavity, pharynx	Quantity–frequency–duration derived quintiles		1 (reference) 2.4 (1.1–5.2) 2.7 (1.2–6.1) 3.4 (1.6–7.4) 14.8 (6.8–32.3) <0.0001		Black cases excluded from analysis
	290 (201 men, 89 women) population-based individually matched on age, sex, neighborhood; response rate, 41%			5 <i>p</i> for trend				

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Mashberg <i>et al.</i> (1993) New Jersey, USA, 1972–83	359 white and black male veterans with invasive cancer and in-situ carcinoma identified in the Department of Veterans Affairs Medical Center; median age, 57 years; histologically confirmed 2280 white or black male patients from the same centre as cases of the same age range as cases (37–80 years); median age, 58 years; excluding patients with cancer or dysplasia of the pharynx, larynx, lung, oesophagus	Interviewer-administered standardized questionnaire	Oral cavity, oropharynx	<i>Total alcohol (in whiskey equiv./day)</i> ^a			Age, race, tobacco smoking	Looked at type of alcoholic beverage and joint effects with smoking; 1 whiskey equivalent = 10.2 g alcohol
				Minimal drinking	17	1 (reference)		
				2–5 per day	37	2.6 (1.4–4.7)		
				6–10 per day	91	6.4 (3.7–11.0)		
				11–21 per day	112	7.9 (4.6–13.4)		
				≥22 per day	98	7.1 (4.1–12.2)		
Former drinker (abstained ≥2 years)	4	1.9 (0.6–5.7)						

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments	
Kabat <i>et al.</i> (1994), USA, 1977–90	1560 (1097 men, 463 women) enrolled in 28 hospitals in eight US cities	Interviewer-administered questionnaire	Oral cavity, pharynx (excluding nasopharynx)	<i>Total alcohol (whiskey equiv.)</i>		<i>Men</i>	Age, education, smoking, race, time period, type of hospital	Looked at type of alcoholic beverage and joint effects of smoking; 1 oz whiskey equivalent = 10.2 g alcohol	
				Non-drinker	50				1
	2948 (2075 men, 873 women) hospital-based; matched on age, sex, race, hospital, date of interview			Occasional	142	1.4 (0.9–2.0)			
				1–2.9 oz/day	246	2.9 (2.0–4.2)			
				4–6.9 oz/day	169	4.7 (3.2–7.1)			
				≥7 oz/day	466	7.3 (5.1–10.7)			
Kabat <i>et al.</i> (1994) (contd)				<i>Women</i>					
				Non-drinker	123				1 (reference)
				Occasional	130				1.2 (0.9–1.6)
				1–3.9 oz/day	108				1.8 (1.3–2.6)
				4–6.9 oz/day	98				4.8 (2.9–7.8)
				≥7 oz/day	–	–			
Maier <i>et al.</i> (1994), Heidelberg, Giessen, Germany, 1987–88	200 men from the ENT departments of the Universities of Heidelberg and Giessen; histologically confirmed	Interviewer-administered questionnaire	Oral cavity, pharynx, larynx	<i>Total alcohol</i>			Tobacco smoking	Beer preferred alcoholic beverage in the area; looked at joint effect of smoking	
	800 male outpatients without known cancer; matched on age, residential area (4:1 controls:cases)			<25 g/day		1 (reference)			
				25–50 g/day		1.7 (1.0–2.7)			
				50–75 g/day		6.7 (3.9–11.3)			
				75–100 g/day		16.2 (7.1–36.8)			
				>100 g/day		21.4 (11.2–40.6)			

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Sanderson <i>et al.</i> (1997) Netherlands, 1980–90	303 women aged ≥ 40 years from the University Hospital's Head Cancer Centre 1779 women from a national survey by National Central Bureau of Statistics; matched on age	Hospital records (cases) and national survey (controls)	Oral cavity, oropharynx (excluding salivary glands and lip)	<i>Total alcohol</i>			Age	Looked at joint effect of smoking
				Non-drinker	153	1 (reference)		
				1–5 units/day	104	3.5 (2.5–4.8)		
				>5 units/day	46	20.8 (11.4–37.8)		
Hayes <i>et al.</i> (1999), Puerto Rico, 1992–95	342 (286 men, 56 women) identified through pathology laboratories and Central Cancer Registry; aged 21–79 years; histologically confirmed; response rate, 70% 521 (417 men, 104 women) population-based; frequency-matched by age, gender; response rate, 83%	Interviewer-administered questionnaire	Oral cavity, pharynx (ICD9 141–143–146, 148, 149)	<i>Total alcohol^a</i>			Age, tobacco use	Looked at cessation of alcoholic beverage consumption and joint effect of smoking
				Non-drinker	9	1 (reference)		
				1–7 drinks/week	19	0.8 (0.3–2.1)		
				8–21 drinks/week	28	1.4 (0.6–3.4)		
				22–42 drinks/week	49	3.3 (1.4–8.0)		
				>42 drinks/week	164	7.7 (3.3–17.9)		
				<i>p</i> for trend		<0.0001		
				<i>Women</i>				
				Non-drinker	26	1 (reference)		
				1–7 drinks/week	13	0.8 (0.3–2.1)		
8–21 drinks/week	1	0.9 (0.0–17.0)						
22–42 drinks/week	12	9.1 (0.9–94.2)						
>42 drinks/week	–	– (–)						
<i>p</i> for trend		0.02						

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (2000), Italy, Switzerland, 1992–97	754 (638 men, 116 women) from major teaching and general hospitals in Pordenone, Rome, Latina (Italy) and Vaud (Switzerland); aged 22–77 years; histologically confirmed; response rate, 95% 1775 (1254 men, 521 women) hospital-based non-cancer from the same network of hospitals as cases; excluded tobacco- and alcohol-related conditions; frequency-matched (5:1 for women, 2:1 for men controls:cases) on age, sex, area of residence; response rate, 95%	Interviewer-administered questionnaire	Oral cavity, pharynx (excluding lip, salivary glands, nasopharynx)	<i>Total alcohol</i>			Age, sex, study centre, education, interviewer, tobacco smoking, drinking status	Study population from Franceschi <i>et al.</i> (1999); looked at alcoholic beverage consumption cessation
				Current drinkers				
				Never	32	1 (reference)		
				1–20 drinks/week	82	0.7 (0.4–1.2)		
				21–62 drinks/week	271	2.6 (1.6–4.2)		
63–90 drinks/week	145	8.9 (5.0–15.9)						
≥91 drinks/week	98	16.7 (8.6–32.7)						
			χ^2 for trend			160.5 $p < 0.001$		

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Garrote <i>et al.</i> (2001), Havana, Cuba, 1996–99	200 (143 men, 57 women) from the Instituto Nacional de Oncología y Radiobiología of Havana; age, 64 years; response rate, 88%. 200 (136 men, 64 women) hospital-based controls admitted to same hospital and three other major hospitals in Havana; excluded patients with alcohol- and tobacco-related conditions; frequency-matched on age, sex; median age, 62 years; response rate, 79%	Interviewer (dentist)-administered questionnaire	Oral cavity, oropharynx	<i>Total alcohol</i>			Age, sex, area of residence, education, tobacco smoking	Looked at cessation, type of alcoholic beverage and joint effect of smoking
				Abstainers	83	1 (reference)		
				Former drinkers (abstained ≥ 12 months)	36	1.04 (0.5–2.1)		
				<i>Current drinkers</i>				
				<7 drinks/week	15	1.1 (0.5–2.6)		
				7–20 drinks/week	25	1.6 (0.7–3.7)		
21–69 drinks/week	21	2.2 (0.9–5.5)						
≥ 70 drinks/week	20	5.7 (1.8–18.5)						
χ^2 for trend		8.75 $p < 0.01$						

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Schwartz <i>et al.</i> (2001), Washington, USA, 1985–95	333 (237 men, 96 women) in-situ and invasive cancers ascertained through the population-based Cancer Surveillance System (participant of SEER); aged 18–65 years from two original studies; response rates, 54% and 63%. 541 (387 men, 154 women) population-based; frequency-matched on age, sex; response rates, 63% and 61%	Interviewer-administered structured questionnaire	Oral cavity, oropharynx (excluding lip)	<i>Total alcohol</i> <1 drink/week 1–7 drinks/week 8–14 drinks/week 15–42 drinks/week ≥43 drinks/week		1 (reference) 1.0 (0.6–1.5) 1.7 (1.0–2.9) 2.8 (1.7–4.8) 4.7 (2.4–9.4)	Age, sex, race, tobacco smoking	Looked at joint effect of smoking and <i>ADH3</i>

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Altieri <i>et al.</i> (2004), Italy, Switzerland, 1992–97	749 (634 men, 115 women) from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland) admitted to major teaching and general hospitals in area under surveillance; aged 22–77 years; histologically confirmed 1772 (1252 men, 520 women) hospital-based from the same network of hospitals as cases; aged 20–78 years; excluded patients with alcohol- and tobacco-related conditions	Interview-administered structured questionnaire	Oral cavity, pharynx	<i>Total alcohol</i>				
				Non-drinkers	33	–		
				1–2 drinks/day	93	1 (reference)		
				3–4 drinks/day	95	2.1 (1.5–2.9)		
				5–7 drinks/day	132	5.0 (3.5–7.1)		
				8–11 drinks/day	199	12.2 (8.4–17.6)		
≥12 drinks/day	196	21.1 (14.0–31.8)						
				χ^2 for trend		272.07		
						$p < 0.0001$		

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Castellsagué <i>et al.</i> (2004), Spain, 1996–99	375 (304 men, 71 women) identified from hospitals in Granada, Sevilla, Barcelona; mean age, 60 years; histologically confirmed; response rate, 76.5% 375 (304 men, 71 women) non-cancer hospital-based from same hospitals as cases; frequency-matched on age, sex; mean age, 60 years; excluded patients with alcohol- and tobacco-related diagnoses; response rate, 91%	Interviewer-administered standardized questionnaire in hospital	Oral cavity, oropharynx (ICDO C1-C10)	<i>Average no. of drinks/day</i>			Age group, sex, education, tobacco smoking, centre	Looked at type of alcoholic beverage and joint effect of smoking
				Never drinker	35	1 (reference)		
				1	59	2.0 (1.1–3.8)		
				2	27	3.7 (1.6–8.6)		
				3–4	49	6.2 (2.8–13.7)		
				5–6	55	10.6 (4.6–24.5)		
				7–10	68	10.3 (4.6–23.2)		
				≥11	82	13.7 (6.0–31.0)		
<i>p</i> for trend		<0.0001						

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Llewellyn <i>et al.</i> (2004a), United Kingdom, 1999–2001	53 (28 men, 25 women) from 14 participating hospitals in the Southeast of England; aged ≤ 45 years; response rate, 80%	Interviewer-administered standardized questionnaire and self-completed questionnaire	Oral cavity, oropharynx (ICD-10 C00–C06, C0, C10)	Total alcohol			Social class, race, ever smoking (matching variables: age, sex, area of residence)	ªRecommended levels: for men, ≤21 units/ week; for women, ≤14 units/ week
				<i>Men</i>	Within recommended levelsª	1 (reference)		
				<i>Women</i>	Over recommended levels	8.1 (1.6–40.1)		
Llewellyn <i>et al.</i> (2004b), United Kingdom, 1990–97	116 (65 men, 51 women) identified by the Thames Cancer Registry; aged ≤ 45 years; response rate, 59%	Self-completed questionnaire	Oral cavity, oropharynx (ICD-10 C00–C06, C0, C10)	Total alcohol			Social class, race, ever smoking (matching variables: age, sex, area of residence)	ªRecommended levels : for men, ≤21 units/ week; for women, ≤14 units/ week
				<i>Men</i>	Within recommended levelsª	1 (reference)		
				<i>Women</i>	Over recommended levels	1.6 (0.8–3.1)		
	207 (112 men, 95 women) non-cancer patients; matched (2:1 controls:cases when feasible) on age, sex, area of residence			<i>Men</i>	Within recommended levelsª	1 (reference)		
				<i>Women</i>	Over recommended levels	1.6 (0.6–4.2)		

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Rodriguez <i>et al.</i> (2004), Italy, Switzerland, 1984–93, 1992–97	137 (113 men, 24 women) from Milan and Pordenone, Italy (1984–93) and Vaud, Switzerland (1992–97), under age 46 years; histologically confirmed; response rate, 95%.	Interviewer-administered questionnaire	Oral cavity, pharynx	<i>Total alcohol</i> Non-drinkers <3 drinks/day 3–<6 drinks/day 6–<10 drinks/day ≥10 drinks/day χ^2 for trend	13 20 19 37 46	1 (reference) 0.7 (0.3–1.8) 1.0 (0.4–2.8) 3.7 (1.2–11.1) 4.9 (1.6–15.1) 17.5 p <0.0001	Age, sex, study centre, education, marital status, body mass index, tobacco smoking, coffee consumption	Study populations from Franceschi <i>et al.</i> (1990, 2000)
	298 (226 men, 72 women) non-cancer hospital-based; matched 2:1 (control:case) for men and 3:1 for women on age, sex, study centre; below age 46 years; excluded patients with alcohol- and tobacco-related conditions; response rate, 95%							

Table 2.5 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment factors	Comments
Shiu & Chen (2004), Taipei, Taiwan, 1988–98	74 (71 men, 3 women) randomly selected from 1688 cancers identified at a medical centre; response rate, 74% 187 patients with periodontal disease free of leukoplakia and oral cancer, randomly selected from 25 882 patients; response rate, 94%	Interviewer-administered questionnaire	Oral cavity, pharynx (140–149, except 142 and 147)	Total alcohol			Tobacco smoking, betel-quid chewing	
				<i>Leukoplakia versus normal</i>				
				No	1 (reference)			
				Yes	0.76 (0.4–1.4)			
				<i>Oral cancer versus leukoplakia</i>				
				No	1 (reference)			
				Yes	2.37 (1.5–3.8)			

ADH3, alcohol dehydrogenase 3 gene; CI, confidence interval; ICD, International Classification of Diseases; SEER, Surveillance, Epidemiology and End Result

65 male and 51 female cases in the latter), which limits the power to detect an association, as well as the inclusion of light drinkers in the baseline comparison group (1–20 g per day in the former and within the recommended level in the latter).

2.2.3 *Types of alcoholic beverage (Table 2.6)*

In a study not described previously, Schildt *et al.* (1998) investigated the effects of snuff, smoking and alcoholic beverage consumption on the risk for cancer of the oral cavity. Among 354 histologically confirmed cases reported to the Cancer Registry from Norrbotten, Vasterbotten, Jamtland and Vasternorrland, Sweden, between 1980 and 1989 and 354 individually matched population controls, beer and liquor were found to be the types of alcoholic beverage associated with a higher risk (odds ratio for beer, 1.5; 95% CI, 0.7–3.2; odds ratio for liquor, 1.5; 95% CI, 0.9–2.3) in a model that contained snuff, smoking and the other types of alcohol. Self-completed questionnaires were completed by proxies for 60% of the participants.

Assessment of risk associated with different types of alcoholic beverage is a difficult task; drinkers rarely consume only one type of alcoholic beverage, and isolating the effects of a single type in the presence of the other types is not easy to accomplish. Furthermore, heterogeneity of effects across different populations further complicates the interpretation of results. Overall, among studies in the USA, the ranking from highest to lowest risk by alcoholic beverage type is beer, hard liquor and wine (Blot *et al.*, 1988; Mashberg *et al.*, 1993; Day *et al.*, 1994b; Kabat *et al.*, 1994). Among the Italian studies, the highest risk was associated with wine consumption (Franceschi *et al.*, 1990). In Latin America, hard liquor was associated with the highest risk among Cuban (Garrote *et al.*, 2001) and Brazilian populations (Schlecht *et al.*, 2001), and wine was associated with the highest risk among Uruguayans (De Stefani *et al.*, 2004). In several studies, the other types of alcoholic beverage were not controlled for in the analyses which may distort the association under study. Generally, the types of alcoholic beverage that are the largest contributors to alcoholic beverage consumption are usually associated with the greatest increases in risk.

2.2.4 *Joint effects (Table 2.7)*

The joint effects of alcoholic beverage consumption and tobacco smoking on cancers of the oral cavity and pharynx have been assessed extensively. The studies varied in their methods and in the approaches used to assess effect modification, which ranged from descriptive to formal estimation of interaction in multivariate models.

For cancers of the oral cavity and pharynx, the evidence comes almost entirely from case–control studies carried out in Asia, Australia, Europe and the USA. Two prospective cohort studies have reported joint effects of alcoholic beverage consumption and tobacco smoking including the European Prospective Investigation into Cancer and Nutrition (EPIC) study (Boeing, 2002) and a cohort study of Japanese men (Chyou

Table 2.6 Consumption of different types of alcoholic beverage and incidence of cancers of the oral cavity and pharynx

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Blot <i>et al.</i> (1988), USA, 1984–85	1114 (762 men, 352 women) cases; identified from the population-based registries covering metropolitan Atlanta (GA), Los Angeles, Santa Clara, San Mateo counties (CA), New Jersey; aged 18–79 years; pathologically confirmed; response rate, 75%; 1268 population controls	Interviewer-administered standardized questionnaire	Oral cavity, pharynx (ICD9 141, 143–146, 148, 149), excluding salivary gland and nasopharynx	Men				Age, race, study location, respondent status (self versus proxy), tobacco smoking, other two types of alcoholic beverage
				<i>Hard liquor</i>	<1 drink/week	40	1 (reference)	
				1–4 drinks/week	71	1.0 (0.7–1.3)		
				5–14 drinks/week	99	1.3 (0.9–1.8)		
				15–29 drinks/week	154	2.6 (1.7–3.9)		
				≥30 drinks/week	389	5.5 (3.4–9.1)		
				<i>Beer</i>	<1 drink/week	146	1 (reference)	
				1–4 drinks/week	130	1.2 (0.8–1.7)		
				5–14 drinks/week	141	1.7 (1.2–2.4)		
				15–29 drinks/week	134	3.4 (2.7–5.1)		
				≥30 drinks/week	195	4.7 (3.0–7.3)		
				<i>Wine</i>	<1 drink/week	497	1 (reference)	
				1–4 drinks/week	114	0.7 (0.5–1.0)		
				5–14 drinks/week	70	0.7 (0.4–1.0)		
15–29 drinks/week	31	0.9 (0.5–1.8)						
≥30 drinks/week	35	2.5 (0.9–6.5)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Blot <i>et al.</i> (1988) (contd)	Population controls from random-digit dialling; aged 18–64 years; frequency-matched on age, sex, race (black, white); response rate, 79% (under 65 years) and 76% (≥65 years)			Women					
				<i>Hard liquor</i>					
				<1 drink/week	135	1 (reference)			
				1–4 drinks/week	78	1.3 (0.9–2.1)			
				5–14 drinks/week	65	1.5 (0.9–2.5)			
				15–29 drinks/week	32	4.9 (1.6–14.3)			
				≥30 drinks/week	41	7.8 (2.1–29.2)			
				<i>Beer</i>					
				<1 drink/week	180	1 (reference)			
				1–4 drinks/week	73	2.2 (1.4–3.6)			
				5–14 drinks/week	48	2.9 (1.5–5.6)			
				15–29 drinks/week	24	2.3 (0.9–6.5)			
				≥30 drinks/week	27	18.0 (2.1–159)			
				<i>Wine</i>					
<1 drink/week	230	1 (reference)							
1–4 drinks/week	60	0.6 (0.4–1.0)							
5–14 drinks/week	41	0.8 (0.4–1.4)							
15–29 drinks/week	1	0.5 (0.1–2.3)							
≥30 drinks/week	7	1.6 (0.2–13.6)							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Merletti <i>et al.</i> (1989), Torino, Italy, 1982–84	122 (86 men, 36 women) cases; histologically confirmed; response rate, 85%. 606 (385 men, 221 women) population-based controls randomly selected from files of residents; stratified by age, sex; response rate, 55%	Interviewer-administered questionnaire	Oral cavity, oropharynx (ICD9 140.3–140.5, 141, 143–146)	Wine only		Men 1 (reference)	Age, education, area of birth, smoking habits, alcoholic beverage consumption	
				Beer		2.1 (1.1–4.0)		
				Aperitifs		1.4 (0.7–2.6)		
				Liquor		0.7 (0.4–1.4)		
				Wine only		Women 1 (reference)		
				Beer		6.1 (1.4–26.5)		
				Aperitifs		0.4 (0.1–1.7)		
				Liquor		0.8 (0.3–2.3)		

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Barra <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–90	305 cases (all men); median age, 58 years; histologically confirmed; refusal rate, 2% 1621 (all men) hospital-based controls; median age, 57 years; matched by area of residence, age; excluded patients with alcohol- and tobacco-related conditions; refusal rate, 3%	Interviewer-administered standardized questionnaire	Oral cavity, pharynx	<i>Wine only</i>			Age, area of residence, occupation, smoking and drinking habits	Includes study population from Franceschi <i>et al.</i> (1990); area of very high wine intake
				≤20 glasses wine/week	17	1		
				21–55 drinks/week	44	1.9 (1.0–3.4)		
				56–83 drinks/week	48	7.3 (3.8–14.1)		
				≥84 drinks/week	14	11.2 (3.8–33.1)		
				<i>Wine and beer</i>				
				≤20 glasses wine/wk	17	1		
				21–55 drinks/week	3	0.7 (0.2–2.5)		
				56–83 drinks/week	13	3.9 (1.6–9.6)		
				≥84 drinks/week	21	7.4 (3.2–17.3)		
				<i>Wine and spirits</i>				
				≤20 glasses wine/wk	17	1		
21–55 drinks/week	13	1.1 (0.5–2.4)						
56–83 drinks/week	34	3.5 (1.7–6.9)						
≥84 drinks/week	32	9.9 (4.3–22.7)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–89	157 male cases; below age 75 years; histologically confirmed; response rate, 98% 1272 hospital-based non-cancer male controls from same hospitals as cases, matched on age, area of residence; excluded patients with alcohol- and tobacco-related conditions; response rate, 97%	Interviewer-administered questionnaire	Oral cavity (ICD9 140, 141, 143–145)	<i>Wine (glasses/week)</i>	12		Age, area of residence, education, occupation, smoking habits	Study population from Barra <i>et al.</i> (1990); area of very high wine intake
				0–6	6	1		
				7–20	20	1.1 (0.5–2.3)		
				21–34	27	1.9 (0.9–3.7)		
				35–55	68	4.9 (2.6–9.5)		
				56–83	24	8.5 (3.6–20.2)		
				≥84		47.68 ($p < 0.01$)		
				χ^2 for trend				
				<i>Beer (glasses/week)</i>	111	1		
				0	20	1.0 (0.6–1.8)		
				1–13	26	0.8 (0.5–1.4)		
				≥14		0.30 (NS)		
				χ^2 for trend				
<i>Hard liquor (glasses/week)</i>	91	1						
0	19	0.7 (0.4–1.3)						
1–6	47	0.9 (0.6–1.3)						
≥7		0.66 (NS)						
χ^2 for trend								

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (1990) (contd)	134 male cases, below age 75 years; histologically confirmed; response rate, 98%		Pharynx (ICD9 146, 148, 161.1)	<i>Wine (glasses/week)</i>				
				0–6	9	1		
				7–20	6	1		
				21–34	16	0.7 (0.3–1.6)		
				35–55	28	1.9 (0.9–3.7)		
				56–83	45	3.1 (1.6–6.1)		
				≥84	30	10.9 (4.7–25.3)		
				χ^2 for trend		46.44 ($p < 0.01$)		
				<i>Beer (glasses/week)</i>				
				0	94	1		
				1–13	11	0.5 (0.3–1.0)		
				≥14	28	0.9 (0.5–1.5)		
				χ^2 for trend		0.47 (NS)		
				<i>Hard liquor (glasses/week)</i>				
				0	73	1		
1–6	10	0.4 (0.2–0.9)						
≥7	51	1.2 (0.8–1.8)						
χ^2 for trend		0.24 (NS)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Zheng <i>et al.</i> (1990), Beijing, China, 1988–89	404 (248 men, 156 women) cases diagnosed at seven participating hospitals in the Beijing area; histologically confirmed; response rate, 100%; 404 randomly selected non-cancer hospital-based controls; individually matched on age, sex, hospital; response rate, 100%.	Interviewer-administered questionnaire	Oral cavity (ICD9 141, 143-145)	<i>Type of alcohol</i> None Spirits only Beer/wine only Mixed	83 144 7 14	1 1.5 (0.9–2.3) 1.0 (0.3–3.1) 1.1 (0.5–2.8)	Age, sex, education, smoking	Most alcoholic beverages in study population were consumed in form of spirits.

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Barra <i>et al.</i> (1991), Pordenone, Italy, 1985–90	272 (236 men, 36 women) cases; median age, 60 years; histologically confirmed; refusal rate, 3% 1884 (1122 men, 762 women) non-cancer, hospital-based controls; median age, 58 years; matched by area of residence, age; excluded patients with alcohol- and tobacco-related conditions; refusal rate, 3%	Interviewer-administered standardized questionnaire	Oral cavity, pharynx	<i>Wine</i>			Age, sex, education, occupation, tobacco	Area of very high wine intake; no mention of controlling for other types of alcoholic beverage; includes participants from Barra <i>et al.</i> (1990)
				≤20 drinks/week	31	1		
				21–34 drinks/week	35	1.7 (1.0–3.1)		
				35–55 drinks/week	46	3.3 (1.8–5.9)		
				56–83 drinks/week	99	6.8 (3.9–12.1)		
				≥84 drinks/week	61	15.6 (8.2–29.7)		
				χ ² for trend		107.9 (<i>p</i> <0.01)		
				<i>Beer</i>				
				0 drink/week	168	1		
				1–13 drinks/week	32	0.7 (0.4–1.0)		
				≥14 drinks/week	72	1.4 (1.0–1.9)		
				χ ² for trend		1.5 (NS)		
<i>Spirits</i>								
0 drink/week	137	1						
1–13 drinks/week	69	0.8 (0.6–1.1)						
≥14 drinks/week	28	1.6 (1.1–2.3)						
χ ² for trend		1.1 (NS)						
Mashberg, <i>et al.</i> (1993), New Jersey, USA, 1972–83	359 white and black men with invasive cancer and in-situ carcinoma 2280 white or black male controls from the same centre as cases	Interviewer-administered questionnaire	Oral cavity, oropharynx	<i>Type of alcohol</i>			Age, race, tobacco smoking, average total alcoholic beverage consumption	
				Minimal drinking	17	1 (reference)		
				Mixed consumption	125	8.3 (4.7–14.8)		
				Whiskey only	32	3.8 (1.8–8.1)		
				Whiskey predominantly	77	5.3 (1.1–26.3)		
				Beer only	40	2.6 (1.3–5.2)		
Beer predominantly	61	8.3 (3.4–20.2)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Ng <i>et al.</i> (1993), USA	173 (100 men, 73 women) non smoking cases 613 (254 men, 359 women) nonsmoking hospital-based controls; matched on age, sex, date of interview		Oral cavity	<i>Men only</i>					
				<i>Beer</i>					
				Non-drinker	24	1 (reference)			
				<1 oz/day	24	1.9 (0.9–3.8)			
				1–2.9 oz/day	16	2.6 (1.1–5.9)			
				≥3 oz/day	9	5.1 (1.8–14.2)			
				χ^2 for trend		13.6 ($p < 0.001$)			
				<i>Wine</i>					
				Non-drinker	38	1 (reference)			
				<1 oz/day	28	0.9 (0.5–1.8)			
				1–2.9 oz/day	6	1.5 (0.5–4.9)			
				≥3 oz/day	0	1.6 (0.0–29.7)			
				χ^2 for trend		0.01 (NS)			
				<i>Liquor</i>					
Non-drinker	13	1 (reference)							
<1 oz/day	20	1.1 (0.6–2.2)							
1–2.9 oz/day	19	2.0 (0.7–5.3)							
≥3 oz/day	13	0.4 (0.0–7.1)							
χ^2 for trend		0.25 (NS)							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments		
Day <i>et al.</i> (1994a), USA, 1984–85	80 (56 men, 24 women) cases with second primary cancers from cohort of 1090 first primary cancers) 189 (132 men, 57 women) controls randomly selected from the cohort that were free of second primary cancer at the end of follow-up (1989) 921 cases and 900 controls who drank hard liquor	Interviewer-administered standardized questionnaire	Oral cavity, pharynx, oesophagus, larynx	<i>Beer</i>	<1 drink/week	14	1 (reference)	Age, stage of disease, lifetime smoking, other two types of alcoholic beverage	Nested case-control study of second primary cancers among cases of Blot <i>et al.</i> (1988) study	
				1–14 drinks/week	18	2.4 (0.8–7.1)				
				≥15 drinks/week	25	3.8 (1.2–12.0)				
				<i>Liquor</i>	<1 drink/week	16	1 (reference)			
				1–14 drinks/week	26	1.2 (0.5–2.9)				
				≥15 drinks/week	15	0.4 (0.1–1.1)				
				<i>Wine</i>	<1 drink/week	46	1 (reference)			
				≥1 drink/week	11	0.6 (0.2–1.3)				
				<i>Dark liquor</i>	<1 drink/week	138	1 (reference)			Age, sex, race, study location, education, smoking, intake of beer and wine
				1–4 drinks/week	120	1.1 (0.7–1.5)				
				5–14 drinks/week	142	1.2 (0.9–1.8)				
				15–29 drinks/week	111	2.7 (1.7–4.3)				
				≥30 drinks/week	139	4.6 (2.7–7.9)				
				<i>Light liquor</i>	<1 drink/week	50	1 (reference)			
1–4 drinks/week	37	1.4 (0.8–2.5)								
5–14 drinks/week	53	1.7 (0.9–3.0)								
15–29 drinks/week	42	5.6 (2.5–12.5)								
≥30 drinks/week	74	13.2 (5.2–33.5)								

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments		
Kabat <i>et al.</i> (1994), USA, 1977–90	1560 (1097 men, 463 women) cases enrolled in 28 hospitals in eight US cities 2948 (2075 men, 873 women) hospital-based controls; matched on age, sex, race, hospital, date of interview	Interviewer-administered standardized questionnaire	Oral cavity, pharynx (excluding nasopharynx)	<i>Whiskey equivalents/day</i>	Men		Age, education, smoking, race, time period, type of hospital	1 oz whiskey equivalent = 10.2 g of alcohol		
				<i>Beer</i>		Non-drinker			178	1 (reference)
						Occasional			254	1.5 (1.2–1.9)
						1–3.9 oz/day			240	2.5 (2.0–3.3)
						4–6.9 oz/day			136	4.1 (2.9–5.7)
						≥7 oz/day			279	5.3 (4.0–7.0)
				<i>Wine</i>		Non-drinker			646	1 (reference)
						Occasional			300	0.8 (0.7–1.0)
						1–3.9 oz/day			83	1.3 (0.9–1.8)
						4–6.9 oz/day			13	1.0 (0.5–2.3)
	≥7 oz/day	50	2.7 (1.6–4.6)							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Kabat <i>et al.</i> (1994) (contd)				<i>Hard liquor</i>				
				Non-drinker	303	1		
				Occasional	228	1.0 (0.8–1.3)		
				1–3.9 oz/day	214	1.7 (1.4–2.3)		
				4–6.9 oz/day	103	2.6 (1.8–3.7)		
				≥7 oz/day	235	3.1 (2.4–4.1)		
				Women				
				<i>Beer</i>				
				Non-drinker	290	1 (reference)		
				Occasional	90	1.3 (1.0–1.9)		
				1–3.9 oz/day	46	1.9 (1.1–3.1)		
				4–6.9 oz/day	37	3.6 (1.7–7.5)		
				<i>Wine</i>				
				Non-drinker	284	1 (reference)		
				Occasional	130	0.8 (0.6–1.1)		
				1–3.9 oz/day	31	0.8 (0.5–1.4)		
				4–6.9 oz/day	16	2.7 (1.0–7.7)		
				<i>Hard liquor</i>				
				Non-drinker	217	1 (reference)		
			Occasional	112	1.1 (0.8–1.5)			
			1–3.9 oz/day	64	1.9 (1.2–2.9)			
			4–6.9 oz/day	70	7.6 (3.9–14.8)			

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Chyou <i>et al.</i> (1995), Hawaii, USA, 1965-93	Cohort of 7995 men of Japanese ancestry, aged 45-68 years; recruitment from 1965-68, incidence follow-up until 1993; 1-2% lost to follow-up.	Interviewer-administered questionnaire	Oral cavity, pharynx, oesophagus, larynx (ICD8 140-150, 161)	<i>Beer</i>	Non-drinker	161	1 (reference)	Age, number of cigarettes/day, years smoked
				<49 oz/month	5	0.7 (0.3-1.8)		
				49-360 oz/month	17	1.9 (1.0-3.8)		
				≥361 oz/month	39	3.7 (2.0-6.7)		
				<i>p</i> for trend	<0.0001			
				<i>Wine</i>	Non-drinker	16	1 (reference)	
				≤4 oz/month	10	2.5 (1.2-5.6)		
				>4 oz/month	12	3.8 (1.8-8.2)		
				<i>p</i> for trend	0.0001			
				<i>Spirits</i>	Non-drinker	16	1 (reference)	
				≤4 oz/month	18	1.6 (0.8-3.2)		
				>4 oz/month	34	3.6 (2.0-6.6)		
<i>p</i> for trend	<0.0001							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Zheng <i>et al.</i> (1997), Beijing, China, 1988–89	111 (65 men, 46 women) cases diagnosed at seven participating hospitals in the Beijing area; aged 20–80 years; histologically confirmed; 111 randomly selected non-cancer hospital-based controls; individually matched on age, sex, hospital	Interviewer-administered questionnaire	Tongue	<i>Type of alcohol</i> None Spirits only Beer/wine	64 41 6	1 (reference) 1.2 (0.3–4.0) 1.2 (0.6–2.4)	Education, smoking (age and sex matched on)	Part of Zheng <i>et al.</i> (1990)

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Grønbaek <i>et al.</i> (1998), Denmark, 1975–94	Cohort of 15 117 men and 13 063 women from prospective population studies of the Copenhagen city heart study the Copenhagen male study, and the Copenhagen county centre of preventive medicine; aged 20–98 years; cases identified by linkage with the Danish Cancer registry; follow-up through to 1993 (mean follow-up, 13.5 years).	Self-administered questionnaire	Oral cavity, pharynx, oesophagus (ICD7 140.0–149.0, 150.0)	<i>Beer</i>	0 drink/week	1 (reference)	Age, sex, smoking, education, other types of alcoholic beverage	One drink = 12 g ethanol
				1–6 drinks/week	1.5 (0.9–2.5)			
					≥7 drinks/week	2.9 (1.8–4.8)		
					<i>Wine</i>	0 drinks/week		
				1–6 drinks/week	0.8 (0.5–1.1)			
					≥7 drinks/week	0.4 (0.2–0.8)		
				<i>Spirits</i>	0 drinks/week	1 (reference)		
1–6 drinks/week	0.7 (0.5–1.1)							
≥7 drinks/week	1.5 (1.2–1.9)							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Garrote <i>et al.</i> (2001), Havana, Cuba, 1996–99	200 (143 men, 57 women) cases identified in the Instituto Nacional de Oncología y Radiobiología of Havana; median age, 64 years; response rate, 88% 200 (136 men, 64 women) hospital-based controls admitted to same institute and three other major hospitals in Havana; excluded patients with alcohol- and tobacco-related conditions; frequency-matched on age, sex; median age, 62 years; response rate, 79%	Interviewer (dentist)-administered questionnaire	Oral cavity, oropharynx	<i>Hard liquor</i>			Age, sex, area of residence, education, smoking, other two types of alcoholic beverage	Looked at cessation, type of alcoholic beverage and joint effect of smoking
				0 drink/week	86	1 (reference)		
				1–7 drinks/week	19	1.3 (0.5–3.3)		
				8–20 drinks/week	25	1.0 (0.4–2.4)		
				21–69 drinks/week	15	4.2 (1.1–16.5)		
				≥70 drinks/week	15	5.1 (1.1–23.3)		
				χ^2 for trend		4.58 ($p < 0.05$)		
				<i>Beer</i>				
				0 drink/week	98	1 (reference)		
				<7 drinks/week	36	1.5 (0.6–3.9)		
				≥7 drinks/week	29	1.5 (0.5–4.6)		
				χ^2 for trend		0.85 ($p = 0.36$)		
<i>Wine</i>								
0 drink/week	129	1 (reference)						
<2 drinks/week	26	1.0 (0.4–2.4)						
≥2 drinks/week	9	0.8 (0.2–3.2)						
χ^2 for trend		0.15 ($p = 0.70$)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Schlecht <i>et al.</i> (2001), Brazil, 1986–89	784 cases selected from hospitals in Sao Paulo, Curitiba, Goiania; histopathologically confirmed 1578 hospital-based non-cancer controls; matched (2:1 controls:case) on age, sex, hospital area, admission period	Interviewer-administered questionnaire	Oral cavity, pharynx, larynx (ICD9 140–149, 161; excluding 142 and 147)	Lifetime consumption			Remaining alcohol consumption, tobacco smoking, income, education, race, beverage temperature, religion, wood stove use, spicy food (matched variables: age, sex, study location, admission period)	Same study population as Schlecht <i>et al.</i> (1999)
				Oral cavity				
				<i>Beer</i>				
				Non-drinker		1 (reference)		
				1–10 g		3.6 (1.9–7.0)		
				11–100 g		2.8 (1.4–5.6)		
				>100 g		3.7 (1.4–10.3)		
				Other than beer		3.1 (1.6–5.8)		
				<i>Wine</i>				
				Non-drinker		1 (reference)		
				1–10 g		3.4 (1.8–6.5)		
				11–100 g		4.3 (1.9–10.1)		
				>100 g		3.0 (1.2–7.3)		
				Other than wine		2.9 (1.6–5.5)		
				<i>Hard liquor</i>				
				Non-drinker		1 (reference)		
				1–10 g		3.3 (1.3–8.2)		
11–100 g		3.1 (1.5–6.6)						
>100 g		6.9 (2.8–17.1)						
Other than hard liquor		3.2 (1.7–5.8)						
<i>Cachaca</i>								
Non-drinker		1 (reference)						
1–10 g		1.4 (0.4–5.4)						
11–100 g		2.0 (1.0–4.2)						
101–500 g		4.5 (2.2–9.2)						
501–1000 g		7.2 (3.5–14.7)						
1001–2000 g		8.7 (4.3–17.6)						
>2000 g		9.9 (3.8–25.5)						
Other than cachaca		3.7 (1.8–7.8)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Schlecht <i>et al.</i> (2001) (contd)				Pharynx				
				<i>Beer</i>				
				Non-drinker		1 (reference)		
				1–10 g		3.2 (1.1–9.2)		
				11–100 g		3.4 (1.1–10.4)		
				>100 g		1.1 (0.3–4.1)		
				Other than beer		3.1 (1.0–9.2)		
				<i>Wine</i>				
				Non-drinker		1 (reference)		
				1–10 g		3.1 (1.0–9.2)		
				11–100 g		2.8 (0.8–9.4)		
				>100 g		3.0 (0.8–11.1)		
				Other than wine		3.6 (1.3–10.5)		
				<i>Hard liquor</i>				
				Non-drinker		1 (reference)		
				1–10 g		4.1 (1.0–17.7)		
				11–100 g		4.6 (1.5–14.1)		
				>100 g		2.5 (0.7–9.8)		
				Other than hard liquor		3.1 (1.1–8.8)		
				<i>Cachaca</i>				
				Non-drinker		1 (reference)		
			1–10 g		2.8 (0.4–19.6)			
			11–100 g		2.9 (0.9–9.1)			
			101–500 g		5.4 (1.7–17.5)			
			501–1000 g		9.2 (2.9–29.3)			
			1001–2000 g		14.3 (4.4–45.8)			
			>2000 g		12.5 (2.9–53.7)			
			Other than cachaca		2.1 (0.6–7.8)			

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Huang <i>et al.</i> (2003), Puerto Rico, 1992–95	286 male cases identified through the Central Cancer Registry and by abstracting patients' medical records; aged 21–79 years; histologically confirmed; response rate, 70% 417 male population controls selected from among all Puerto Ricans; frequency-matched on age; response rate, 83%.	Interviewer-administered questionnaire	Oral cavity, pharynx (ICD9 141, 143–146, 148, 149)	<i>Beer</i>	Non-drinker	47	1 (reference)	Age, tobacco use, raw fruit and vegetable intake, education, other types of alcoholic beverage	Same population as Hayes <i>et al.</i> (1999)
				>0–<8 drinks/week	70	0.5 (0.3–1.0)			
				8–<43 drinks/week	119	1.1 (0.6–2.0)			
				≥43 drinks/week	42	1.8 (0.8–4.1)			
				<i>p</i> for trend	0.004				
				<i>Wine</i>	Non-drinker	194	1 (reference)		
				>0–<8 drinks/week	62	1.0 (0.6–1.7)			
				≥8 drinks/week	27	1.8 (0.8–4.3)			
				<i>p</i> for trend	0.2				
				<i>Liquor</i>	Non-drinker	22	1 (reference)		
				>0–<8 drinks/week	40	1.7 (0.9–3.2)			
				8–<43 drinks/week	90	3.5 (1.8–6.7)			
≥43 drinks/week	128	13.2 (6.5–26.6)							
<i>p</i> for trend	<0.0001								

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Altieri <i>et al.</i> (2004), Italy, Switzerland, 1992–97	749 (634 men, 115 women) cases from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland) admitted to major teaching and general hospitals in area under surveillance; aged 22–77 years; histologically confirmed 1772 (1252 men, 520 women) hospital controls from the same network of hospitals as cases; aged 20–78 years; excluded patients with alcohol- and tobacco-related conditions	Interview-administered structured questionnaire	Oral cavity, pharynx	<i>Beer</i>				Age, sex, study centre, education, smoking habit, other types of alcoholic beverage
				Non-drinkers	284	1 (reference)		
				1–2 drinks/day	380	1.2 (1.0–1.5)		
				≥3 drinks/day	84	2.3 (1.4–3.7)		
				χ^2 for trend		9.86 ($p = 0.02$)		
				<i>Wine</i>				
				Non-drinkers	43	–		
				1–2 drinks/day	110	1 (reference)		
				3–4 drinks/day	127	2.2 (1.6–3.0)		
				5–7 drinks/day	157	7.1 (5.0–10.1)		
				8–11 drinks/day	177	11.8 (8.1–17.2)		
				≥12 drinks/day	134	16.1 (10.2–25.3)		
χ^2 for trend		221.83 ($p < 0.0001$)						
<i>Spirits</i>								
Non-drinkers	297	1 (reference)						
1–2 drinks/day	386	1.0 (0.8–1.2)						
≥3 drinks/day	66	1.9 (1.1–3.3)						
χ^2 for trend		1.14 ($p = 0.29$)						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Castellsagué et al. (2004), Spain, 1996–99	375 (304 men, 71 women) cases identified from hospitals; histologically confirmed; response rate, 76.5% 375 (304 men, 71 women) non-cancer hospital controls from same hospitals as cases; frequency-matched on age, sex; mean age, 60 years; excluded patients with alcohol- and tobacco-related diagnoses; response rate, 91%	Interviewer-administered questionnaire	Oral cavity, oropharynx (ICDO C1-C10)	<i>Type of alcohol</i> Only beer Only wine and beer Only wine Spirits with or without wine/beer <i>p</i> for trend	12 47 32 248	1.2 (0.5–2.8) 2.0 (1.0–4.0) 2.7 (1.3–5.6) 7.3 (3.7–14.5)	Age group, sex, education, tobacco smoking, centre	
					<0.0001			

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2004), Montevideo, Uruguay, 1997–2003	85 male cases identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97.5% 640 hospital-based male controls from the same hospitals as cases; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; frequency matched (2:1 controls:cases) on age, residence; response rate, 97%	Interviewer-administered questionnaire	Hypopharynx	Ethanol/day (mL)			Age, residence, urban/rural status, education, body mass index, smoking, other types of alcoholic beverage	
				<i>Beer</i>				
				Beer abstainers	75	1 (reference)		
				1–60	8	0.8 (0.3–1.9)		
				≥61	2	0.2 (0.1–1.1)		
				<i>p</i> for trend	0.08			
				<i>Red wine</i>				
				Wine abstainers	9	1 (reference)		
				1–60	20	2.3 (0.9–5.5)		
				61–120	29	5.2 (2.2–12.4)		
				≥121	27	4.5 (1.9–10.8)		
				<i>p</i> for trend	0.0001			
				<i>Hard liquor</i>				
Liquor abstainers	45	1 (reference)						
1–60	12	0.9 (0.4–1.9)						
61–120	10	2.2 (0.9–5.2)						
≥121	18	3.3 (1.6–6.8)						
<i>p</i> for trend	0.0008							

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2007), Montevideo, Uruguay, 1988–2000	335 male cases identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97% 1501 hospital-based non-cancer male controls; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; response rate, 97%	Interviewer-administered questionnaire	Oral cavity (excluding lip)	Ethanol/day (mL)			Age, residence, urban/rural status, hospital, year of diagnosis, education, family history of cancer, occupation, vegetable and fruit consumption, mate, smoking, total alcoholic beverage	
				<i>Beer</i>				
				Beer abstainers		1 (reference)		
				1–22		0.5 (0.3–0.9)		
				≥23		0.4 (0.2–0.9)		
				<i>p</i> for trend		0.004		
				<i>Wine</i>				
				Wine abstainers		1 (reference)		
				1–60		0.8 (0.6–1.2)		
				61–120		1.5 (1.0–2.1)		
				≥121		1.4 (0.9–2.4)		
				<i>p</i> for trend		0.03		
<i>Hard liquor</i>								
Liquor abstainers		1 (reference)						
1–60		0.8 (0.6–1.2)						
61–120		1.8 (1.2–2.7)						
≥121		1.4 (0.8–2.2)						
<i>p</i> for trend		0.03						

Table 2.6 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2007) (contd)	441 male cases identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97%		Pharynx (excluding nasopharynx)	<i>Beer</i> Beer abstainers 1–22 ≥23 <i>p</i> for trend <i>Wine</i> Wine abstainers 1–60 61–120 ≥121 <i>p</i> for trend <i>Hard liquor</i> Liquor abstainers 1–60 61–120 ≥121 <i>p</i> for trend		1 (reference) 0.8 (0.4–1.3) 0.3 (0.2–0.7) 0.001 1 (reference) 1.1 (0.8–1.5) 2.7 (1.9–3.8) 2.5 (1.6–3.9) <0.0001 1 (reference) 0.9 (0.7–1.3) 1.6 (1.1–2.3) 0.9 (0.5–1.4) 0.5		

CI, confidence interval; ICD, International Classification of Diseases; NS, not significant

Table 2.7 Joint effects of alcoholic beverage consumption and tobacco smoking on cancers of the oral cavity and pharynx

Reference, study location, period	Tobacco	Alcoholic beverages					Comments/ adjustment factors
		<1 drink/week	1–4 drinks/week	5–14 drinks/week	15–29 drinks/week	≥30 drinks/week	
Blot <i>et al.</i> (1988), USA, 1984–85		No. of cases (odds ratio)					ªQuit for ≥10 years or smoked for <20 years; adjusted for age, race, study location, respondent status (self vs next-of-kin)
	Men						
	Nonsmoker	12 (1)	12 (1.3)	15 (1.6)	5 (1.4)	6 (5.8)	
	Short duration/ formerª	8 (0.7)	24 (2.2)	21 (1.4)	25 (3.2)	43 (6.4)	
	1–19/day for ≥20 years	2 (1.7)	7 (1.5)	8 (2.7)	16 (5.4)	22 (7.9)	
	20–39/day for ≥20 years	8 (1.9)	17 (2.4)	28 (4.4)	52 (7.2)	145 (23.8)	
	≥40/day for ≥20 years	9 (7.4)	6 (0.7)	19 (4.4)	43 (20.2)	148 (37.7)	
	Pipe/cigar only	1 (0.6)	5 (1.0)	8 (3.7)	13 (4.7)	25 (23.0)	
	Women						
	Nonsmoker	36 (1)	11 (0.7)	7 (1.3)	0 (0.0)	0 (0.0)	
	Short duration/ formerª	7 (1.0)	8 (1.6)	4 (0.4)	3 (1.1)	3 (~)	
	1–19/day for ≥20 years	4 (0.9)	22 (5.1)	11 (2.8)	3 (4.6)	9 (11.0)	
	20–39/day for ≥20 years	12 (2.2)	20 (2.7)	35 (6.9)	31 (12.4)	38 (46.0)	
	≥40/day for ≥20 years	4 (~)	14 (9.3)	15 (7.8)	18 (18.0)	37 (107.9)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
		No. of cases/odds ratio (95% CI)				
Tuyns <i>et al.</i> (1988), France, Italy, Spain, Switzerland, 1980–83		0–40 g/day	41–80 g/day	81–120 g/day	≥121 g/day	Adjusted for age, place, age/place interaction
	0–7 cigarettes/day	4 (1)	10 (3.0)	7 (5.5)	11 (15.0)	
	8–15 cigarettes/day	9 (4.7)	32 (14.6)	28 (27.5)	39 (71.6)	
	16–25 cigarettes/day	27 (13.9)	42 (19.5)	52 (48.3)	56 (67.8)	
	≥26 cigarettes/day	5 (4.9)	15 (18.4)	22 (37.6)	50 (135.5)	
Merletti <i>et al.</i> (1989), Torino, Italy, 1982–84		No. of cases/odds ratio (95% CI)				Adjusted for age, education, area of birth
		0–40g/day	41–120g/day	>120g/day		
	Men					
	0–7 g/day	4/1.0 (reference)	4/0.6 (0.2–2.0) (categories combined)			
	8–15 g/day	7/3.3 (0.9–12.4)	15/3.6 (1.1–12.0)	5/8.6 (1.9–39.0)		
	>16 g/day	10/2.5 (0.7–8.5)	25/3.6 (1.2–11.3)	16/21.4 (5.9–77.7)		
	Women					
0 g/day	6/1.0 (reference)	5/1.1 (0.3–4.1)	2/0.8 (0.1–4.2)			
≥1 g/day	5/2.8 (0.7–11.1)	8/6.5 (1.7–24.5)	10/21.3 (5.1–88.6)			

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
Franceschi <i>et al.</i> (1990), Milan, Pordenone, Italy, 1986–89		No. of cases (odds ratio)				Adjusted for age, area of residence, education, occupation; oral cavity and pharynx cases combined
		<35 drinks/week	35–59 drinks/week	≥60 drinks/week		
	Nonsmoker	3 (1)	2 (1.6)	1 (2.3)		
	Light smoker	7 (3.1)	7 (5.4)	12 (10.9)		
	Intermediate smoker	39 (10.9)	79 (26.6)	102 (36.4)		
Heavy smoker	7 (17.6)	8 (40.2)	19 (79.6)			
Zheng <i>et al.</i> (1990), Beijing, China, 1988–89		No. of cases (odds ratio)				Adjusted for age, education
		Lifetime consumption of spirit equivalents				
		0 kg	<217 kg	217–801 kg	>801 kg	
	0 pack–years	20 (1)	9 (1.2)	4 (0.8)	4 (2.4)	
	1–18 pack–years	15 (1.4)	15 (2.8)	13 (5.6)	4 (15.2)	
	19–32 pack–years	12 (2.1)	14 (4.9)	9 (1.7)	19 (10.1)	
>32 pack–years	13 (2.5)	2 (5.9)	14 (5.9)	31 (17.4)		
Nam <i>et al.</i> (1992), USA, 1986		Odds ratio (<i>p</i> -value)			Adjusted for sex	
		0–3 drinks/week	4–23 drinks/week	≥24 drinks/week		
	≤30 pack–years	1	0.6	1.4		
	31–59 pack–years	1.5	2.3 (<0.05)	2.6 (<0.01)		
≥60 pack–years	2.2 (<0.05)	2.3 (<0.05)	5.2 (<0.01)			

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages					Comments/adjustment factors	
		No. of cases/odds ratio (95% CI)						
Maier <i>et al.</i> (1994), Heidelberg, Giessen, Germany, 1987–88	<5 tobacco–years	<25 g/day	25–75 g/day	>75 g/day				
		5/1	5/2.3 (0.6–8.8)	3/10.3 (1.9–55.8)				
		27/5.7 (1.9–17.3)	50/14.6 (4.8–43.9)	44/153.2 (44.1–532)				
	5–50 tobacco–years	14/23.3 (6.6–82.5)	27/52.8 (15.8–176.6)	25/146.2 (37.7–566)				
Mashberg <i>et al.</i> (1993), New Jersey, USA, 1972–83	Minimal smokers Cigar/pipe 6–15 cigarettes/day 16–25 cigarettes/day 26–35 cigarettes/day ≥36 cigarettes/day	No. of cases (odds ratio)					Adjusted for age, race	
		Minimal drinkers	2–5 WE/day	6–10 WE/day	11–21 WE/day	≥22 WE/day		
		1 (1)	1 (2.7)	2 (11.9)	3 (12.5)	2 (8.3)		
		6 (20.5)	6 (17.0)	13 (53.4)	6 (27.3)	5 (23.1)		
		3 (10.8)	7 (24.2)	17 (50.9)	8 (30.9)	6 (27.5)		
		4 (7.6)	16 (29.7)	23 (28.9)	34 (44.8)	31 (61.7)		
		0 (–)	2 (5.3)	18 (61.9)	18 (79.5)	22 (70.3)		
1 (3.2)	4 (10.2)	17 (26.8)	40 (98.4)	30 (32.0)				

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/ adjustment factors
		Non-drinker/ occasional	1–3.9 oz/day	4–6.9 oz/day	≥7 oz/day	
Kabat <i>et al.</i> (1994), USA, 1977–90	Men					
	Never	1	1.6 (0.9–2.7)	1.2 (0.4–3.7)	2.9 (1.1–8.1)	
	Former smoker (abstained for ≥12 months)	1 (0.7–1.6)	1.7 (1.1–2.6)	3.1 (1.9–5.2)	5.1 (3.3–7.8)	
	1–20 cigarettes/ day	1.5 (0.9–2.51)	5.8 (3.7–9.1)		11.9 (7.7–18.4)	
	21–30 cigarettes/ day	2.2 (1.1–4.3)	6.8 (3.6–12.7)		13.5 (7.9–23.2)	
	≥31 cigarettes/ day	2.0 (1.1–3.7)	6.9 (3.9–12.4)		20.1 (12.9–31.5)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages			Comments/ adjustment factors
		Non-drinker/ occasional	≥4 oz/day	1–3.9 oz/day	
Kabat <i>et al.</i> (1994) (cont)	Women				Adjusted for age, education, race, time period, type of hospital
	Never	1	3.5 (0.9–13.4)	0.7 (0.3–1.4)	
	Former smoker (abstained for ≥12 months)	1.3 (0.9–2.0)	2.7 (1.0–7.9)	2.1 (1.2–3.8)	
	1–20 cigarettes/ day	2.9 (1.9–4.3)	17.6 (8.1–37.5)	5.8 (3.5–9.8)	
	≥21 cigarettes/ day	3.8 (2.3–6.2)	26.7 (12.3–58.6)	22.3 (9.6–51.8)	
Chyou <i>et al.</i> (1995), Hawaii, USA		No. of cases/odds ratio (95% CI)			Study population from Kato <i>et al.</i> (1992c); adjusted for age
		0 oz/month	>0–<14 oz/month	≥14 oz/month	
	0 cigarette/ day	3/1 (reference)	3/1.3 (0.3–6.3)	6/6.5 (1.6–26.0)	
	>0–≤20 cigarettes/ day	8/3.0 (0.8–11.3)	6/1.9 (0.5–7.7)	24/10.7 (3.2–35.4)	
	>20 cigarettes/ day	5/3.2 (0.8–13.4)	7/4.6 (1.2–17.7)	28/14.4 (4.4–47.4)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
Murata <i>et al.</i> (1996), Japan 1984–93	Nonsmoker Smoker	No. of cases (odds ratio; <i>p</i> -value)				In sake-equivalents (180 mL sake contains ~27 mL ethanol)
		0 cup/day	0.1–1.0 cup/day	≥1 cup/day		
		7 (1)	6 (1.2)	5 (2.1)		
		10 (1.9)	7 (1.4)	16 (<i>p</i> < 0.01)		
Sanderson, <i>et al.</i> (1997), Netherlands, 1980–90	Nonsmoker Smoker Nonsmoker and smoker	No. of cases/odds ratio (95% CI)				
		Non-drinker	1–5 units/day	>5 units/day		
		125 Ref	39/2.4 (1.6–3.6)			
		28/1 (0.6–1.5)	65/6.5 (4.4–9.7)			
			46/32.9 (18.3–59.2)			
Zheng <i>et al.</i> (1997), Beijing, China, 1988–89	Never ≤ 20 pack–years >20 pack–years	No. of cases (odds ratio; <i>p</i> -value)				Adjusted for education (matching variables: age, sex)
		(Lifetime intake, spirit equivalents in kg)				
		Never	≤255 kg	>255 kg		
		39 (1)	6 (1.9)	3 (2.4)		
	10 (1.2)	9 (1.6)	4 (3.0)			
		15 (7.6; <i>p</i> < 0.05)	8 (23.3; <i>p</i> < 0.05)	17 (4.1)		
Schildt <i>et al.</i> (1998), Sweden, 1980–89	Never Low consumption High consumption	No. of cases/odds ratio (95% CI)				
		Never liquor	Low liquor intake	Medium liquor intake	High liquor intake	
		80/1.0	50/1.2 (0.8–1.9)	7/1.4 (0.8–2.6)	4/4.2 (1.8–9.4)	
		15/1.0 (0.6–1.6)	26/1.2 (0.6–2.1)	19/1.4 (0.7–2.7)	4/4.0 (1.6–9.8)	
		8/1.4 (0.8–2.3)	30/1.6 (0.9–2.9)	27/2.0 (1.0–3.6)	30/5.7 (2.4–14)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages					Comments/adjustment factors	
		Odds ratio (95% CI) for lifetime consumption						
Schlecht <i>et al.</i> (1999), Brazil, 1986–89	<i>Oral cavity</i>	0–5 pack–years	1	1.2 (0.4–3.4)	2.3 (0.6–9.1)			Same study population as Schlecht <i>et al.</i> (2001); adjusted for race, beverage temperature, religion, wood stove use, spicy food intake (matching variables: age, sex, study location, admission period) Adjusted for age
		6–42 pack–years	2.9 (1.2–6.8)	6.2 (2.7–14.1)	19.5 (2.6–147)			
		>42 pack–years	7.8 (2.9–21.0)	11.2 (4.8–26.3)	20.3 (9.0–45.3)			
	<i>Pharynx</i>	0–5 pack–years	1	6.2 (0.7–56.6)	22.3 (2.1–238)			
		6–42 pack–years	2.4 (0.2–24.0)	21.7 (2.6–180)	66.3 (1.7–2,556)			
		>42 pack–years	69.4 (6.9–694)	43.0 (4.9–340)	77.3 (9.2–625)			
Hayes <i>et al.</i> (1999), Puerto Rico, 1992–95	None Low 10–19 cigarettes/day 20–39 cigarettes/day ≥40 cigarettes/day	No. of cases/odds ratio (95% CI)						
		None	1–7 drinks/week	8–21 drinks/week	22–42 drinks/week	≥42 drinks/week		
		6/1.00 (reference)	1/0.2 (0.0–1.5)	2/0.6 (0.1–3.5)	2/1.6 (0.3–9.6)	4/6.4 (1.3–31.9)		
		0	10/1.6 (0.5–4.8)	3/1.3 (0.3–5.7)	11/3.7 (0.8–16.4)	9/5.5 (1.6–19.0)		
		1/11.3 (0.6–213.0)	2/1.3 (0.2–7.2)	3/1.8 (0.4–8.3)	8/18.6 (4.1–84.0)	10/12.2 (3.3–45.6)		
		1/1.8 (0.2–19.0)	10/3.8 (1.2–12.0)	13/6.2 (2.0–19.3)	19/11.3 (3.7–34.0)	60/50.2 (16.6–152.0)		
1/2.4 (0.2–27.6)	6/4.3 (1.1–16.7)	4/7 (0.9–18.7)	10/10.5 (2.9–37.9)	67/38.7 (13.6–110.0)				

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/ adjustment factors
		No. of cases/odds ratio (95% CI)				
Franceschi <i>et al.</i> (1999), Italy, Switzerland, 1992–97		0–20 drinks/week	21–48 drinks/week	49–76 drinks/week	≥77 drinks/week	Study population from Franceschi <i>et al.</i> (2000); adjusted for age, area of residence, interviewer, education, vegetable and fruit intake, total energy intake *categories combined
	<i>Oral cavity</i>					
	Never smoker	3/1 (reference)	5/2.7 (0.6–11.6)	3/4.5 (0.8–24.2)*	3/4.5 (0.8–24.2)*	
	1–14 cigarettes/ day	2/2.2 (0.4–13.5)	6/5.9 (1.4–25.1)	11/30.6 (7.3–128.2)	8/52.4 (10.4–264.2)	
	15–24 cigarettes/ day	4/3.0 (0.6–13.8)	28/22.9 (66.6–79.4)	35/62.5 (17.4–224.2)	31/110.3 (29.1–418.1)	
	≥25 cigarettes/ day	4/5.6 (1.2–26.3)	12/22.7 (5.9–86.9)	25/103.1 (26.4–402.7)	31/227.8 (54.6–950.7)	
Former smoker (abstained ≥12 months)	12/3.9 (1.1–14.1)	20/6.0 (1.7–21.0)	17/10.5 (2.9–38.6)	17/25.4 (6.7–96.0)		

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
Franceschi <i>et al.</i> (1999) (contd)	<i>Pharynx</i>					*Categories combined
	Never smoker	6/1 (reference)	2/0.4 (0.1–2.3)	1/0.5 (0.1–4.3)*	1/0.5 (0.1–4.3)*	
	1–14 cigarettes/day	4/2.3 (0.6–8.4)	11/4.5 (1.5–13.4)	17/16.3 (5.3–50.5)	13/27.5 (7.2–105.1)	
	15–24 cigarettes/day	12/4.4 (1.6–12.5)	32/11.7 (4.6–30.2)	40/26.9 (10.0–72.3)	48/58.3 (20.3–167.3)	
	≥25 cigarettes/day	7/5.5 (1.7–17.8)	22/18.6 (6.8–51.3)	18/32.2 (10.3–100.4)	36/100.4 (30.8–327.7)	
Former smoker (abstained ≥12 months)	11/1.7 (0.6–4.9)	22/2.7 (1.0–7.1)	31/6.8 (2.6–17.8)	31/14.8 (5.4–40.9)		
Schwartz <i>et al.</i> (2001), Washington, USA, 1985–95		No. of cases/odds ratio (95% CI)				Adjusted for age, sex, race
		<1 drink/week	1–14 drinks/week	≥15 drinks/week		
	Never	26/1 (reference)	19/0.8 (0.4–1.5)	5/1.2 (0.4–3.6)		
	1–20 pack–years	9/0.8 (0.3–1.8)	27/0.9 (0.5–1.6)	13/3.8 (1.5–9.4)		
	≥20 pack–years	10/1.8 (0.7–4.5)	94/3.3 (1.9–5.7)	130/9.9 (5.5–17.9)		

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages			Comments/adjustment factors
Garrote <i>et al.</i> (2001), Havana, Cuba, 1996–99	Never smokers 1–29 cigarettes/day ≥ 30 cigarettes/day	No. of cases/odds ratio (95% CI)			Adjusted for age, sex, area of residence, education, smoking (former smokers only)
		0 drink/week	<21 drinks/week	≥21 drinks/week	
		14/1 (reference)	1	0	
		35/6.6 (2.8–15.7)	17/11.0 (3.7–32.8)	15/26.7 (7.2–99.9)	
		15/10.5 (2.9–38.2)	15/42.3 (8.4–212.3)	21/111.2 (22.7–543.7)	
Balaram <i>et al.</i> (2002); southern India, 1996–99	Never paan chewer Current paan chewer	No. of cases/odds ratio (95% CI)			Adjusted for age, centre, education, oral hygiene, smoking, chewing, drinking habits
		Never drinker	Current drinker		
		64/1 (reference)	48/2.8 (1.6–5.1)		
		48/7.3 (3.8–14.1)	46/8.6 (4.1–18.1)		
Boeing (2002), Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, Netherlands, United Kingdom	Nonsmoker 1–20 cigarettes/day >20 cigarettes/day	No. of cases/hazard rate ratio (95% CI)			Adjusted for sex, follow-up time, education, body mass index, vegetable and fruit intake, energy intake
		0–30 g/day	>30–60 g/day	>60 g/day	
		58/1 (reference)	7/2.6 (1.1–6.0)	4/6.9 (2.3–2.7)	
		22/2.0 (1.2–3.5)	6/5.1 (2.1–12.7)	6/22.0 (8.3–58.1)	
		7/6.8 (3.0–15.5)	7/20.7 (8.7–49.0)	7/48.7 (20.0–118.9)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
Rodriguez <i>et al.</i> (2004), Italy, Switzerland, 1984–93, 1992–97	Never/former smokers (abstained \geq 12 months)	No. of cases/odds ratio (95% CI)				Study populations from Franceschi <i>et al.</i> (1990, 1999); adjusted for education, marital status, body mass index, coffee consumption (matched variables: age, sex, study centre)
		<6 drinks/day	6–<10 drinks/day	\geq 10 drinks/day		
		22/1 (reference)	4/1.9 (0.5–7.1)	5/15.7 (3.6–67.9)		
Castellsagué <i>et al.</i> (2004), Spain, 1996–99	Never smoker	No. of cases/ odds ratio (95% CI)				Adjusted for age, sex, centre, education
		Never drinker	1–2 drinks/day	3–5 drinks/day	\geq 6 drinks/day	
		28/1 (reference)	23/2.0 (0.9–4.4)	2/1.1 (0.9–6.4)	2/6.2 (1.0–39.2)	
1–10 cigarette/day	3/2.9 (0.6–14.8)	14/4.7 (1.7–12.9)	10/32.2 (8.1–127.1)	1/2.7 (0.3–26.5)		
	11–20 cigarette/day	2/1.0 (0.2–6.0)	27/11.1 (4.0–30.6)	22/26.6 (8.6–82.0)	46/43.1 (15.0–123.8)	
\geq 21 cigarettes/day	2/1.9 (0.3–11.1)	22/8.2 (2.9–22.9)	40/22.0 (8.0–61.0)	131/50.7 (19.1–134.2)		

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages			Comments/ adjustment factors
De Stefani, <i>et al.</i> (2004), Montevideo, Uruguay, 1997–2003		Odds ratio (95% CI)			Adjusted for age, residence, urban/ rural status, education, body mass index
		0–60 mL/day	61–120 mL/day	≥121 mL/day	
	0–14 cigarettes/day	1 (reference)	5.1 (1.1–23.3)	4.6 (0.8–25.6)	
	15–24 cigarettes/day	1.9 (0.3–12.8)	16.3 (4.2–62.9)	22.3 (5.8–86.3)	
	≥25 cigarettes/day	4.3 (0.8–23.5)	5.6 (2.4–13.1)	43.9 (11.5–116.8)	

Table 2.7 (continued)

Reference, study location, period	Tobacco	Alcoholic beverages				Comments/adjustment factors
		0–60 mL/day	61–120 mL/day	121–240 mL/day	≥ 241 mL/day	
De Stefani <i>et al.</i> (2007), Montevideo, Uruguay, 1988–2000	Odds ratio (95% CI)					Adjusted for age, residence, urban/rural status, hospital, year at diagnosis, education, family history of cancer, occupation, vegetable and fruit intake, mate intake
	<i>Oral cavity</i>					
	0–9 cigarettes/day	1	3.5 (1.2–10.5)	2.9 (90.8–11.2)	1.9 (0.2–15.9)	
	10–19 cigarettes/day	4.4 (2.1–9.4)	8.9 (3.9–20.4)	14.5 (6.1–34.2)	24.5 (8.3–72.1)	
	20–29 cigarettes/day	4.8 (2.3–10.2)	24.1 (11.5–50)	21.2 (9.6–46.8)	50.5 (21–119)	
	≥30 cigarettes/day	6.5 (3.1–13.8)	29.6 (13.7–64)	42.5 (19.9–90)	33.4 (15.8–70)	
	<i>Pharynx</i>					
	0–9 cigarettes/day	1	0.9 (0.2–4.4)	2.5 (0.8–8.2)	9.8 (3.7–26.3)	
	10–19 cigarettes/day	2.8 (1.4–5.6)	8.8 (4.3–17.9)	18.6 (9.1–38.0)	12.4 (4.0–38.7)	
	20–29 cigarettes/day	3.7 (1.9–7.1)	16.8 (8.6–33)	31.4 (16.0–62)	53.2 (25–114)	
≥30 cigarettes/day	4.7 (2.4–9.2)	24.0 (12.8–48)	36.4 (18.7–71)	43.8 (23.0–84)		

CI, confidence interval; WE whiskey equivalent

et al., 1995). The evaluation of effect modification was descriptive, without formal assessment of multiplicative interaction in most of studies.

Overall, a large majority of studies on joint exposure to alcoholic beverage and tobacco consumption demonstrated a synergistic effect. Many studies demonstrated a greater than multiplicative interaction (Tuyns *et al.*, 1988; Merletti *et al.*, 1989; Franceschi *et al.*, 1990; Zheng *et al.*, 1990; Mashberg *et al.*, 1993; Kabat *et al.*, 1994; Franceschi *et al.*, 1999; Hayes *et al.*, 1999; Schlecht *et al.*, 1999; Garrote *et al.*, 2001; Schwartz *et al.*, 2001; Boeing, 2002; Castellsagué *et al.*, 2004; De Stefani *et al.*, 2007). In contrast, some other studies demonstrated a greater than additive but less than multiplicative interaction (Maier *et al.*, 1992a; Chyou *et al.*, 1995; Schildt *et al.*, 1998). Among tobacco chewers in India, there appears to be no interaction between chewing and alcoholic beverage consumption (Balaram *et al.*, 2002).

2.2.5 *Effect of cessation of alcoholic beverage consumption (Table 2.8)*

Studies of cessation of alcoholic beverage consumption may be confounded by the fact that precursors and early malignancies of the oral cavity and pharynx may lead to such cessation. Nevertheless, this type of confounding may result in underestimation of the effect of cessation. For recent quitters, the risk for oral and pharyngeal cancers increases above that of current drinkers; as the number of years since quitting increases, however, that elevated risk gradually drops to below that of current drinkers and near to the levels of non-drinkers in some studies. Hayes *et al.* (1999) observed that risk could drop to near the levels of non-drinkers after 20 years of quitting among men. Castellsagué *et al.* (2004) showed that risk can be reduced to near levels of never drinkers after 14 years and De Stefani *et al.* (2004) showed that this occurs after 10 years of quitting. In contrast, Franceschi *et al.* (2000) showed that a reduction in risk with quitting compared with current drinkers is not attained even 11 years after quitting.

2.2.6 *Effect of alcoholic beverage consumption in nonsmokers (Table 2.9)*

Because tobacco smoking is a major risk factor for oral and pharyngeal cancer, the study of nonsmoking subjects can avoid the strong confounding effect of tobacco smoking. Of the studies that focused on the effects of alcoholic beverage consumption in nonsmokers, an increase in risk in relation to alcoholic beverages was consistent. Talamini *et al.* (1990a) compared 27 nonsmoking cases identified between 1986 and 1989 in Milan and Pordenone and 572 nonsmoking hospital-based controls matched on age and area of residence. A significant dose–response relationship between alcoholic beverage consumption and cancer of the oral cavity and pharynx was observed ($P=0.04$). Ng *et al.* (1993) identified 173 white nonsmoking cases of oral and hypopharyngeal cancer between 1977 and 1991 in eight US cities and compared them with 613 hospital-based controls matched on age, sex and date of interview. A significant dose–response relationship was also observed in this study ($P<0.001$). Sixty nonsmoking

Table 2.8 Effect of cessation of alcoholic beverage consumption on the incidence of cancers of the oral cavity and pharynx

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Day <i>et al.</i> (1994a), USA, 1984–85	80 (56 men, 24 women) with second primary cancers from cohort of 1090 (first primary cancers) 189 (132 men, 57 women) randomly selected from cohort that were free of second primary cancer at the end of follow-up (1989)	Interviewer-administered questionnaire	Oral cavity, pharynx, oesophagus, larynx	<i>Years since last drank alcohol</i>			Age, stage of disease, amount smoked and drunk	
				Current drinker	29	1 (reference)		
				<5 years	17	5.4 (1.6–18.0)		
				≥5 years	7	1.9 (0.6–6.7)		

Table 2.8 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hayes <i>et al.</i> (1999), Puerto Rico, 1992–95	342 (286 men, 56 women) identified through pathology laboratories and Central Cancer Registry; aged 21–79 years; histologically confirmed; response rate, 70% 521 (417 men, 104 women) population-based controls; frequency-matched by age, gender; response rate, 83%	Interviewer-administered questionnaire	Oral cavity, pharynx (ICD9 141–143–146, 148, 149)	<i>Years since last drink</i>			Age, tobacco use	
				Men				
				Non-drinker	9	1 (reference)		
				Recent use	163	2.4 (0–5.4)		
				Quit 2–9 years	60	3.6 (1.5–9.0)		
				Quit 10–19 years	34	2.7 (1.0–7.0)		
				Quit ≥20 years	20	1.3 (0.5–3.6)		
				Women				
				Non-drinker	26	1 (reference)		
				Recent use	15	1.2 (0.4–3.4)		
				Quit 2–9 years	6	1.0 (0.2–5.4)		
Quit 10–19 years	5	1.1 (0.2–6.4)						
Quit ≥20 years	4	0.9 (0.2–4.8)						

Table 2.8 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (2000), Italy, Switzerland, 1992–97	754 (638 men, 116 women) cases from major teaching and general hospitals in Pordenone, Rome, Latina (Italy) and Vaud (Switzerland); aged 22–77 years; histologically confirmed; response rate, 95%	Interviewer-administered questionnaire	Oral cavity, pharynx (excluding lip, salivary glands, nasopharynx)	<i>Years since quit drinking</i>			Age, sex, study centre, education, interviewer, tobacco smoking, total alcoholic beverage consumption	Study population from Franceschi <i>et al.</i> (1999)
				1–3 years	27	1.2 (0.6–2.4)		
				4–6 years	37	1.8 (1.0–3.5)		
				7–10 years	36	3.3 (1.5–7.3)		
				≥11 years	26	1.9 (1.0–3.8)		
			χ^2 for trend		1.6 ($p = 0.21$)			

Table 2.8 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Garrote <i>et al.</i> (2001), Havana, Cuba, 1996–99	200 (143 men, 57 women) cases identified in the Instituto Nacional de Oncología y Radiobiología of Havana; median age, 64 years; response rate, 88% 200 (136 men, 64 women) hospital-based controls admitted to same institute and three other major hospitals in Havana; excluded patients with alcohol- and tobacco-related conditions; frequency-matched on age, sex; median age, 62 years; response rate, 79%	Interviewer (dentist)-administered questionnaire	Oral cavity, oropharynx	<i>Years since quit drinking</i>			Age, sex, area of residence, education, smoking	
				Current drinker	81	1		
				<10 years	21	0.7 (0.3–1.8)		
				≥10 years	14	0.3 (0.1–0.8)		
			χ^2 for trend			5.00 ($p=0.03$)		

Table 2.8 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Balaram, <i>et al.</i> (2002), southern, India, 1996–99	591 (309 men, median age, 56 years; 282 women, median age, 58 years) from three centres in Bangalore, Madras, Trivandrum; response rate, 97% 582 (292 men, 290 women) hospital-based from the same hospitals as cases; frequency-matched by centre, age, sex; response rate, 90%	Interviewer-administered questionnaire	Oral cavity	Men only			Centre, age, education, paan chewing, smoking, drinking	
				<i>Years since quit drinking</i>				
				Current drinkers	84	1		
				<10 years	49	0.94 (0.43–2.09)		
				≥ 10 years	16	0.62 (0.19–2.05)		
<i>p</i> for trend		0.55						
Castellsagué, <i>et al.</i> (2004), Spain, 1996–99	375 (304 men, 71 women); mean age, 60 years; response rate, 76.5% 375 (304 men, 71 women); mean age, 60 years; response rate, 91%	Interviewer-administered questionnaire	Oral cavity, oropharynx	<i>Years since quit drinking</i>			Age group, sex, education, centre, average number of cigarettes per day	
				Never drinker	35	1 (reference)		
				Current drinker	251	3.5 (1.9–6.5)		
				1–2 years	28	3.9 (1.7–9.1)		
				3–7 years	22	1.7 (0.8–3.9)		
				8–13 years	20	2.3 (1.0–5.3)		
				≥14 years	19	1.5 (0.7–3.3)		
				<i>p</i> for trend		0.003		

Table 2.8 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2004), Montevideo, Uruguay, 1997–2003	85 men identified in the four major hospitals in Montevideo; microscopically confirmed; response rate, 97.5% 640 hospital-based men from the same hospitals as cases; excluded patients with alcohol- and tobacco-related conditions with no recent changes in diet; frequency-matched (2:1 controls:cases) on age, residence; response rate, 97%	Interviewer-administered questionnaire	Hypopharynx	<i>Years since quit drinking</i>			Age, residence, urban/rural status, education, body mass index, smoking	Looked at oral cavity, type of alcoholic beverage and joint effect of smoking
				Current drinker	66	1 (reference)		
				1–4 years	8	1.4 (0.6–3.2)		
				5–9 years	4	1.3 (0.4–4.3)		
				≥10 years	3	0.4 (0.1–1.5)		
Never drinker	4	0.2 (0.1–0.5)						
			<i>p</i> for trend			0.0007		

CI, confidence interval; ICD, International Classification of Diseases

Table 2.9 Risk of consumption of alcoholic beverages for cancers of the oral cavity and pharynx among nonsmokers

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Talamini <i>et al.</i> (1990a), Milan, Pordenone, Italy, 1986–89	27 (six men, 21 women) 572 (288 men, 284 women) hospital-based; matched on age, area of residence	Interviewer-administered questionnaire	Oral cavity, pharynx	<i>Total alcohol</i> <14 drinks/week 14–55 drinks/week >55 drinks/week χ^2 for trend	11 14 2	1 (reference) 1.5 (0.6–3.7) 2.2 (0.2–27.9) 4.08 ($p=0.04$)	Age, sex	Includes study population from Franceschi <i>et al.</i> (1990); reference group included '0' drinks/week and <14 drinks/week

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Ng <i>et al.</i> (1993), USA, 1977–91	173 (100 men, 73 women) whites in eight US cities; histologically confirmed 613 (254 men, 359 women) hospital-based; matched (up to 4:1 controls:cases) on age, sex, date of interview; excluded patients with tobacco-related conditions	Interviewer-administered questionnaire	Oral cavity, pharynx (ICD9 141, 143–146, 148, 149)	<i>Total alcohol (oz. of whiskey equiv./day)</i> Men Non-drinker <1 oz/day 1–2.9 oz/day 3–6.9 oz/day ≥7 oz/day χ^2 for trend Women Non-drinker <1 oz/day 1–2.9 oz/day 3–6.9 oz/day ≥7 oz/day χ^2 for trend	13 20 19 13 8	1 (reference) 1.3 (0.6–3.1) 2.4 (1.0–5.6) 2.9 (1.1–7.6) 4.4 (1.4–13.7) 11.7 ($p<0.001$) 1 (reference) 0.9 (0.5–1.6) 0.9 (0.3–2.6) 0.4 (0.0–7.1) 2.6 (0.5–13.3) 0.00 (NS)		Nonsmokers of study from Kabat <i>et al.</i> (1994)

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Talamini <i>et al.</i> (1998), Italy, Switzerland, 1992–97	60 (20 men, 40 women) from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland); aged 22–77 years; histologically confirmed; response rate, 95% 692 (346 men, 346 women) hospital-based; response rate, 95%	Interviewer-administered questionnaire	Oral cavity, pharynx	<i>Total alcohol</i>			Age, sex, education, study centre	Study population from Franceschi <i>et al.</i> (2000)
				Never drinkers	16	1 (reference)		
				<21 drinks/week	23	0.8 (0.4–1.6)		
				21–34 drinks/week	4	0.8 (0.2–2.7)		
				35–55 drinks/week	7	5.0 (1.5–16.1)		
				≥56 drinks/week	3	5.3 (1.1–24.8)		
Former drinkers (abstain ≥1 year)	7	2.0 (0.7–5.4)						
			χ^2 for trend			6.2 (0.01)		

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Fioretti <i>et al.</i> (1999), Milan, Pordenone, Italy, 1984–93	42 (10 men, 32 women) lifelong nonsmokers from a network of general hospitals in Milan and Pordenone; histologically confirmed 864 (442 men, 422 women) hospital-based non-cancer nonsmokers; matched on age, area of residence; excluded patients with tobacco-related conditions	Interviewer-administered questionnaire	Oral cavity, pharynx	<i>Total alcohol</i>				Age, sex, education, study centre	Study population from Franceschi <i>et al.</i> (1990)
				Non-drinkers	4	1 (reference)			
				>0–<3 drinks/day	25	3.4 (1.1–10.1)			
				≥3 drinks/day	13	2.6 (0.7–9.3)			
				Wine drinkers	37	3.3 (1.1–9.6)			
Beer drinkers	7	3.3 (0.7–16.4)							
Spirit drinkers	5	1.0 (0.2–6.1)							

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hashibe <i>et al.</i> (2007a), International Consortium of Head and Neck Cancer; combined analysis of 15 studies from USA, South and Central American, European countries	383 who never used tobacco 5775 who never used tobacco	Interview or self-administered questionnaire	Oral cavity (ICD9 140, 141, 143–5)	<i>Total alcohol</i>			Adjusted for age, sex, race/ethnicity, education, study centre	
				Never	243	1.00 (reference)		
				Ever	137	1.17 (0.92–1.48)		
				<1 drink/day	44	1.14 (0.8–1.63)		
				1–2 drinks/day	60	1.64 (1.19–2.25)		
				3–4 drinks/day	10	1.11 (0.57–2.15)		
				≥5 drinks/day	8	1.23 (0.59–2.57)		
				<i>p</i> for trend		0.032		
				<i>Duration</i>				
				1–10 years	21	2.36 (1.43–3.88)		
				11–20 years	17	1.09 (0.65–1.85)		
				21–30 years	19	0.81 (0.49–1.33)		
31–40 years	35	1.29 (0.88–1.9)						
>40 years	32	1.15 (0.77–1.73)						
<i>p</i> for trend		<0.001						

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hashibe <i>et al.</i> (2007a) (contd)	369 who never used tobacco 5775 who never used tobacco		Oro-pharynx/ hypo-pharynx (ICD9 146, 148)	<i>Total alcohol</i>				
				Never	153	1.00 (reference)		
				Ever	216	1.38 (0.99–1.94)		
				<1 drink/day	73	1.39 (0.99–1.96)		
				1–2 drinks/day	83	1.66 (1.18–2.34)		
				3–4 drinks/day	24	2.33 (1.37–3.98)		
				≥5 drinks/day	29	5.50 (2.26–13.36)		
				<i>p</i> for trend		<0.001		
				<i>Duration</i>				
				1–10 years	18	1.76 (0.99–3.14)		
				11–20 years	28	1.34 (0.81–2.11)		
				21–30 years	63	1.95 (1.37–2.77)		
				31–40 years	61	1.44 (0.78–2.66)		
>40 years	37	1.51 (0.68–3.37)						
<i>p</i> for trend		<0.001 (0.003)						

Table 2.9 (continued)

Reference, study location, period	Characteristics of study population	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hashibe <i>et al.</i> (2007a) (contd)	155 who never used tobacco 4983 who never used tobacco		Oral cavity or pharynx NOS (ICD9)	<i>Total alcohol</i>				
				Never	80	1.00 (reference)		
				Ever	72	1.09 (0.77–1.54)		
				<1 drink/day	25	1.08 (0.67–1.75)		
				1–2 drinks/day	26	1.24 (0.77–1.99)		
				3–4 drinks/day	13	2.32 (1.24–4.34)		
				≥5 drinks/day	4	0.77 (0.27–2.18)		
				<i>p</i> for trend		<0.891		
				<i>Duration</i>				
				1–10 years	13	2.59 (1.38–4.86)		
				11–20 years	11	1.09 (0.56–2.11)		
				21–30 years	18	1.26 (0.73–2.17)		
				31–40 years	14	0.86 (0.47–1.57)		
>40 years	13	0.92 (0.49–1.71)						
<i>p</i> for trend		<0.014						

CI, confidence interval; ICD, International Classification of Diseases; NOS, not otherwise specified; NS, not significant

cases from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland) were identified from 1992 to 1997 and compared with 692 hospital-based controls (Talamini *et al.*, 1998). Again, a dose–response relationship was seen between alcoholic beverage consumption and cancer of the oral cavity and pharynx ($P=0.01$). The Pooling Project, the International Head and Neck Cancer Epidemiology Consortium, reported associations between alcoholic beverage consumption and oral and pharyngeal cancer among nonsmokers (Hashibe *et al.*, 2007a). The study included 384 cases of oral cancer, 369 oropharyngeal or hypopharyngeal cancers, 155 cases of oral and pharyngeal (not otherwise specified) cancer and 5775 controls. A significant dose–response relationship was observed for oro- and hypopharyngeal cancer for both frequency and duration of alcoholic beverage consumption. The adjusted odds ratios were 1.66 (95% CI, 1.18–2.34) for 1–2 drinks per day, 2.33 (95% CI, 1.37–3.98) for 3–4 drinks per day and 5.5 (95% CI, 2.26–13.36) for five or more drinks per day. The association was weaker for cancer of the oral cavity.

In addition, among 25 studies of effect modification listed in Table 2.7, the effect of alcoholic beverage consumption was presented in 17 (Blot *et al.*, 1988; Franceschi *et al.*, 1990; Zheng *et al.*, 1990; Kabat *et al.*, 1994; Chyou *et al.*, 1995; Murata *et al.*, 1996; Sanderson *et al.*, 1997; Zheng *et al.*, 1997; Schildt *et al.*, 1998; Franceschi *et al.*, 1999; Hayes *et al.*, 1999; Schlecht *et al.*, 1999; Garrote *et al.*, 2001; Schwartz *et al.*, 2001; Balaram *et al.*, 2002; Boeing, 2002; Castellsagué *et al.*, 2004). The majority of these studies found a strong association with alcoholic beverage consumption among nonsmokers with a dose–response relationship. A strong association and a dose–response relationship between alcoholic beverage consumption and the risk for oral and pharyngeal cancers demonstrated strong evidence for the carcinogenic effect of alcoholic beverage consumption.

2.3 Cancer of the larynx

The consumption of alcoholic beverages and tobacco smoking are the two major risk factors for laryngeal cancer (Austin & Reynolds, 1996; Doll *et al.*, 1999). A relationship between the consumption of alcoholic beverages and cancer of the larynx was first suggested in the early 1900s by mortality statistics and clinical reports, and was subsequently supported by ecological studies that compared per-capita alcoholic beverage consumption and trends in the incidence of and mortality from laryngeal cancer (Wynder, 1952; Tuyns, 1982). However, the definition of alcoholic beverages as an independent etiological factor for laryngeal cancer and its quantification was not obtained until the late 1950s and early 1960s following ad-hoc epidemiological investigations (Schwartz *et al.*, 1962; Wynder *et al.*, 1976; Jensen, 1979).

Several case–control studies found an independent dose–risk relationship between alcoholic beverage consumption and the risk for laryngeal cancer, as well as a synergistic effect with tobacco smoking. Studies published up to 1988 were reviewed in a previous monograph (IARC, 1988). These included six prospective studies (Sundby, 1967;

Hakulinen *et al.*, 1974; Monson & Lyon, 1975; Robinette *et al.*, 1979; Jensen, 1980; Schmidt & Popham, 1981) and 14 case-control studies conducted in North America and Europe (Wynder *et al.*, 1956; Schwartz *et al.*, 1962; Vincent & Marchetta, 1963; Wynder *et al.*, 1976; Spaljckovic, 1976; Williams & Horm, 1977; Burch *et al.*, 1981; Herity *et al.*, 1982; Elwood *et al.*, 1984; Olsen *et al.*, 1985; Zagraniski *et al.*, 1986; Brugère *et al.*, 1986; Tuyns *et al.*, 1988). Four of the six prospective studies showed significant increases in risk. Furthermore, all of the case-control studies showed an association with alcoholic beverage consumption, and a trend in risk for the amount consumed, but no indication of a difference in risk for various types of alcoholic beverage. The previous IARC Working Group concluded that the occurrence of malignant cancer of the larynx was causally related to the consumption of alcoholic beverages (IARC, 1988).

However, several important aspects of the relationship between alcoholic beverage consumption and the risk for laryngeal cancer remained unsolved. These included the role of time-related variables, such as duration of the habit, age at starting, time since cessation of consumption for former drinkers and the effect of different types of alcoholic beverage. Further, the risk may differ by anatomical subsite, such as the supraglottis and the glottis/subglottis.

The epidemiological evidence for an association between alcoholic beverage consumption and the risk for laryngeal cancer includes at least four cohort and 18 case-control studies that have been published since 1988.

2.3.1 Cohort studies (Table 2.10)

Since 1988, six prospective studies have examined the relationship between alcohol beverage consumption and laryngeal cancer.

A study from Sweden (Adami *et al.*, 1992b) of 9353 individuals discharged from care facilities with a diagnosis of alcoholism, including 11 cases of laryngeal cancer, showed an SIR of 3.3 for this cancer type. No information on individual consumption of alcoholic beverages was available, although the level of consumption of these subjects was presumably much higher and of longer duration than that of the general population. Moreover, no adjustment was available for tobacco consumption or for other potentially confounding factors such as socioeconomic status or diet, although an unfavourable risk pattern in alcoholics is probable. In the largest study of subjects who had a hospital discharge diagnosis of alcoholism in Sweden (Boffetta *et al.*, 2001), the relative risk for laryngeal cancer was 4.21 (95% CI, 3.78–4.68; based on 347 cases).

The Honolulu Heart Program study (Chyou *et al.*, 1995) was based on 7995 American men of Japanese ancestry who lived in Hawaii, and included 93 cases of cancers of the oral cavity and pharynx, oesophagus and larynx. A strong dose-risk relationship with alcoholic beverage consumption was found with a relative risk of 4.7 for ≥ 25 oz/month of total alcoholic beverage intake, compared with non-drinkers. In a prospective study of 10 960 Norwegian men followed from 1962 through to 1992 (Kjaerheim

Table 2.10 Selected prospective studies of laryngeal cancer and alcoholic beverage consumption

Reference, location	Study subjects	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Adami <i>et al.</i> (1992b), Uppsala, Sweden	9353 patients, 8340 men, 1013 women diagnosed with alcoholism from the Uppsala In-patient Register	Not reported	<i>Men</i>	3.1 (1.5–5.7)	Age, sex	SIR reported
			10			
			<i>Women</i>	23.2 (0.3–129.1)		
			1			
<i>Total</i>	11	3.3 (1.7–6.0)				
Chyou <i>et al.</i> (1995), Japan	7995 men of Japanese-American descent; interviewed and examined from 1965–1968; aged 45–68 years; identified through continuous surveillance of Oahu hospitals and linkage with the Hawaiian Tumor Registry	Non-drinkers <4 oz/month 4–24.9 oz/month ≥25 oz/month	16	1.00	Age, number of cigarettes/day, number of years smoked	
			5	0.57 (0.21–1.57)		
			18	1.74 (0.88–3.41)		
			52	4.67 (2.62–8.32)		
				$p < 0.0001$		
Kjaerheim <i>et al.</i> (1998), Oslo, Norway	10 960 Norwegian men born between 1893 and 1929; no prior diagnosis of upper aerogastric tract disease	<i>Total alcohol</i> Never or <1 time/week Previously 1–3 times/week 4–7 times/week Unknown	26	1.00	Age, smoking level	
			4	0.9 (0.3–2.7)		
			18	1.1 (0.6–1.9)		
			19	3.9 (2.1–7.1)		
			4	0.6 (0.2–1.8)		
	$p = 0.003$					

Table 2.10 (continued)

Reference, location	Study subjects	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Boffetta <i>et al.</i> (2001), Sweden	182 667 patients with a diagnosis of alcoholism aged 20 years or over and hospitalized during 1965–1994; identified in the In-patient Register and the National Cancer Register	Not reported	347	4.21 (3.78–4.68)	Not reported	SIR reported

CI, confidence interval; SIR, standardized incidence ratio

et al., 1998) that included 71 incident cases of upper digestive tract and respiratory neoplasms, the relative risk for the highest level of alcoholic beverage consumption (4–7 times/week) was 3.9 compared with never or occasional drinkers. These results were not confounded by marital status, occupational group or body-mass index. In the two latter prospective studies, no separate risk estimates were given for laryngeal cancer.

2.3.2 Case-control studies (Table 2.11)

Twenty case-control studies published since 1988 have included information on alcoholic beverage consumption and laryngeal cancer. All of these included overall allowance for tobacco use. Two additional case-control studies from China of 99 and 116 patients also found an excess risk in heavy alcoholic beverage drinkers, but did not allow for tobacco smoking.

The dose-risk relationship between alcoholic beverage consumption and major digestive and respiratory tract neoplasms was estimated from the data of a series of Italian case-control studies using regression spline models, and showed substantial increases in risk for laryngeal cancer with regular consumption of more than 50 g ethanol per day (Polesel *et al.*, 2005).

A meta-analysis of 20 case-control studies (Bagnardi *et al.*, 2001) included over 3500 cases of laryngeal cancer and reported a strong direct trend in risk, with multivariate relative risks of 1.38 (95% CI, 1.32–1.45) for 25 g alcohol per day, 1.94 (95% CI, 1.78–2.11) for 50 g per day and 3.95 (95% CI, 3.43–4.57) for 100 g per day, based on a dose-risk regression model. Corrao *et al.* (2004) found significantly increased risks for laryngeal cancer when comparing point-based and model-based relative risks to that of meta-pooled relative risks from studies that provided information on low doses (i.e., ≤ 25 g of alcohol per day), thus confirming the evidence of an association for modest doses as well.

2.3.3 Subsites of the larynx (Table 2.12)

The larynx can be divided into the supraglottis (also called extrinsic larynx) and epilarynx, which border on the hypopharynx, and the glottis (also called intrinsic larynx) and subglottis, which lie wholly within the respiratory system (Spleissl *et al.*, 1990). These various subsites of the larynx are exposed to potential carcinogens at different levels: the glottis and subglottis are more highly exposed to inhaled agents and the supraglottis to ingested agents, while the junctional area between the larynx and the pharynx is exposed to both inhaled and ingested agents. Thus, each site could react differently to different etiological factors.

At least seven case-control studies (Brugère *et al.*, 1986; Guénel *et al.*, 1988; Falk *et al.*, 1989; Maier *et al.*, 1992b; Muscat & Wynder, 1992; Talamini *et al.*, 2002; Menvielle *et al.*, 2004) and one meta-analysis (Bagnardi *et al.*, 2001) suggested that the risk from alcoholic beverage consumption was stronger for cancer of the supraglottis than for

Table 2.11 Case-control studies of laryngeal cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Burch <i>et al.</i> (1981), Canada, 1977-79	204 newly diagnosed cases of laryngeal cancer; 100% histologically confirmed	204 individually matched neighbourhood controls, matched on age (± 5 years), sex		<i>Ounces of ethanol in lifetime</i> 0 <10 000 10 000-25 000 ≥ 26 000		1.0 2.0 3.9 7.7	Smoking	Presented results were limited to men
Elwood <i>et al.</i> (1984), Canada 1977-1980	374 patients diagnosed primary epithelial cancers of the oral cavity, oro- and hypopharynx and larynx	374 patients diagnosed with another cancer within 3 months of the date of diagnosis of the study patient; diagnoses were not related to smoking, alcohol or occupational exposure; 1:1 matched for age (± 2 years), sex; interview time of patient (within 3 years)	Larynx (ICD0 161)	See Table 2.12	See Table 2.12	See Table 2.12	Socioeconomic status, marital status, dental care, history of tuberculosis, smoking	Including age and sex in the multivariate model did not substantially change the estimates.
Olsen <i>et al.</i> (1985), Denmark 1980-82	326 newly diagnosed cases of laryngeal cancer	1134 matched for sex and closest date of birth	ICD161.1, 161.2, 161.0	See Table 2.12	See Table 2.12	See Table 2.12		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Brugère <i>et al.</i> (1986), France 1975–82	2540 male patients with cancer of larynx, pharynx and mouth, selected from male and female patients treated in the Neck and Head Department of the Institut Curie in Paris	National Institute of Statistics and Economic Studies data; more than 4000 men; stratified by age and cancer location for analysis		See Table 2.12	See Table 2.12	See Table 2.12	Smoking	Data collected by different methods between patients and controls
Guénel <i>et al.</i> (1988), France, 1975–85	197 glottis, 214 supraglottis; males >25 years old; cases with squamous-cell carcinoma	4135 controls from the population	ICD-8 161.5, 161.4	See Table 2.12	See Table 2.12	See Table 2.12	Age, tobacco	Relative risk for combined heavy tobacco and alcoholic beverage consumption, 289.4 (83.0–705.8) for glottis and 1094 (185.8–2970.7) for supraglottis
Tuyns <i>et al.</i> (1988), France, Italy, Spain, Switzerland	727 endolarynx, 188 epilarynx	3057 men from the population		0–20 g/day 21–40 g/day 41–80 g/day 81–120 g/day ≥121 g/day		1 (reference) 0.9 (0.7–1.3) 1.1 (0.8–1.5) 1.7 (1.2–2.4) 2.6 (1.8–3.6)	Age, residence, smoking	Relative risk for >120 g/day: 2.6 for endolarynx, 10.6 for epilarynx

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Falk <i>et al.</i> (1989), Texas, USA, 1975–80	151 men from 56 hospitals in Texas and identified through hospital records	235 identified from Texas Department of Public Safety drivers license files or HCFA medicare recipients roster; frequency-matched by residence, age, ethnicity	ICD-9 161.X, 231.0	Non-drinkers	13	1 (reference)	Age, residence, employment, smoking, fruit and vegetable consumption	No consistent linear trend in risk, but relatively low consumption
				<2 drinks/week	8	0.8 (0.3–2.6)		
				2–3 drinks/week	6	0.5 (0.2–1.6)		
				4–6 drinks/week	17	2.1 (0.8–5.3)		
				7–10 drinks/week	19	2.3 (0.9–5.8)		
				11–15 drinks/week	17	1.5 (0.6–3.8)		
				16–21 drinks/week	22	1.8 (0.7–4.6)		
				22–29 drinks/week	14	1.3 (0.5–3.4)		
≥30 drinks/week	35	2.1 (0.9–5.0)						
Franceschi <i>et al.</i> (1990), Italy, 1986–89	162 men with laryngeal cancer from hospitals in northern Italy	1272 men admitted with acute illnesses not related to alcohol or tobacco consumption	ICD-9 161	<i>Total number of drinks per week</i>			Age, smoking, residence, education, occupation	Combined effect with tobacco compatible with a multiplicative effect
				≤19	39	1 (reference)		
				20–34	27	0.8 (0.5–1.4)		
				35–59	51	1.3 (0.8–2.1)		
				≥60	45	2.1 (1.2–3.8)		
Sankaranarayanan <i>et al.</i> (1990), India, 1983–84	191 men with squamous cell cancer	549 hospital patients attending the Regional Cancer Centre	ICD-0 161	Never	98	1 (reference)		No data on dose
				≥20 years	13	2.7 (0.9–4.5)		
				>21 years	47	4.2 (1.5–4.3) <i>p</i> -trend<0.001		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Ahrens <i>et al.</i> (1991), Germany, 1986–87	100 prevalent male cases of laryngeal cancer; cases recruited from Ear, Nose and Throat Clinic; 100% histologically confirmed	100 hospital controls with diseases not related to alcohol, smoking or occupational exposures; same age distribution as cases; admission diagnosis with an expected length of stay in hospital comparable with that of laryngeal cancer		Non-drinkers Occasional drinkers Daily drinkers	28	1 (reference) 3.2 (1.4–7.5) 1.1 (0.5–2.3)	Age, smoking, occupation	Number of cases among non-drinkers or daily drinkers not given
Choi & Kahyo (1991a), Seoul, Republic of Korea, 1986–89	94 male cases of laryngeal cancer; 100% histologically confirmed	282 hospital controls from Korea Cancer Center Hospital; non-cancer, non-alcohol or tobacco-related diseases	161	Non-drinkers Light Moderate Medium–heavy Heavy	17 5 28 29 15	1 (reference) 0.3 (0.1–0.7) 1.2 (0.6–2.5) 2.4 (1.2–4.9) 11.1 (3.8–32.4)	Age (matched), smoking	Data related to alcohol consumption among women were limited.

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Zatonski <i>et al.</i> (1991), Warsaw, Poland, 1986–87	249 men with cancer of the larynx; 70% supraglottis, 30% glottis; response rate, 88%	965 men from the general population aged 25–65 years; response rate, 94%		Irregular	142	1 (reference)	Age, residence, education, smoking	Vodka main type of alcoholic beverage; higher risk for regular than for irregular drinkers
				1–15 years	18	3.4 (1.6–7.0)		
				16–30 years	65	9.5 (5.2–17.2)		
Freudenheim <i>et al.</i> (1992), New York, USA, 1975–85	250 pathologically confirmed cases of laryngeal cancer; white men	250 age- and neighbourhood-matched controls		0–339 drinks/year	32	1 (reference)	Education, smoking	Race and gender differences
				340–1243 drinks/year	33	1.5 (0.7–3.2)		
				1244–2925 drinks/year	48	1.1 (0.6–2.1)		
				≥2926 drinks/year	137	3.5 (1.8–6.9)		
						<i>p</i> -trend<0.001		
Maier <i>et al.</i> (1992b), Germany, 1988–89	164 men with histologically proven squamous-cell carcinoma	656 matched male controls with no known tumorous disease selected from outpatient clinics		<25 g/day 25–75 g/day ≥75 g/day		1 (reference) 2.6 (1.6–4.0) 9.0 (5.2–15.53)	Age, residence, smoking	Number of cases not reported

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Muscat & Wynder (1992), USA, 1985–90	194 men with histologically confirmed laryngeal cancer; Memorial Sloan-Ketterling and 7 other hospitals	184 hospital controls admitted for unrelated tobacco-induced disease; age matched (± 5 years)		Never/	40	1 (reference)	Age (matched), education, smoking, quetelet index	Relative risk 14.8 for binge drinkers
				<29.6 mL/day	19	1.1 (0.6–2.3)		
				29.7–88.9 mL/day	41	2.8 (1.5–5.2)		
				89–206 mL/day	55	4.8 (2.5–9.4)		
Zheng <i>et al.</i> (1992), China, 1988–90	201 male residents of urban Shanghai; aged 20–75 years diagnosed with laryngeal cancer	414 hospital controls; age and sex matched; Shanghai Resident Registry	ICD-9 161.0–161.9	Binge drinkers	31	14.8 (1.6–46.3)	Age, education, smoking	Absence of association attributed to alcoholic beverage consumption during meals; data for female alcohol consumption not presented
				Never drinkers	80	1 (reference)		
				<144 g/week	16	0.8 (0.4–1.7)		
				144–284 g/week	22	1.0 (0.5–2.0)		
				285–479 g/week	27	0.9 (0.5–1.9)		
Hedberg <i>et al.</i> (1994), western Washington, USA, 1983–87	235 patients with laryngeal cancer aged 20–74 years; from 3 counties in western Washington state; response rate, 81%	547 controls identified through random-digit dialing; response rate, 75%	ICD-9 161.0–161.9	≥ 480 g/week	32	0.8 (0.4–1.6)	Age, sex, smoking, MAST score	
				<7 drinks/week	89	1 (reference)		
				7–13 drinks/week	42	1.9 (1.1–3.2)		
				14–20 drinks/week	27	2.1 (1.0–4.4)		
				21–41 drinks/week	37	2.8 (1.4–5.7)		
>42 drinks/week	24	3.1 (1.2–7.9)						

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Dosemeci <i>et al.</i> (1997), Istanbul, Turkey, 1979–84	832 men with laryngeal cancer; selected from oncology treatment centre	829 hospital patients with selected cancers not related to alcohol or tobacco use	ICD-0 161.0–161.3; 161.9	Never drinkers	625	1 (reference)	Age, smoking	Possible underestimation of alcohol drinking due to low social acceptance; females excluded due to low prevalence of smoking and alcohol use among women in Turkey
				1–35 cL/week	46	1.7 (1.0–3.2)		
				36–140 cL/week	85	1.8 (1.1–2.9)		
				>141 cL/week	41	1.5 (0.8–2.9)		
Rao <i>et al.</i> (1999), India, 1980–84	427 men diagnosed with cancer of vocal cords, supraglottis and larynx	635 male hospital patients free from cancer, infectious disease and benign lesions	ICD-9 161.0, 161.1, 161.9	Non-drinkers	308	1 (reference)		Multivariate relative risk for drinkers versus non-drinkers, adjusted for tobacco smoking and chewing and education, 1.64 (1.16–2.31; $p=0.005$)
				Once per day	85	1.5 (1.0–2.2)		
				Twice per day	17	2.8 (1.4–7.5)		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Schlecht <i>et al.</i> (2001), Brazil, 1986–89	784 newly diagnosed cases of carcinoma of the oral cavity, pharynx and larynx; selected from hospitals in 3 metropolitan areas in Brazil	1578 controls 2:1 matched by age (± 5 years), gender, trimester of admission	ICD-9 140–145, 146–149, 161	>100 kg of lifetime condumption versus non-drinker Beer Wine Hard liquor	39 60 61	1.8 (0.6–5.7) 1.5 (0.6–4.0) 1.3 (0.6–5.4)	Age, study location, admission period, tobacco smoking, remaining alcohol consumption, income, education, race, beverage temperature, religion, wood stove use, consumption of spicy food Smoking	
Bosetti <i>et al.</i> (2002), Italy, Switzerland, 1986–92; 1992–2000	40 non smoking cases and 68 non-drinking cases of laryngeal cancer; aged 30–74 years	160 nonsmoking and 161 non-drinking controls matched on study, sex, age, study centre; aged 31–79 years; admitted for acute, non-neoplastic conditions		Drinks per day <8 ≥ 8	31 9	1 2.46 (0.98–6.20)		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Talamini <i>et al</i> (2002), Italy, Switzerland, 1992–2000	527 cases of squamous-cell carcinoma of the larynx; <79 years old; response rate, 97%	1297 hospital subjects admitted for non-alcohol-or tobacco-related illnesses	ICD-9 161.0–161.3, 161.8, 161.9	Abstainers	19	1 (reference)	Age, sex, centre, education, smoking	No clear risk for duration; association in women too
				>0–13 drinks/week	37	0.9 (0.5–1.8)		
				14–27 drinks/week	68	1.2 (0.6–2.2)		
				28–55 drinks/week	159	2.6 (1.4–4.7)		
Corrao <i>et al.</i> , (2004) 1966–1998	Meta analyses of 99 case-control and 57 cohort studies published between 1966–88; for larynx, 20 case-control studies were the basis of the analysis			≥56 drinks/week	184	5.9 (3.1–11.3)		
						<i>p</i> -trend<0.0001		
				25 g/day		1.43 (1.38–1.48)		
				50 g/day		2.02 (1.89–2.16)		
			100 g/day		3.86 (3.42–4.35)			

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Menvielle <i>et al.</i> (2004), France, 1989–91	504 men (125 glottis, 80 supraglottis, 97 epiglarynx, 201 hypopharynx)	242 men with non-respiratory cancers; frequency-matched by age	ICD-10 C32	Occasional drinkers	22	1 (reference)	Age, tobacco	Relative risk higher for hypopharynx compared with the glottis, supraglottis and epipharynx
				1–2 drinks/day	56	1.4 (1.2–1.6)		
				3–4 drinks/day	80	2.0 (1.5–2.7)		
				5–8 drinks/day	156	2.9 (1.9–4.4)		
				9–12 drinks/day	109	4.1 (2.4–7.2)		
				≥13 drinks/day	81	5.9 (2.9–11.8)		
Lee <i>et al.</i> (2005), Taiwan, China, 2000–03	128 male laryngeal cancer patients	255 hospital controls non-frequency matched; 40 years of age and older	ICD-10 C32	Non-drinkers	56	1 (reference)	Age, tobacco, use of betel quid	
				≤750 mL	52	3.1 (1.7–5.8)		
				>750 mL	15	10.3 (3.0–42.5) <i>p</i> -trend<0.0001		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Polesel <i>et al.</i> (2005), Italy, Switzerland, 1982–99	588 histologically confirmed cases of laryngeal cancer	1663 patients <80 years of age, admitted to the same network of hospitals as cases, any acute non-neoplastic condition frequency matched by area of residence, age and year of interview						Spline models showed an increased risk with increasing alcohol consumption. See Polesel <i>et al.</i> (2005) for details regarding the estimation of spline model fit.
Garavello <i>et al.</i> (2006), Italy, 1986–2000	672 cases of laryngeal cancer (613 men and 59 women) aged 30–80 years; histologically confirmed; admitted to major teaching and general hospitals	3454 hospital-based controls (2646 men, 808 women); admitted to same network of hospitals as cases for non-neoplastic conditions not associated with smoking or alcohol		<i>Total alcohol</i>			Study centre, sex, age, education, body mass index, smoking	Pattern of increasing risk with increasing number of drinks was similar for drinkers of wine only and of wine plus beer and spirits; *for multivariate models, abstainers (0 drinks/day) or light drinkers (1–2 drinks/day) were compared with other levels of drinking.
				0	46	1.00		
				1–2 drinks/day	96	*		
				3–4 drinks/day	111	1.12 (0.83–1.50)		
				5–7 drinks/day	149	2.43 (1.79–3.28)		
				8–11 drinks/day	180	3.65 (2.68–4.98)		
				≥12 drinks/day	84	4.83 (3.18–7.33)		
						$p < 0.0001$		

Table 2.11 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hashibe <i>et al.</i> (2007a), central and eastern Europe, 2000–02	384 incident (254 glottis, 108 supraglottis)	918 hospital	ICD-10 C32.0, C32.1, C32.2, C32.8, C32.9	Non-drinker	6	0.6 (0.22–1.65)	Age, sex, education, body mass index, fruit intake, study centre, pack-years of tobacco use	Significant trend in risk with dose; direct relation of borderline significance with duration of drinking
				1–139.9 g/week	161	1 (reference)		
				140–279 g/week	94	1.57 (1.05–2.33)		
				280–419 g/week	29	1.13 (0.62–1.99)		
≥420 g/week	80	1.45 (0.92–2.26)	<i>p</i> -trend=0.08					

CI, confidence interval; HCFA, Health Care Financing Administration; ICD, International Classification of Diseases; MAST, Michigan alcoholism-screening test

Table 2.12 Selected case–control studies of alcoholic beverage consumption and cancer of the larynx by anatomical subsite

Reference	Amount of alcohol consumption	Relative risk (95% CI)					
		No. of cases	Epilarynx	No. of cases	Supraglottis	No. of cases	Glottis/subglottis
Elwood <i>et al.</i> (1984)	≥20 oz/week vs <1			46	6.4	108	2.2
Olsen <i>et al.</i> (1985)	≥301 g/week vs 0–100			191	3.0	103	5.0
Brugère <i>et al.</i> (1986)	≥160 g/day vs 0–40	217	101.4 (44–233.9)	224	42.1 (20.5–86.4)	242	6.1 (3.4–10.9)
Guénel <i>et al.</i> (1988)	≥160 g/day vs ≤39 g/day			81	35.7 (19.2–66.5)	61	14.9 (8.7–25.4)
Tuyns <i>et al.</i> (1988)	≥121 g/day vs 0–20	118	10.6 (4.4–25.8)	426	2.0 (1.3–3.0)	270	3.4 (2.1–5.6)
Falk <i>et al.</i> (1989)	20 drinks/week vs non-drinkers			9	4.6 (0.6–39.1)	40	1.8 (0.8–4.0)
Maier <i>et al.</i> (1992b)	>75 g/day versus <25				11.8 (4.5–29.6)		7.9 (3.5–17.7)
Muscat & Wynder (1992)	>207 mL/day vs never/<29.6			33	9.6 (3.3–27.6)	72	2.5 (1.0–6.2)
Dosemeci <i>et al.</i> (1997)	>141 cL/week vs never drinker			385	1.3 (0.6–2.8)	183	1.5 (0.6–3.6)
Talamini <i>et al.</i> (2002)	≥56 drinks/week vs 0–13			49	11.7 (3.2–42.3)	95	4.9 (2.1–11.7)
Menvielle <i>et al.</i> (2004)	>13 glasses/day vs 1–2	13	6.6 (2.4–17.7)	12	4.1 (1.4–11.5)	14	2.9 (1.1–7.1)

CI, confidence interval

cancer of the glottis/subglottis. Conversely, other studies reported similar risks for both supraglottis and glottis/subglottis (Flanders & Rothman, 1982; Tuyns *et al.*, 1988; Hedberg *et al.*, 1994). In a multicentric study in France, Italy, Spain and Switzerland (Tuyns *et al.*, 1988) and in two French studies (Brugère *et al.*, 1986; Menvielle *et al.*, 2004), a stronger effect of alcoholic beverage consumption was found for the epilarynx.

The available evidence thus indicates that the highest risks related to the consumption of alcoholic beverages tend to occur in tissues that come into close contact with both alcoholic beverages and tobacco smoke. Thus, alcoholic beverage consumption may influence the risk for laryngeal cancer particularly through its direct contact or solvent action, perhaps by enhancing the effects of tobacco or other environmental carcinogens.

2.3.4 *Types of alcoholic beverage (Table 2.13)*

Several studies have investigated whether the risk for laryngeal cancer depends on the type of alcoholic beverage consumed. In a cohort study in Hawaii (Chyou *et al.*, 1995) of 93 cancers of the upper digestive and respiratory tract, no substantial difference in risk was found between the highest levels of consumption of beer (relative risk, 3.7), wine (relative risk, 3.8) or spirits (relative risk, 3.6). Another prospective study in Norway (Kjaerheim *et al.*, 1998) of upper digestive and respiratory tract cancers found a higher risk for elevated consumption of beer (relative risk, 4.4) compared with that of spirits (relative risk, 2.7). However, due to the limited number of cases, specific analysis of laryngeal cancer was not possible in these two cohort studies.

Among case–control studies, a Canadian study (Burch *et al.*, 1981) found an increase in risk among heavy beer drinkers (odds ratio, 4.8), but no consistent increase for spirit (odds ratio, 1.3) or wine drinkers (odds ratio, 0.5). Similarly, a case–control study from Denmark (Olsen *et al.*, 1985) of 326 cases of laryngeal cancer and 1134 controls reported a higher risk in drinkers who preferably consumed beer (odds ratio, 1.4) than in those who preferred wine (odds ratio, 0.6) or spirits (odds ratio, 1.0). A case–control study in Uruguay (De Stefani *et al.*, 1987) of 107 cases of laryngeal cancer and 290 controls showed a higher risk for wine (odds ratio, 7.4) than for hard liquors (odds ratio, 4.0). In an Italian study (Franceschi *et al.*, 1990), wine was associated with the highest risk (odds ratio, 4.2), whereas a lower risk was reported for beer (odds ratio, 1.5) and hard liquors (odds ratio, 0.8). In a case–control study conducted in the USA (Muscat & Wynder, 1992), based on 250 cases, an increased risk for laryngeal cancer was found for heavy drinkers of beer (odds ratio, 2.7) and hard liquors (odds ratio, 2.2), but not for wine drinkers (odds ratio, 1.1). No strong differences were seen between consumption of beer, hard liquors or wine in a case–control study in Brazil (Schlecht *et al.*, 2001) that included 194 cases of laryngeal cancer: the relative risk was 1.8 for high consumption of hard liquors and beer and 1.5 for that of wine. Higher risks were observed for cachaça (relative risk, 9.9), a typical Brazilian hard liquor. In a case–control study in Italy and Switzerland (Talamini *et al.*, 2002),

Table 2.13 Selected case–control studies of laryngeal cancer and consumption of different types of alcohol beverage

Reference, study location	Level of alcohol intake	Relative risk (95% CI)					
		No. of cases	Beer	No. of cases	Wine	No. of cases	Hard liquors
Burch <i>et al.</i> (1981), Canada	Beer/spirits: ≥ 4 drinks/day versus non-drinker Wine: ever used versus never		4.8 (2.4–9.8)		0.5 (0.2–0.9)		1.3 (0.5–3.4)
Olsen <i>et al.</i> (1985), Denmark	Preferred type of alcohol		1.4 (1.1–1.9)		0.6 (0.4–0.9)		1.0 (0.6–1.8)
De Stefani <i>et al.</i> (1987), Uruguay	>201 mL/day versus non-drinker		–		7.4 (3.0–18.1)		4.0 (1.9–8.2)
Franceschi <i>et al.</i> (1990), Italy	Beer: >14 drinks/week versus 0 Wine: ≥ 84 versus 0–6 Hard liquors: >7 versus 0	25	1.5 (0.8–2.5)	10	4.2 (1.6–10.6)	35	0.8 (0.5–1.3)
Freudenheim <i>et al.</i> (1992), USA	Beer: ≥ 1873 drinks/year versus 0–32 Wine: ≥ 139 versus 0 Hard liquors: ≥ 438 versus 0	123	2.7 (1.4–5.1)	67	1.1 (0.6–2.0)	117	2.2 (1.2–4.0)
Schlecht <i>et al.</i> (2001), Brazil	>100 kg of lifetime consumption versus non-drinkers	39	1.8 (0.6–5.7)	60	1.5 (0.6–4.0)	61	1.8 (0.6–5.4)
Talamini <i>et al.</i> (2002), Italy, Switzerland	Beer: >1 drinks/week versus 0–1 Wine: ≥ 42 versus 0–13 Hard liquors: >3 versus 0–3	167	3.3 (1.8–6.1)	210	5.2 (2.8–9.9)	182	2.9 (1.5–5.8)
Garavello <i>et al.</i> (2006), Italy	Beer: ≥ 3 drinks/day Wine: ≥ 12 drinks/day Spirits: ≥ 3 drinks/day	37	1.3 (0.9–2.2)	56	5.9 (3.5–10.0)	37	1.2 (0.7–2.0)

CI, confidence interval

the risk was slightly higher for wine drinkers than for beer and hard liquor drinkers (odds ratios, 5.2, 3.2 and 2.9, respectively). Case-control studies conducted in Italy between 1986 and 2000 (Franceschi *et al.*, 1990; Talamini *et al.*, 2002; Garavello *et al.*, 2006) included 672 cases of laryngeal cancer and 3454 hospital controls, admitted for acute, non-neoplastic conditions that were unrelated to smoking or alcoholic beverage consumption. Significant trends in risk were found for total alcoholic beverage intake, with multivariate odds ratios of 1.12 for drinkers of 3–4 drinks per day, 2.43 for 5–7, 3.65 for 8–11 and 4.83 for >12 drinks per day compared with abstainers or light drinkers. Corresponding odds ratios for wine drinkers were 1.12, 2.45, 3.29 and 5.91. After allowance was made for wine intake, the odds ratios for beer drinkers were 1.65 for 1–2 drinks per day and 1.36 for ≥ 3 drinks per day compared with non-beer drinkers; corresponding values for spirit drinkers were 0.88 and 1.15. Thus, in the Italian population which is characterized by frequent wine consumption, wine is the beverage most strongly related to the risk for laryngeal cancer.

Taken together, these data suggest, however, that the most frequently consumed beverage in each population tends to be that which yields the highest risk, and that ethanol is the main component of alcoholic beverages that determines the risk for cancer.

2.3.5 *Joint effects*

Several investigations have considered the combined effect of tobacco smoking and alcoholic beverage consumption on the etiology of cancer of the larynx (Flanders & Rothman, 1982; Elwood *et al.*, 1984; Olsen *et al.*, 1985; De Stefani *et al.*, 1987; Guénel *et al.*, 1988; Tuyns *et al.*, 1988; Franceschi *et al.*, 1990; Choi & Kahyo, 1991a; Zatonski *et al.*, 1991; Maier *et al.*, 1992a; Zheng *et al.*, 1992; Chyou *et al.*, 1995; Dosemeci *et al.*, 1997; Schlecht *et al.*, 1999; Bagnardi *et al.*, 2001; Talamini *et al.*, 2002). These studies gave risk estimates for the highest level of consumption for both factors compared with the lowest level of between approximately 10 and over 100, and indicated that a multiplicative model rather than an additive model or risk could explain the level of risk from combined exposure to both factors. Separating the effects of alcoholic beverages and tobacco remains difficult, however, since heavy drinkers tend to be heavy smokers and vice versa. Furthermore, most studies included very few cases who neither smoked nor drank.

An example of the combined effect of alcoholic beverages and tobacco on laryngeal cancer was given by Talamini *et al.* (2002). Compared with never smokers/abstainers or light drinkers, the relative risk for laryngeal cancer increased with increasing alcoholic beverage consumption in each stratum of smoking habit to reach 177.2 in heavy drinkers and smokers compared with moderate drinkers and nonsmokers. Similar results were found for smoking within strata of alcoholic beverage intake. The odds ratio for the highest level of alcoholic beverage consumption and current smoking was 177.2. In a French study (Guénel *et al.*, 1988), the relative risk for combined heavy alcoholic beverage and tobacco consumption was 289.4 (95% CI, 83.0–705.8) for glottic and 1094.2

(95% CI, 185.8–2970.7) for supraglottic cancers. In a case–control study in Taiwan, China, the odds ratio for users of alcoholic beverages, betel quid and cigarettes compared with non-users was 40.3 (95% CI, 14.8–123.6) (Lee *et al.*, 2005).

2.3.6 *Effect of cessation of alcoholic beverage consumption*

The risk for laryngeal cancer declines steeply with time since stopping smoking (Olsen *et al.*, 1985; Guénel *et al.*, 1988; Tuyns *et al.*, 1988; Franceschi *et al.*, 1990; Freudenheim *et al.*, 1992; Kjaerheim *et al.*, 1993; Bosetti *et al.*, 2006). Data exist from only one study on time since stopping alcoholic beverage consumption. In a case–control study in Italy (Altieri *et al.*, 2002) that included a total of 59 former drinkers, the odds ratios were 1.24 for 1–5 years, 1.29 for 6–19 years and 0.53 for ≥ 20 years since cessation of drinking compared with current drinking. The risk approached that of never drinkers only after 20 years since cessation (odds ratio, 0.56).

Thus, while the favourable effect of stopping smoking is evident within a few years after cessation, that of stopping drinking becomes apparent only in the long term. Among current smokers that have stopped drinking, the persistence of exposure to tobacco may play an important role in limiting the benefits from cessation of drinking. These findings must, however, be interpreted with caution, since former drinkers may represent a select group of individuals whose average alcoholic beverage intake had exceeded that of current drinkers.

2.3.7 *Effect of Alcoholic beverage consumption in nonsmokers (Table 2.14)*

An independent role of alcoholic beverages on the incidence of laryngeal cancer has been suggested, but is difficult to quantify (Austin & Reynolds, 1996). In developed countries, cancer of the larynx is rare in nonsmokers, and only a few studies have included enough cases to provide useful information on the effect of alcoholic beverages in nonsmokers.

A case–control study from Canada (Burch *et al.*, 1981) of 204 cases and 204 matched controls reported an increased risk for laryngeal cancer in relation to alcoholic beverage consumption (odds ratio, 7.7 for $\geq 26\ 000$ oz ethanol in a lifetime) in never smokers based, however, on three case–control pairs only. A multicentric case–control study in France, Italy, Spain and Switzerland (Tuyns *et al.*, 1988) reported odds ratios of 1.7 for ≥ 80 g per day of alcohol among nine never-smoker cases of cancer of the endolarynx and of 6.7 for ≥ 40 g per day of alcohol among 22 nonsmoking cases of cancer of the epilarynx/hypopharynx. In a case–control in Italy conducted on 40 never-smoking cases, an excess risk (odds ratio, 2.5) for ≥ 8 drinks per day was found (Bosetti *et al.*, 2002).

A pooled analysis of never-tobacco users from 11 case–control studies, including 121 cases of laryngeal cancer and 4602 controls, showed an increased risk for laryngeal

Table 2.14 Selected case–control studies of laryngeal cancer and alcoholic beverage consumption in nonsmokers

Reference, study location	Exposure Categories	Number of cases	Relative risk (95% CI)
Burch <i>et al.</i> (1981), Canada	0 oz ethanol in lifetime	3	1 ^a (3)
	<10 000 oz ethanol in lifetime	3	2.0 (3)
	10 000–25 000 oz ethanol in lifetime	3	3.9 (3)
	≥26 000 oz ethanol in lifetime	3	7.7 (3)
Tuyns <i>et al.</i> (1988) ^b , France, Italy, Spain, Switzerland	0–40 g/day	7	1 ^a (7)
	40–80 g/day	3	1.5 (3)
	≥80 g/day	6	1.7 (6)
Bosetti <i>et al.</i> (2002), Italy, Switzerland	<8 drinks/day	31	1 ^a (31)
	≥8 drinks/day	9	2.5 (9)
Hashibe <i>et al.</i> (2007b), pooled analysis	Never drinkers		1.00 ^a
	<1 drink/day		0.92 (0.50–1.69)
	1–2 drinks/day		1.26 (0.77–2.07)
	3–4 drinks/day		1.24 (0.62–2.45)
	≥5 drinks/day		2.98 (1.72–5.17)
			<i>p</i> for trend <0.001

CI, confidence interval ^a Reference category ^b Relative risks are presented for endolarynx.

cancer with the consumption of ≥5 drinks per day (odds ratio, 2.98; 95% CI, 1.72–5.17) (Hashibe *et al.*, 2007b).

Thus, these studies confirmed that, even in a population of never smokers, elevated alcoholic beverage consumption increases the risk for laryngeal cancer. There is, however, no reason to suppose that tobacco smoking is the only carcinogenic agent to which the human upper respiratory and digestive tract is exposed, and ethanol may facilitate the effect of other unrecognized carcinogenic agents in nonsmokers, just as it commonly facilitates the effect of tobacco smoking (Doll *et al.*, 1999).

2.4 Cancer of the oesophagus

The evidence for the carcinogenic effects of alcoholic beverage consumption on the risk for oesophageal cancer was considered to be sufficient by a previous Working Group (IARC, 1988). Several epidemiological studies have been published since that time, and this section evaluates the risk for oesophageal cancer based on the relevant cohort and case–control studies after 1988.

The 18 cohort and 38 case–control studies conducted in Argentina, China, Denmark, Europe, India, Italy, Japan, Norway, Sweden, the United Kingdom, Uruguay and the

USA summarized in this section are described in Tables 2.15, 2.16 (literature originally in the Chinese language) and 2.17.

2.4.1 Cohort studies (Table 2.15)

(a) Special populations

Five cohort studies were based on either individuals who had high exposure to alcoholic beverages, such as alcoholics or workers in the brewery industry, or who had lower alcoholic beverage consumption, such as teetotalers (Carstensen *et al.*, 1990; Adami *et al.*, 1992b; Kjaerheim *et al.*, 1993; Tønnesen *et al.*, 1994; Boffetta *et al.*, 2001). This type of study does not usually consider individual exposure levels. The point estimates were either the SIRs or SMRs with no adjustment for tobacco smoking. The four studies of alcoholics or brewery workers reported a statistically significant association, and the point estimates of the SIR ranged from 2.5 to 5.5 (Carstensen *et al.*, 1990; Adami *et al.*, 1992b; Tønnesen *et al.*, 1994; Boffetta *et al.*, 2001); the point estimate was 0.26 for teetotalers (Kjaerheim *et al.*, 1993).

(b) General population

Thirteen cohort studies of the general population have been published, including two in the Chinese literature (Table 2.16), most of which adjusted for tobacco smoking. Ten cohort studies reported a statistically significant association between alcoholic beverage consumption and the risk for oesophageal cancer after controlling for tobacco smoking. In addition, these studies were carried out in different geographical regions of the world. The adjusted relative risks ranged from 2.8 in the USA (Thun *et al.*, 1997) to 14.5 in Japan (Kono *et al.*, 1987) for two or more drinks per day after adjusting for tobacco smoking. One study (Lindblad *et al.*, 2005) reported a positive association for adenocarcinoma of the oesophagus with a relative risk of 1.76 (95% CI, 1.16–2.66) for heavy drinkers.

The two cohort studies in Linxian County, China, based on the same population reported a null association (Guo *et al.*, 1994; Tran *et al.*, 2005). The null association between alcoholic beverage consumption and oesophageal cancer in rural high-risk areas of China is probably due to the relatively low consumption of alcoholic beverages in these areas or other strong risk factor(s) which may mask or highly confound the association between alcoholic beverage consumption and oesophageal cancer. Another study from the Chinese literature (Wang *et al.*, 2005a; Table 2.16) reported that an increased risk for oesophageal cancer was associated with elevated alcoholic beverage consumption (relative risk, 5.08 for >70 g/day or 5 or more drinks/day) after adjusting for tobacco smoking; however, no 95% CI was provided.

In summary, the results of the majority of the prospective cohort studies support that alcoholic beverage consumption can cause cancer of oesophagus.

Table 2.15 Cohort studies of oesophageal cancer and consumption of alcoholic beverages

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Special populations								
Kono <i>et al.</i> (1987), Japan, Japanese Physicians' Study	5130 male Japanese physicians, aged 27–89 years; followed up for 19 years, 1965–83; response rate, 51%	Self-administered questionnaire;	Oesophagus	Never and occasional Daily <2 go Daily ≥2 go		1.00 1.53 (0.14–16.83) 14.46 (3.00–69.71)	Age, smoking	No significant interaction with smoking ($p>0.05$); 1 go of sake ≈ 27 mL alcohol
Carstensen <i>et al.</i> (1990), Sweden	6230 men employed in the Swedish brewery industry in 1960, aged 20–69 years; followed-up 1961–79	Population census	Oesophagus	Not reported	20	2.46 (1.51–3.81)	Not reported	All Swedish men used as a reference group.
Adami <i>et al.</i> (1992b), Sweden, Uppsala Alcoholics Study	9353 (8340 men, 1013 women) with a discharge diagnosis of alcoholism in 1965–83; 94% confirmed microscopically; followed up for 19 years (mean, 7.7 years)	Record-linkage to the nationwide Registry of Causes of Death;	Oesophagus	<i>Years of follow-up</i> 1–4 5–9 10–19		SIR 11.7 (6.9–18.4) 3.7 (1.2–8.7) 4.6 (1.5–10.7)	Expected rates were derived from the study population.	

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kjaerheim <i>et al.</i> (1993), Norway	5332 members of International Organization of Good Templars, Norwegian teetotalers; followed-up 1980–89	Cancer registry	Oesophagus	Not reported	1	0.26 (1–145)		Compared with that of the total Norwegian population
Tønnesen <i>et al.</i> (1994), Denmark, Alcohol Abusers Study	18 368 non-hospitalized alcohol abusers during 1954–87; 15 214 men were observed for 12.9 years and 3093 women for 9.4 years.	Central population registry	Oesophagus	Not reported		Men	Compared with that of Danish population	
					57	5.3 (4.0–6.9) $p \leq 0.01$		
					2	4.9 (0.6–17.7)		
		59	5.3 (4.0–6.8) $p \leq 0.01$	Total				

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Boffetta <i>et al.</i> (2001), Sweden, Uppsala Alcoholics Study	173 665 patients (138 195 men, 35 470 women) with a hospital discharge diagnosis of alcoholism during 1965–94, aged >20 years; followed up for 10.2 years	Linkage between the Swedish In-patient Register and the National Cancer Register	Oesophagus	Diagnosed alcoholics		SIR		Compared with incidence in the national population
					521	<i>Both genders</i>	5.54 (5.07–6.04)	
					465	<i>Men</i>	5.26 (4.79–5.76)	
				56	<i>Women</i>	10.0 (7.57–13.0)		
General populations								
Boffetta & Garfinkel (1990), USA, American Cancer Society Cancer Prevention Study I	276 802 white men, aged 40–59 years, volunteers for the American Cancer Society enrolled in 1959 and followed for 12 years	A detailed four-page questionnaire; vital status checked yearly; death certificates of deceased participants obtained from state health departments	Oesophagus	Non-drinkers	59	1.0	Age, smoking	
				Occasional	9	1.12 (0.55–2.28)		
				1 drink/day	20	1.37 (0.81–2.30)		
				2 drinks/day	18	1.61 (0.94–2.77)		
				3 drinks/day	19	3.52 (2.05–6.02)		
				4 drinks/day	19	5.35 (3.08–9.27)		
				5 drinks/day	6	3.53 (1.47–8.48)		
≥6 drinks/day	22	5.79 (3.44–9.74)						
Irregular	13	1.64 (0.89–3.01)						

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kato <i>et al.</i> (1992c), USA, Hawaii, American Men of Japanese Ancestry Study	6701 American men of Japanese ancestry, born in 1900–19, and residing on the Hawaiian island of Oahu; 19 year follow-up survey, 1965–90	Structured interview	Oral cavity, pharynx, oesophagus, larynx	0 mL/day <30 mL/day ≥30 ml/day	13 21 36	1.0 1.2 (0.6–2.3) 5.4 (2.8–10.4)	Age, smoking	
Guo <i>et al.</i> (1994), China, Lin Xian Nutrition Intervention Trial	Nested case–control study; a cohort of 29 584 adults in a randomized intervention trial, aged 40–69 years; follow-up 1986–91; 640 cases; 3200 controls; 5 controls per case matched by age and sex	Structured interview	Oesophagus	Lifetime use of alcoholic beverages	640	Not reported	Not reported	Drinking alcoholic beverages was relatively uncommon in Lin Xian residents, but was reported by 22% of the cancer patients; no significant association between oesophageal and alcohol drinking found.

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments		
Thun <i>et al.</i> (1997), USA, American Cancer Society Cancer Prevention Study II	490 000 (251 420 women, 238 206 men), mean age, 56 years (range, 30–104); study subjects were recruited by American Cancer Society volunteers; followed up from 1982–91	Self-reported alcoholic beverage and tobacco use	Alcohol-related (mouth, oesophagus, pharynx, larynx, liver)	None	<i>Men</i> 69	1.0	Age, race, education, body mass index, smoking	Study subjects were recruited by American Cancer Society volunteers; they were also more likely than the general US population to be college educated, married, middle class and white; number of case or risk related to oesophageal cancer can not be determined.		
				Less than daily	106	1.4 (1.0–1.9)				
				1 drink/day	58	1.4 (1.0–2.0)				
				2–3 drinks/day	101	1.5 (1.1–2.1)				
				4 drinks/day	144	2.8 (2.1–3.8) <i>p</i> <0.001				
						<i>Women</i>				
				None	43	1.0				
				Less than daily	30	1.1 (0.7–1.8)				
				1 drink/day	10	0.8 (0.4–1.6)				
				2–3 drinks/day	26	1.5 (0.9–2.5)				
4 drinks/day	21	3.0 (1.7–5.3) <i>p</i> <0.002								

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Grønbaek <i>et al.</i> (1998), Denmark, The Copenhagen Centre for Prospective Population Studies	15 117 men, 13 063 women, aged 20–98 years; follow-up of 13.5 years, –1994; mean participation rate, 80%	Self-administered questionnaire; health examination	Oropharynx, oesophagus	See Tables 2.19a, b		See Tables 2.19a, b	Age, sex, smoking habits, educational level	There was a strong dose-dependent increase in risk for upper digestive tract cancer with increased alcoholic beverage intake.
Kinjo <i>et al.</i> (1998), Japan, Six-Prefecture Study	220 272 residents (100 840 men, 119 432 women), aged 40–69 years at the baseline of 1965, from 29 public health districts in six Prefectures of Japan; followed up 1966–81	Structured questionnaire	Oesophagus	None	149	1.0	Age, Prefecture, occupation, sex	Joint effect of alcohol and tobacco, 3.9 (2.7–5.4); dose–response relationship, <i>p</i> for trend <0.001
				1–3 times/month	31	0.7 (0.5–1.1)		
				1–3 times/week	76	1.1 (0.8–1.5)		
				4 times/week or more	184	2.4 (1.8–3.1)		
						<i>p</i> <0.001		

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kjaerheim <i>et al.</i> (1998), Norway, Norwegian Cohort Study	10 960 Norwegian men, born in 1893–1929, who had answered questionnaires, were alive and living in Norway on 1 January 1968 and had no diagnosis of upper aerogastric tract cancer prior to this date; mean age at start of follow-up, 59 years; followed up 1968–92; histological verification, 95.8%	Structured questionnaire; cancer registry	Oral cavity, pharynx, larynx, oesophagus	<i>Times/week</i>	<i>Upper aerogastric tract cancer</i>		Age, smoking	
				Never or <1	22	1.0		
				Previously	3	0.8 (0.2–2.7)		
				1–3	17	1.1 (0.6–2.1)		
4–7	18	3.2 (1.6–6.1)	$p=0.01$					

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lindblad <i>et al.</i> (2005), United Kingdom, General Practitioner Research Database	Nested case-control study; 287 oesophageal adenocarcinomas and 10 000 controls, aged 40–84 years; controls randomly selected, frequency-matched by sex, age, same calendar year from the pool; 5 controls per case; 1994–2001	Patients reviewed by one investigator kept blinded to exposure information during the review process	Oesophagus	<i>Units/day</i> 0–2 3–15 16–34 >34 Unknown use	294 156 54 30 375	1.0 1.06 (0.86–1.30) 1.04 (0.76–1.43) 1.76 (1.16–2.66) 1.04 (0.82–1.32)	Sex, age, smoking, body mass index, reflux, calendar year	One unit of an alcoholic beverage = 10 mL (7.9 g) pure ethanol.

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments			
Sakata <i>et al.</i> (2005), Japan, Japan Collaborative Cohort Study	110 792 (46 465 men, 64 327 women), aged 40–79 years; followed-up 1988–99; a baseline survey conducted in 45 areas throughout Japan	Self-administered questionnaire; death and cause of death confirmed annually or biannually	Oesophagus	Non-drinkers	9	1.0	Age, centre	42 578 men for analysis; one unit of alcohol contains about 22 g alcohol			
				<1.0 units/day	2	1.47 (0.28–7.68)					
				1.0–1.9 units/day	16	1.58 (0.65–3.86)					
				2.0–2.9 units/day	31	3.74 (1.62–8.66)					
				≥3.0 units/day	18	6.39 (2.54–16.12) <i>p</i> =0.028					
				Years of drinking							
				Non-drinkers	9	1.00					
				≤25.0	14	1.71 (0.64–4.60)					
				25.1–35.0	19	3.23 (1.32–7.92)					
				35.1–45.0	18	3.23 (1.33–7.81)					
				≥45.1	7	2.77 (0.85–9.03) <i>p</i> =0.100					
				Cumulative intake							
				Non-drinkers	9	1.0					
1–29.9 unit-years	4	0.68 (0.19–2.42)									
31.0–39.9 unit-years	6	2.31 (0.75–7.06)									
≥40.0 unit-years	46	3.80 (1.70–8.46) <i>p</i> =0.089									

Table 2.15 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Cancer site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Tran <i>et al.</i> (2005), China, Linxian Intervention Trial Study	Population-based prospective study of 29 584 adults in the Linxian General Population Trial, 40–69 years of age at baseline; follow-up, 15 years; case ascertainment considered complete and loss to follow-up minimal ($n=176$ or 1%)	Structured interviewed;	Oesophagus	Alcoholic in previous 12 months	450	0.92 (0.82–1.03)	Sex, age	No association

CI, confidence interval; ICD, International Classification of Diseases; SIR, standardized incidence

Table 2.16 Analytical studies of oesophageal cancer and alcoholic beverage consumption published in the Chinese literature

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Cohort studies	<i>Characteristics of the cohort</i>						
Zhang <i>et al.</i> (1998), Shandong, 1982–94	15 803 residents from 29 villages, aged 20 years; followed 1982–94	-	Questionnaire	<i>Alcoholic beverage intake (g)</i>		Not specified	
				0–49	1.00		
				50–149	2.05 (1.37–3.06)		
				150–249	1.20 (0.65–2.21)		
				≥250	1.03 (0.53–1.99)		
				<i>Duration (years)</i>			
				15–24	1.00		
				25–34	0.75 (0.27–2.10)		
				35–44	1.18 (0.44–3.20)		
				45–54	2.59 (0.99–6.73)		
				55–64	4.10 (1.52–11.08)		
				≥65	2.02 (0.51–8.06)		

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Wang <i>et al.</i> (2005a), Shanghai, 1986–2002	18 244 cancer-free men; followed 1986–2000	-	Interview	<i>Alcoholic beverage intake (g/day)</i> 0 <30 30–70 >70	1.00 1.33 2.47 5.08	Age, smoking, education	Significant result, but with no CI
Case–control studies							
Chen <i>et al.</i> (2000), Jiangsu, 1997–98	100 new cases from 11 hospitals	100 healthy controls matched on village of residence, gender, age	Questionnaire	<i>Alcoholic beverage consumption</i> <25 g/day >25 g/day	1.00 2.09 (1.21–4.29)	Crude analysis	
Liu <i>et al.</i> (2000), TianJing, 1999	86 randomly sampled men	158 from the general population	Questionnaire	<i>Duration of drinking (years)</i> 0 1–10 10–20 >20 <i>Volume consumed (mL)</i> 0–50 50–99 100–249 ≥250	1.00 1.85 (0.70–4.85) 2.15 (1.23–4.79) 3.10 (1.55–6.97) 1.00 1.23 (0.56–2.69) 4.31 (1.89–10.07) 18.66 (5.23–27.56)	Age, occupation, education, smoking	

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Lu <i>et al.</i> (2000b), LinZhou, 1995–96	352 from cancer registry	352; matched on age, sex, neighborhood	Questionnaire	<i>Alcoholic beverage consumption</i> No Yes	1.00 2.67 (1.04–6.81) <i>p</i> <0.05	Crude analysis	
Zhang <i>et al.</i> (2000), Ci, HeBei, 1973–97	350 hospital patients; categorized by geographical area	350 cancer-free; matched on village of residence, gender, occupation, age	Interviewer-administered questionnaire	<i>Alcoholic beverage consumption</i> No Yes	1.0 0.62 (0.41–0.93)	Crude analysis	Alcoholic beverage consumption appears to be a protective factor for oesophageal cancer in this study.
Cui <i>et al.</i> (2001a), JiangYan, Jiangsu, 1995–99	156 living	156 healthy residents from the same community as cases, matched on age	Interviewer-administered questionnaire	<i>Alcoholic beverage consumption</i> No Yes	1.0 3.58 (0.68–5.08)	Hot food, spicy food, smoking	
Ding <i>et al.</i> (2001a,b), TaiXing, Jiangsu, 1998–99	591 cases	591 from the same community; matched on gender, age	Interviewer-administered questionnaire	<i>Consumption of distilled spirits</i> No Yes	1.00 2.71 (1.09–7.64)	Crude analysis	

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gao <i>et al.</i> (2001), HuaiAn, 1997–2000	141 hospital patients	223 cancer-free from the general population; matched on age	Interview	<i>Alcoholic beverage consumption</i> <1 per week ≥1 per week	1.00 1.65 (0.90–3.03)	Gender, age, smoking	
Li <i>et al.</i> (2001), ChaoShan, Guangdong, 1997–2000	1248 from four hospitals within 3 months of diagnosis; residents of ChaoShan for over 10 years	1248 hospital patients; matched on age	Questionnaire	<i>Alcohol beverage consumption</i> No Yes	Result insignificant; number not reported		The study was primarily on smoking. A possible effect modification between smoking and alcohol beverage was detected (not significant). Cases and controls from 3 time periods were analysed separately in this study.
Chen <i>et al.</i> (2003a), Lin Xian, 1984–97	3 periods: 1244 in 1985 640 in 1991 702 in 1997	3 periods: 1314 in 1985 3200 in 1991 702 in 1997	Interview		Result insignificant; number not reported		
Ding <i>et al.</i> (2003), Shanghai, 2000	204 hospital patients	397 healthy controls from general population	Interview	<i>Alcoholic beverage consumption</i> No Yes	1.00 16.31 (5.57–47.77)	Education, gastritis, eating speed, smoking, drinking tea, personality	

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mu <i>et al.</i> (2003), TaiXing, Jiangsu, 2000	218	415 from the general population	Questionnaire	Alcoholic beverage consumption stratified by green tea consumption <i>Green tea drinker</i> Alcoholic beverages No Yes <i>Green tea non-drinker</i> Alcoholic beverages No Yes	1.00 1.21 (0.65–2.28) 1.00 1.98 (1.00–3.91)	Age, gender, education	
Wang <i>et al.</i> (2003a), XiAn	Meta-analysis; 530 cases	Meta-analysis; 4005 controls		<i>Alcoholic beverage consumption</i> No Yes	1.00 1.72 (1.27–2.33)		This study is a meta-analysis.

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zhao <i>et al.</i> (2003), FeiCheng	185	204 cancer-free from the general population	Interviewer-administered questionnaire	<i>Alcohol consumed each month (kg*years)</i> 0 1–280 >280	1.00 1.00 (0.58–1.74) 1.74 (0.88–3.42)	Age, gender, education, smoking	
Wang <i>et al.</i> (2004)	78 hospital patients	118 cancer-free from general population; matched on age	Interview	<i>Alcoholic beverage consumption</i> No Yes	1.00 6.41 (2.81–14.62)	Not specified	
Yan <i>et al.</i> (2004), ZhangYe, 1999–2000	125 hospital patients, residents of ZhangYe for over 20 years	145 cancer-free hospital patients	In-hospital interview with questionnaires	<i>Alcoholic beverage consumption</i> No Yes	1.00 2.55 (1.47–4.43)	Not specified	
Huang <i>et al.</i> (2005), Shandong	92 hospital patients	115 healthy controls from general population	Questionnaire	<i>Alcohol consumed each month (kg*years)</i> 0 <100 100–300 >300	1.00 2.73 (1.04–7.20) 6.61 (2.34–18.67) 23.40 (5.62–97.49)	Age, gender, smoking	

Table 2.16 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Wang <i>et al.</i> (2005b), Inner Mongolia, 2004	50 hospital-based	100 (1:2); matched on sex, neighbourhood, race/ethnicity, age \pm 5 years, time of visit	Questionnaire interview	Univariate history of alcoholic beverage consumption	4.43 (2.64–8.90)	Multivariate with years of alcoholic beverage drinking, years of smoking, difficulty in swallowing, history of psychological event, worsening of financial state, stool with blood	
				Multivariate years of alcoholic beverage consumption	5.41 (3.89–6.79)		
Zhao <i>et al.</i> (2005), Jiangsu, 2002	95 hospital patients	95; matched on gender, age	Interviewer-administered questionnaire	<i>Alcoholic beverage consumption</i>		Hot food, eating garlic, eating nuts	
				No	1.00		
				Yes	3.94 (1.81–8.59)		

CI, confidence interval

2.4.2 Case-control studies (Table 2.17)

Among the 38 case-control studies, 20 studies were published in the English literature and 18 in the Chinese literature. Of the 20 studies published in the English literature, 18 adjusted for tobacco smoking, 8 were population-based and 12 were hospital-based. Sixteen of the 20 studies in the English literature on alcoholic beverage consumption and the risk for oesophageal cancer reported a statistically significant association. The adjusted odds ratios ranged from 1.7 to 3.5 for ever drinkers and from 5.4 to 37.3 for heavy drinkers. Among the case-control studies identified in the Chinese literature (Table 2.16), the majority were hospital-based and 10 studies did not adjust for tobacco smoking (Chen *et al.*, 2000; Lu *et al.*, 2000b; Zhang *et al.*, 2000; Ding *et al.*, 2001a,b; Li *et al.*, 2001; Mu *et al.*, 2003; Wang B *et al.*, 2003a; Wang *et al.*, 2004; Yan *et al.*, 2004; Zhao *et al.*, 2005). Eight of these reported a positive association with alcoholic beverage consumption; the odds ratios ranged from 1.72 to 6.41 for ever drinkers of alcoholic beverages and from 3.1 to 23.4 for heavy drinkers. The evidence for alcoholic beverage consumption and the risk for oesophageal cancer in the Chinese literature are consistent with that in the English literature. In addition, the results from case-control studies are also consistent with those from prospective cohort studies.

2.4.3 Histological types (Tables 2.17 and 2.18)

Consumption of alcoholic beverages is an established cause of oesophageal cancer and is strongly associated with the risk for squamous-cell carcinoma of the oesophagus and, to a lesser degree, with the risk for oesophageal adenocarcinoma (Brown *et al.*, 1994; Gammon *et al.*, 1997; Lagergren *et al.*, 2000; Wu *et al.*, 2001; Lindblad *et al.*, 2005; Hashibe *et al.*, 2007a).

One prospective study of alcoholics (Boffetta *et al.*, 2001), one nested case-control study (Lindblad *et al.*, 2005) and eight case-control studies of adenocarcinoma of the oesophagus (Table 2.18) in relation to alcoholic beverage consumption have been published. A cohort study of alcoholics in Sweden (Boffetta *et al.*, 2001) reported an SIR of 1.45 (95% CI, 0.96–2.11) for oesophageal adenocarcinoma and 6.76 (95% CI, 6.15–7.41) for oesophageal squamous-cell carcinoma. The nested case-control study on adenocarcinoma of the oesophagus observed a null association (Lindblad *et al.*, 2005). Among the eight case-control studies, two reported a significant association between alcoholic beverage consumption and oesophageal adenocarcinoma. The increased risk for adenocarcinoma of oesophagus was associated with a higher level of alcoholic beverage consumption in two studies (Kabat *et al.*, 1993; Vaughan *et al.*, 1995), but not in the other six. Thus, the evidence for alcoholic beverage consumption and the risk for adenocarcinoma of the oesophagus was considered to be insufficient.

Table 2.17 Case-control studies of oesophageal cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
DeStefani <i>et al.</i> (1990), Uruguay, 1985–88	261 squamous-cell carcinomas (199 men, 62 women); clinical and/or radiological diagnosis; in four main hospitals in Montevideo; response rate, 92%	522 hospital patients (398 men, 124 women), without diagnosis of tobacco- and/or alcohol-related diseases; 1:2 matched by sex, age, hospital	Interviewer-administered standardized questionnaire	<i>Alcohol (mL per day)</i>			Sex, age, residence, smoking	Joint effect of alcoholic beverage and tobacco consumption; odds ratio for those who smoked and drank heavily compared with that of light smokers and drinkers, 22.6
					<i>Men</i>			
				0	26	1.00		
				1–24	16	0.85 (0.4–1.8)		
				25–49	12	0.71 (0.3–1.6)		
				50–149	50	1.37 (0.8–2.4)		
				150–249	46	3.57 (1.9–6.7)		
				≥250	49	5.27 (2.7–10.2)		
					<i>Women</i>			
				0	38	1.00		
				1–24	12	1.04 (0.4–2.4)		
				25–49	–	–		
				50–149	–	–		
150–249	12	1.89 (0.7–4.9)						
≥250	–	–						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Franceschi <i>et al.</i> (1990), northern Italy, 1986–89	288 men, aged <75 years; histologically confirmed; interviews generally (90%) conducted within 2 months from diagnosis; no next-of-kin respondents; refusal rate, 2%	1272 hospital-based men; 26% non-traumatic orthopaedic conditions, 25% trauma, 17% eye disorders, 13% other illness; matched by area of residence, hospital, age; no next-of-kin respondents; refusal rate, 3%	Interviewer-administered standardized questionnaire	≤19 drinks/week	45	1.0	Age, residence, education, occupation, smoking	High level of combined alcoholic beverage and cigarette consumption increased the risk to 18 times that of the lowest levels of consumption; the effect of drinking 60 or more alcoholic drinks per week in nonsmokers was slightly stronger than that of heavy smoking in light drinkers (odds ratio, 7.9 versus 6.4).
				20–34 drinks/week	41	1.0 (0.6–1.7)		
				35–59 drinks/week	115	3.1 (2.0–4.7)		
				≥60 drinks/week	87	6.0 (3.7–10.0) <i>p</i> <0.01		
				<i>Years of alcohol use</i>				
<30	60	1.0						
30–39	93	1.1 (0.7–1.7)						
≥40	116	0.9 (0.6–1.5) <i>p</i> =0.24						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Castelletto <i>et al.</i> (1992), Argentina, 1985–86	170 (99 men, 71 women), >15 years old; patients from 1 hospital and 9 private clinics; patients had various gastrointestinal symptoms	226 (109 men, 117 women) with histologically normal oesophagus	Of 406 study subjects, 396 completed information on the variable under study using a simple questionnaire	Men			Age, smoking	All subjects had various gastrointestinal symptoms; patients with oesophageal cancer or with severe erosions, ulcerations and stenosis associated with gastric reflux were not included.
				<i>Drinking status</i>				
				Non-drinkers	41	1.0		
				Drinkers	58	2.4 (1.3–4.3)		
				<i>Amount</i>				
				0–39 mL/day	41	1.0		
				40–79 mL/day	15	1.9 (0.8–4.7)		
				≥80 mL/day	43	2.5 (1.2–5.1)		

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Cheng <i>et al.</i> (1992), Hong Kong, China, 1989–90	400 (345 men, 55 women); histologically confirmed; 85% squamous-cell carcinomas; participation rate, 86.8%	1598 (800 hospital and 798 general practice; 1378 men, 220 women); 1:4 matched by age, sex; 2 controls admitted to the same surgical departments; patients with tobacco- or alcohol-related cancers were excluded; 2 controls selected from private or general practice clinics in the area where case was originally referred to the physician; response rate, 95%	Interviewer-administered standardized questionnaire	Never drinker	53	1.00	Age, education, birthplace, smoking	Cases or controls with diabetes mellitus were excluded.
				<50 g/week	57	1.07 (0.66–1.75)		
				50–99 g/week	16	1.36 (0.67–2.74)		
				100–199 g/week	30	1.82 (0.99–3.35)		
				200–299 g/week	48	3.40 (1.92–6.01)		
				400–599 g/week	44	5.05 (2.72–9.39)		
				600–799 g/week	39	11.11 (5.4–22.85)		
800–999 g/week	25	18.07 (7.40–44.13)						
≥1000 g/week	66	9.93 (5.27–18.74)						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Negri <i>et al.</i> (1992), northern Italy, 1984–90	300 (244 men, 56 women), aged 29–74 years; histologically confirmed newly diagnosed cancer of the oesophagus, admitted to the National Cancer Institute	1203 (901 men, 302 women) hospital patients, aged 25–74 years; 34% traumas, 26% non-traumatic orthopaedic conditions, 28% acute surgical disease, 12% various other diseases; diseases related to alcohol or tobacco consumption excluded	Interviewer-administered standardized questionnaire	<4 drinks/day 4–6 drinks/day >6 drinks/day	111 58 131	1.0 1.6 (1.1–2.4) 3.5 (2.5–5.1) <i>p</i> <0.001	Age, sex, education, smoking, β -carotene intake	Compared with the lowest risk category (nonsmokers, moderate alcohol drinkers and high β -carotene consumers), relative risk rose to 45.9 for men and to 36.4 for women who were heavy drinkers, heavy smokers and had a diet poor in β -carotene.

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Kabat <i>et al.</i> (1993), USA, 1981–90	Adenocarcinoma of oesophagus/cardia (160 men, 21 women), squamous-cell carcinoma of oesophagus (122 men, 78 women) and adenocarcinoma of distal stomach (113 men, 30 women); newly diagnosed, histologically confirmed	Hospitalized patients with disease not related to smoking and of organ systems other than the gastrointestinal tract (4162 men, 2222 women); matched by age, sex, race, hospital	Interviewer-administered structured questionnaire; all subjects interviewed in 28 hospitals in 8 cities in the USA between 1981 and 1990	<i>Squamous-cell carcinoma</i>			Age, education, smoking, hospital, time period (1981–84, 1985–90)	Non-drinker, <1 drink/week; occasional, ≥1 drink/week but <1 drink/day; WE = whiskey-equivalent per day; the analysis was limited to whites; joint effect of smoking and drinking (analysis limited to men), 7.6 (3.1–18.6) for squamous-cell carcinoma of oesophagus and 2.4 (1.3–4.2) for adenocarcinoma of oesophagus/cardia
				Men				
				Non-drinker	1.0			
				Occasional	1.4 (0.6–3.5)			
				1–3.9 oz WE/day	2.3 (1.0–5.4)			
				≥4 WE/day	10.9 (4.9–24.4)			
Women								
Non-drinker	1.0							
Occasional	1.4 (0.7–2.9)							
1–3.9 oz WE/day	4.4 (2.2–8.7)							
≥4 WE/day	13.2 (6.1–28.8)							

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Brown <i>et al.</i> (1994), USA, 1986–89	174 white men with adenocarcinoma of oesophagus (median age, 63 years); residents of geographical areas covered by the population-based cancer registries; response rate, 74%	750 (median age, 61 years) living in three areas of the USA selected by random-digit dialling for those aged 30–64 years (response rate, 72%) and random sampling from computerized listings of Medicare recipients (response rate, 76%)	Structured questionnaire administered by trained interviewers	<i>Adenocarcinoma of oesophagus and oesophagogastric junction</i>			Age, area, smoking, income	
				Never drank	32	1.0		
				Drank	142	0.9 (0.6–1.4)		
				<8 drinks/week	38	0.7 (0.4–1.3)		
				8–21 drinks/week	42	0.8 (0.4–1.3)		
22–56 drinks/week	43	1.1 (0.6–1.9)						
>56 drinks/week	18	1.5 (0.7–3.1)						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments		
Cheng <i>et al.</i> (1995), Hong Kong, China 1989–90	400 consecutive patients during a 21-month period in 1989–90; histologically confirmed; response rate, 87%	1598 patients from the same surgical departments as the cases and from general practices from which the cases were originally referred; matched by age, sex; response rate, 95%	Interviewer-administered structured questionnaire	Never drinkers	53	1.0	Age, sex, education, smoking			
				1–199 g/week	103	1.1 (0.7–1.8)				
				200–599 g/week	92	3.3 (2.0–5.4)				
				≥600 g/week	130	9.2 (5.4–15.7)				
				<i>Duration</i>						
				Never drinkers	53	1.0				
				1–19 years	24	2.0 (1.0–3.8)				
				20–39 years	175	2.1 (1.4–3.2)				
				≥40 years	131	2.4 (1.6–3.8)				
				<i>Years since stopped drinking</i>						
				Current drinkers	207	1.0				
				0–1 year	47	2.5 (1.4–4.4)				
				1–4 years	36	1.5 (0.9–2.6)				
5–9 years	22	0.5 (0.3–0.9)								
10–14 years	22	0.8 (0.4–1.5)								
≥15 years	11	0.2 (0.1–0.6)								
Never drinkers	33	0.6 (0.4–1.0)								

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Gammon <i>et al.</i> (1997), USA, 1993–95	Oesophageal adenocarcinoma (245 men, 48 women), gastric cardia adenocarcinoma (223 men, 38 women), oesophageal squamous-cell carcinoma (176 men, 45 women), other gastric adenocarcinoma (254 men, 114 women); histologically confirmed; newly diagnosed; all cases identified by use of established rapid reporting systems	695 population-based (555 men, 140 women), aged 30–64 years; frequency-matched by age (± 5 years), sex; identified by use of Waksberg's random-digit dialling method; overall response rate, 70.2%	Structured questionnaire administered by trained interviewers	<i>Oesophageal squamous-cell carcinoma</i>			Age, sex, geographical centre, race, body mass index, income, cigarette smoking, all other types of alcohol use	Interviews were administered directly to subjects rather than to closest next of kin (usually the spouse) for 70.4% of target cases, 67.8% of comparison cases and 96.6% of controls.
				Never	19	1.0		
				Ever	195	3.5 (1.9–6.2)		
				<5 drinks/week	16	0.8 (0.4–1.6)		
				5–11 drinks/week	25	1.8 (0.9–3.5)		
12–30 drinks/week	48	2.9 (1.5–5.4)						
>30 drinks/week	106	7.4 (4.0–13.7)						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Lagergren <i>et al.</i> (2000), Sweden, 1995–97	618 (81% of all eligible) patients (189 oesophageal adenocarcinoma, 262 cardia adenocarcinoma, 167 oesophageal squamous-cell carcinoma) (median ages at diagnosis, 69, 66 and 67 years, respectively); men constituted 87%, 85% and 72%, respectively	820 randomly selected population (median age, 68 years); frequency-matched on age, sex; men constituted 83%; participation rate, 73%	Structured questionnaire administered by trained interviewers	<i>Oesophageal squamous-cell carcinoma</i>			Age, sex, tobacco smoking, educational level, body mass index, reflux symptoms, intake of fruit and vegetables, energy intake, physical activity	Increase in the risk of 1.95-fold ($p < 0.01$) with habit of daily bidi smoking
				Never	16	1.0		
				Ever	151	1.1 (0.6–2.1)		
				<i>Ethanol (g) per week</i>				
				1–15	34	0.9 (0.4–1.8)		
				16–70	39	0.8 (0.4–1.8)		
>70	78	3.1 (1.4–6.7)						
			None			1	Age, sex, smoking	
			Occasional			1.36 (0.68–2.70)		
			Daily			7.81 (2.38–25.6)		

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Gallus <i>et al.</i> (2001), Italy, Switzerland	114 women aged <79 years (median age, 63 years); newly diagnosed; histologically confirmed squamous-cell oesophageal cancer; admitted to the major hospitals in the areas under study	425 women (median age, 62 years) admitted for acute, non-neoplastic conditions to the same hospitals: 40% trauma, 21% non-traumatic orthopaedic conditions, 24% acute surgical disorders, 15% miscellaneous other illnesses (including skin, eye or ear disorders); frequency-matched to cases by age, study centre; control: case ratio, 4	Interviewer-administered standardized questionnaire	<1 drink/day 1–2 drinks/day ≥3 drinks/day		1.0 1.99 (1.15–3.44) 5.40 (2.70–10.80)	Age, education, body mass index, smoking	Data from three case-control studies of squamous-cell oesophageal cancer: first conducted in 1984–93 in the provinces of Milan and Pordenone (Fioretti <i>et al.</i> , 1999); second in 1992–97 in the provinces of Padua and Pordenone, and the greater Milan area, northern Italy (Franceschi <i>et al.</i> , 2000); third in 1992–99 in the Swiss Canton of Vaud (Levi <i>et al.</i> , 2000).

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No.of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Wu <i>et al.</i> (2001), Los Angeles, USA, 1992–97	222 incident oesophageal adenocarcinoma (202 men, 20 women), 277 gastric cardia and 443 distal gastric adenocarcinoma, aged 30–74 years; histologically confirmed; identified by Cancer Surveillance Program	1356 multiethnic population-based (999 men, 357 women); matched by sex, race, date of birth; diagnosis of oesophageal or stomach cancer excluded; neighbourhood control sought by use of a systematic algorithm based on the address of the case patient	Interviewer-administered structured questionnaire; interviews completed by 55% of those identified and 77% of those approached	<i>Adenocarcinoma of oesophagus</i>			Age, sex, race, birthplace, education, smoking	
				1–7 drinks/week		0.72 (0.5–1.2)		
				8–21 drinks/week		0.57 (0.3–0.9)		
				22–35 drinks/week		0.77 (0.4–1.4)		
				≥36 drinks/week		0.93 (0.5–1.6) <i>p</i> -trend=0.79		
				<i>Alcoholic beverage</i>				
				Never		1.0		
				Former		0.74 (0.5–1.2)		
				Current		0.70 (0.5–1.1)		
Znaor <i>et al.</i> (2003), Chennai and Trivandrum, South India, 1993–99	566 men; histologically confirmed	3638 men (1711 non-tobacco-related cancer controls, 1927 healthy hospital visitors); histologically confirmed	Interviewer-administered structured questionnaire	Never	304	1.0	Age, centre, education, smoking, chewing habit	Joint effect between smoking and alcoholic beverage drinking: odds ratio, 7.33 (5.06–10.62); joint effect of smoking, chewing with tobacco and alcoholic beverage drinking: odds ratio, 8.65 (5.50–13.62) (ICD-9 150)
				Ever	262	1.70 (1.36–2.13)		
				<20 mL/day	70	1.13 (0.83–1.55)		
				20–50 mL/day	80	1.83 (1.31–2.55)		
				>50 mL/day	110	2.53 (1.85–3.46)		
				<i>Duration (years)</i>				
				<20	69	1.21 (0.88–1.67)		
20–29	82	1.69 (1.23–2.34)						
30–39	91	2.80 (1.95–4.01)						
≥40	20	1.88 (0.98–3.59)						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Yang <i>et al.</i> (2005), Japan, 2001–04	165 (148 men, 17 women; 159 squamous-cell carcinoma, 6 adenocarcinoma), aged 18–80 years; histologically diagnosed	495 hospital-based (444 men, 51 women) randomly selected; matched 1:3 for age, sex	Interviewer-administered structured questionnaire; 7-mL of blood; 95% of eligible subjects completed the questionnaire and about 60% provided blood samples	Non-drinker Moderate drinker Heavy drinker Never Former Current	8 63 94 8 12 145	1.00 5.16 (2.33–11.4) 27.8 (12.2–63.5) 1.0 6.20 (2.34–16.4) 9.44 (4.36–20.4)	Age, sex	Significant gene–environment interaction between alcoholic beverage drinking and <i>ALDH2</i> polymorphism
Lagergren <i>et al.</i> (2006), Sweden, 1995–97	189 oesophageal adenocarcinoma (88% of all eligible), 262 adenocarcinoma (84%); all histologically classified	Controls randomly selected from the total population register; frequency-matched by age, sex; 820 (73%) interviewed in person	A computer-aided face-to-face interview	<i>Carbonated low-alcohol beer (times/week)</i> See Table 2.18		See Table 2.18	Age, sex, smoking status, socioeconomic status, dietary intake of fruits and vegetables (in quartiles), body mass index	No association between consumption of carbonated soft drinks and risk for oesophageal adenocarcinoma

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Wu <i>et al.</i> (2006a), Taiwan, China [dates not reported]	165 men (oesophageal squamous-cell carcinoma), aged 35–92 years; pathologically proven	255 hospitalized men, aged 40–92 years; none had malignant tumours or any condition known to be associated with betel chewing, cigarette smoking or alcoholic beverage consumption; refusal rate, 11.8%	Interviewer-administered structured questionnaire	<i>Daily quantity</i>			Cigarette smoking, betel chewing, age, years of education	Dose–response effects found in daily quantity of drinking and smoking; synergistic effect between alcoholic beverage intake and cigarette use (odds ratio, 108.0; 35.1–478.0)
				Non-drinker	17	1.0		
				750 mL/day	113	15.8 (8.3–31.7)		
				>750 mL/day	30	65.1 (20.0–264.8)		
						<i>p</i> -trend<0.001		
				<i>Drinking status</i>				
				Non-drinker	17	1.0		
				Former drinker	13	5.4 (1.9–15.4)		
				Current drinker	135	23.3 (12.0–47.7)		
				<i>Starting age</i>				
				Non-drinker	17	1.0		
				≥25 years old	103	15.7 (8.1–32.0)		
				<25 years old	43	30.8 (12.5–82.1)		
				<i>Duration (years)</i>				
Non-drinker	17	1.0						
30	75	14.9 (7.2–32.4)						
>30	68	23.0 (10.6–52.9)						
		<i>p</i> -trend=0.001						
<i>Cumulative exposure (mL/year)</i>								
Non-drinker	17	1.0						
<7500	22	6.8 (3.0–15.9)						
7500–15 000	24	13.7 (5.3–37.8)						
>15 000	45	37.3 (14.8–105.1)						
		<i>p</i> -trend<0.001						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Wu <i>et al.</i> (2006b), Jiangsu, China, 2003–04	531 (381 men, 150 women); 45% and 72% of all newly registered cases recruited and interviewed in Dafeng (high risk area) and Ganyu (low risk area), respectively	531 population-based (381 men, 150 women); randomly selected by a computer from the demographic database of the general population; response rate, 70%	Interviewer-administered structured questionnaire; a 5-mL blood sample	<i>Dafeng (high-risk area)</i>		0.87 (0.49–1.54)	Age, gender, education, economic status, tobacco smoking	In Ganyu (low-risk area), odds ratio for oesophageal cancer versus non-drinker category was 1.71 (1.02–2.88).
				1–249 mL/week		1.06 (0.60–1.89)		
				250–499 mL/week		0.97 (0.52–1.79)		
				500–749 mL/week		1.10 (0.63–1.93)		
				≥750 mL/week		<i>p</i> -trend=0.74		
				<i>Alcohol drinking</i>				
				Never	175	1.0		
				Ever	116	1.01 (0.70–1.46)		
						<i>p</i> -trend=0.964		
				<i>Age of first drink (years)</i>				
<20		0.83 (0.44–1.58)						
20–34		1.23 (0.79–1.91)						
≥35		0.81 (0.48–1.35)						
		<i>p</i> -trend=0.815						
<i>Duration of drinking (years)</i>								
1–24		0.96 (0.56–1.59)						
25–34		0.89 (0.48–1.64)						
35–44		1.57 (0.92–2.70)						
≥45		0.77 (0.43–1.40)						
		<i>p</i> -trend=0.834						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Yokoyama <i>et al.</i> (2006), Japan, 2000–04	52 women with primary oesophageal squamous-cell carcinoma at the National Cancer Center Hospital, aged 40–79 years; histological diagnosis; none of the patients refused to participate.	412 cancer-free women, aged 40–79 years; most of the controls were ordinary residents or workers living in Tokyo or neighbouring areas; 82% of the eligible subjects who were contacted were enrolled in the study.	Self-administered structured questionnaire	Never/rare	24	1.0	Age	Never/rare, <1 unit/week; light, 1–8.9 units/week; moderate, 9–17.9 units/week; heavy, ≥18 units/week; 1 unit=22 g ethanol
				Light	11	1.81 (0.81–4.05)		
				Moderate	6	3.97 (1.40–11.26)		
				Heavy	7	15.35 (4.85–48.62)		
				Former drinker	4	4.58 (1.25–16.79)		
						<i>p</i> -trend<0.0001		
						<i>Strong alcoholic beverages</i>		
Never	46	1.0						
Sometimes	4	2.58 (0.80–8.33)						
Frequently	2	12.47 (0.97–160.06)						
		<i>p</i> -trend=0.012						

Table 2.17 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Hashibe <i>et al.</i> (2007c), central and eastern Europe, 2000–02	192 squamous-cell carcinoma (170 men, 22 women), 35 adenocarcinoma (31 men, 4 women) of the oesophagus diagnosed at 5 centres in the Czech Republic, Poland, Romania, Russia, confirmed histologically or cytologically; recruited into the study within 3 months of diagnosis; response rate, 96%	1114 (846 men, 268 women); frequency-matched from same hospital as the cases with a recent diagnosis of disease unrelated to tobacco and alcohol; in Moscow, frequency-matched to cases by age, sex, centre, referral or residence area; in other centres, overlapped with those in study of lung cancer; interviewed more than 6 months before the beginning of recruitment of cases; response rate, 97%	Face-to-face interviews using a structured questionnaire	<i>Squamous-cell carcinoma</i>			Centre, age, sex, education, body mass index, fruit intake, vegetable intake, pack-years of tobacco	A synergistic interaction between tobacco and alcohol was observed for the risk for oesophageal squamous-cell carcinoma. (ICD-0-2 C 15)
				No drinking	5	1.00		
				Ever drinking	181	2.86 (1.06–7.74)		
				<i>Intake of ethanol (g/week)</i>				
				No drinking	5	1.00		
				1–139	69	3.08 (1.11–8.60)		
				140–279	34	4.51 (1.46–13.94)		
				280–419	20	8.14 (2.45–27.04)		
				≥420	55	9.78 (3.08–31.04)		
				<i>Years of drinking</i>				
				No drinking	5	1.00		
				1–19	12	2.25 (0.63–8.04)		
				20–39	131	4.80 (1.68–13.72)		
≥40	35	2.39 (0.83–6.90)						
			<i>p</i> -trend=0.08					
<i>Cumulative consumption (grams)</i>								
No drinking	5	1.00						
1–1399	23	1.70 (0.59–4.87)						
1400–2799	33	4.91 (1.62–14.84)						
2800–4199	16	3.29 (1.01–10.72)						
4200–5599	16	6.62 (1.99–22.08)						
≥ 5600	93	7.21 (2.37–21.98)						
			<i>p</i> -trend<0.01					

ALDH, acetaldehyde dehydrogenase; CI, confidence interval; WE, whiskey equivalent

2.4.4 *Type of alcoholic beverage (Table 2.19a and Table 2.19b)*

The types of alcoholic beverage consumed were examined in several studies. Consumption of beer or hard liquor led to a higher relative risk than consumption of wine (Kato *et al.*, 1992c; Brown *et al.*, 1994; Gammon *et al.*, 1997; Grønbaek *et al.*, 1998; Kjaerheim *et al.*, 1998; Lagergren *et al.*, 2000), whereas two studies (Barra *et al.*, 1990; Sakata *et al.*, 2005) also found an excess risk for wine drinkers. Most of the studies that investigated types of alcoholic beverage showed no substantial difference in risk.

2.4.5 *Evidence of a dose–response*

The risk for oesophageal cancer was shown to increase with increasing number of drinks per day or the number of days per week on which alcoholic beverages were consumed in 10 cohort and 21 case–control studies. Some studies found a relationship between the duration of alcoholic beverage consumption in years and the risk for oesophageal cancer (Cheng *et al.*, 1995; Zhang *et al.*, 1998; Liu *et al.*, 2000; Znaor *et al.*, 2003; Sakata *et al.*, 2005; Wu *et al.*, 2006a; Hashibe *et al.*, 2007a). Using non-drinkers as the baseline, the influence of the cumulative amount of alcoholic beverage consumed was apparent (Lagergren *et al.*, 2000; Sakata *et al.*, 2005; Wu *et al.*, 2006a; Hashibe *et al.*, 2007a). A dose–response relationship was found between the frequency of alcoholic beverage intake and the risk for oesophageal cancer (Grønbaek *et al.*, 1998; Kinjo *et al.*, 1998; Wu *et al.*, 2006a; Hashibe *et al.*, 2007a). In two studies (Yang *et al.*, 2005; Wu *et al.*, 2006a), the relative risks were lower in former drinkers than in current drinkers but remained significantly elevated.

2.4.6 *Effect of cessation of alcoholic beverage consumption (Table 2.20)*

Studies on the cessation of alcoholic beverage consumption may be confounded by the fact that the precursors and early malignancies of the oesophagus may lead to such cessation. Nevertheless, this type of confounding may result in an underestimation of the effect. For recent quitters, the risk for oesophageal cancer increased above that of current drinkers; as the number of years of having quit increased, however, the risk gradually decreased to below that of current drinkers or even to close to the levels of non-drinkers in some studies.

Cheng *et al.* (1995) observed that risk could decrease to nearly the levels of non-drinkers after more than 10 years of quitting. Castellsagué *et al.* (2000) showed that risk can be reduced to 50% of that of current drinkers after more than 10 years of cessation. Bosetti *et al.* (2000) observed an odds ratio of 0.37 (95% CI, 0.14–0.99) after 10 or more years of cessation. All three case–control studies suggested a reduction in risk after cessation of alcoholic beverage consumption for more than 10 years.

Table 2.18 Selected cohort and case–control studies of oesophageal cancer by histological type and alcoholic beverage intake

Reference	Exposure categories	Histological type and risks				
Cohort studies						
Boffetta <i>et al.</i> (2001)		Adenocarcinoma		Squamous-cell carcinoma		
		<i>Cases</i>	<i>SIR (95% CI)</i>	<i>Cases</i>	<i>SIR (95% CI)</i>	
		27	1.45 (0.96–2.11)	449	6.76 (6.15–7.41)	
Lindblad <i>et al.</i> (2005) (nested case–control)	<i>Units/day</i>	Adenocarcinoma		Squamous-cell carcinoma		
		<i>Cases</i>	<i>Relative Risk (95% CI)</i>	<i>Cases</i>	<i>Relative Risk (95% CI)</i>	
		0–2	95	1.00	49	1.00
		3–15	59	1.06 (0.76–1.49)	20	1.01 (0.59–1.72)
		16–34	15	0.69 (0.39–1.20)	13	2.44 (1.26–4.71)
		>34	9	1.25 (0.61–2.55)	5	3.39 (1.28–8.99)
Unknown use	109	1.21 (0.81–1.79)	53	0.79 (0.42–1.49)		
Case–control studies						
Kabat <i>et al.</i> (1993)		Distal oesophagus/cardia		Squamous-cell carcinoma		
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	<i>Cases</i>	<i>Odds ratio (95% CI)</i>	
		Men				
		Non-drinker	16	1.0	7	1.0
		Occasional	55	2.0 (1.1–3.5)	15	1.4 (0.6–3.5)
		1–3.9 oz WE/day	61	2.1 (1.2–3.6)	27	2.3 (1.0–5.4)
		≥4 oz WE/day	41	2.3 (1.3–4.3)	86	10.9 (4.9–24.4)
		Women				
		Non-drinker	10	1.0	16	1.0
		Occasional	5	0.6 (0.2–1.9)	17	1.4 (0.7–2.9)
1–3.9 oz WE/day	3	0.9 (0.2–3.5)	25	4.4 (2.2–8.7)		
≥4 oz WE/day	3	3.8 (0.9–16.6)	20	13.2 (6.1–28.8)		

Table 2.18 (continued)

Reference	Exposure categories	Histological type and risks			
Brown <i>et al.</i> (1994)		Adenocarcinoma of oesophagus and oesophagogastric junction			
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>		
	Never drinker	32	1.0		
	Drinker	142	0.9 (0.6–1.4)		
	<8 drinks/week	38	0.7 (0.4–1.3)		
	8–21 drinks/week	42	0.8 (0.4–1.3)		
	22–56 drinks/week	43	1.1 (0.6–1.9)		
	>56 drinks/week	18	1.5 (0.7–3.1)		
Vaughan <i>et al.</i> (1995)		Adenocarcinoma		Squamous-cell carcinoma	
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	<i>Cases</i>	<i>Odds ratio (95% CI)</i>
	0–6 drinks/week	147	1.0	27	1.0
	7–13 drinks/week	39	1.1 (0.7–1.8)	20	6.0 (2.7–13.5)
	14–20 drinks/week	18	1.2 (0.6–2.3)	11	6.3 (2.2–17.9)
	≥21 drinks/week	44	1.8 (1.1–3.1)	30	9.5 (4.0–22.3)
Gammon <i>et al.</i> (1997)		Adenocarcinoma		Squamous-cell carcinoma	
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	<i>Cases</i>	<i>Odds ratio (95% CI)</i>
	Never	79	1.0	19	1.0
	Ever	210	0.7 (0.5–1.0)	195	3.5 (1.9–6.2)
	<5 drinks/week	56	0.7 (0.4–1.0)	16	0.8 (0.4–1.6)
	5–11 drinks/week	45	0.6 (0.4–0.9)	25	1.8 (0.9–3.5)
	12–30 drinks/week	57	0.7 (0.4–1.1)	48	2.9 (1.5–5.4)
	>30 drinks/week	52	0.9 (0.5–1.4)	106	7.4 (4.0–13.7)
Lagergren <i>et al.</i> (2000)		Adenocarcinoma		Squamous-cell carcinoma	
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	<i>Cases</i>	<i>Odds ratio (95% CI)</i>
	Never	41	1.0	16	1.0
	Ever	148	0.5 (0.3–0.9)	151	1.1 (0.6–2.1)
	1–15 g/week	54	0.6 (0.4–1.1)	34	0.9 (0.4–1.8)
	16–70 g/week	51	0.4 (0.2–0.7)	39	0.8 (0.4–1.8)
	>70 g/week	43	0.6 (0.3–1.1)	78	3.1 (1.4–6.7)

Table 2.18 (continued)

Reference	Exposure categories	Histological type and risks		
Wu <i>et al.</i> (2001)		Adenocarcinoma of oesophagus		
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	
		Not reported	0.72 (0.5–1.2)	
	1–7 drinks/week		0.57 (0.3–0.9)	
	8–21 drinks/week		0.77 (0.4–1.4)	
	22–35 drinks/week		0.93 (0.5–1.6)	
	≥36 drinks/week		<i>p</i> =0.79	
	<i>Alcohol use</i>			
	Never		1.0	
	Former		0.74 (0.5–1.2)	
	Current		0.70 (0.5–1.1)	
Lagergren <i>et al.</i> (2006)		Adenocarcinoma of oesophagus		
		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	
		Unexposed (0)	40	1.00
		Low (≤1)	44	1.05 (0.60–1.83)
		Medium (>1–4)	46	1.16 (0.65–2.07)
		High (>4)	50	1.33 (0.74–2.40)
			<i>p</i> =0.78	

Table 2.18 (continued)

Reference	Exposure categories	Histological type and risks			
		Adenocarcinoma		Squamous-cell carcinoma	
Hashibe <i>et al.</i> (2007c)		<i>Cases</i>	<i>Odds ratio (95% CI)</i>	<i>Cases</i>	<i>Odds ratio (95% CI)</i>
	No drinking	3	1.00	5	1.00
	Ever drinking	32	1.21 (0.31–4.77)	181	2.86 (1.06–7.74)
	1–139 g/week	13	1.06 (0.25–4.58)	69	3.08 (1.11–8.60)
	140–279 g/week	6	2.22 (0.40–12.39)	34	4.51 (1.46–13.94)
	280–419 g/week	4	5.39 (0.73–39.93)	20	8.14 (2.45–27.04)
	≥420 g/week	6	2.31 (0.30–17.58)	55	9.78 (3.08–31.04)
			<i>p</i> =0.20		<i>p</i> <0.01
	Years of drinking				
	No drinking	3	1.00	5	1.00
	1–19	1	0.38 (0.02–6.09)	12	2.25 (0.63–8.04)
	20–39	17	1.08 (0.24–4.94)	131	4.80 (1.68–13.72)
	≥40	11	1.44 (0.31–6.66)	35	2.39 (0.83–6.90)
			<i>p</i> =0.55		<i>p</i> =0.08
	Cumulative consumption (grams)				
	No drinking	3	1.00	5	1.00
	1–1399	7	1.08 (0.24–4.82)	23	1.70 (0.59–4.87)
1400–2799	6	1.48 (0.29–7.41)	33	4.91 (1.62–14.84)	
2800–4199	4	1.16 (0.21–6.51)	16	3.29 (1.01–10.72)	
4200–5599	0	–	16	6.62 (1.99–22.08)	
≥5600	15	1.96 (0.39–9.88)	93	7.21 (2.37–21.98)	
		<i>p</i> =0.54		<i>p</i> <0.01	

CI, confidence interval; SIR, standardized incidence ratio; WE, whiskey equivalent

Table 2.19a. Selected cohort studies of oesophageal cancer and consumption of different types of alcoholic beverages

Reference, location, name of study	Exposure categories	Beer		Wine		Hard liquors	
		No. of exposed cases	Relative risk (95% CI)	No. of exposed cases	Relative risk (95% CI)	No. of exposed cases	Relative risk (95% CI)
Cohort studies							
Kato <i>et al.</i> (1992c), USA, Hawaii, American Men of Japanese Ancestry Study	<i>Alcohol intake</i> 0 mL/day <500 mL/day ≥500 mL/day	24 16 30	1.0 0.7 (0.4–1.4) 2.6 (1.5–4.6) <i>p</i> 0.01		Not reported		Not reported
Grønbaek <i>et al.</i> (1998), Denmark, The Copenhagen Centre for Prospective Population Studies	<i>Frequency of drinking</i> 0 drinks/week 1–6 drinks/week ≥7 drinks/week	Not reported	1.0 1.5 (0.9–2.5) 2.9 (1.8–4.8)	Not reported	1.0 0.8 (0.5–1.1) 0.4 (0.2–0.8)	Not reported	1.0 0.7 (0.5–1.1) 1.5 (1.2–1.9)
Kjaerheim <i>et al.</i> (1998), Norway, Norwegian Cohort Study	<i>Frequency of drinking (times/week)</i> Never or <1 Previously 1–3 4–7	37 11 8 14	1.0 1.0 (0.5–1.9) 1.4 (0.7–3.1) 4.4 (2.4–8.3) <i>p</i> 0.001	Not reported	Not reported	42 15 5 5	1.0 1.3 (0.7–2.3) 1.4 (0.6–7.0) 2.7 (1.1–7.0) <i>p</i> =0.06
Sakata <i>et al.</i> (2005), Japan, Japanese Collaborative Cohort Study		17	1.42 (0.58–3.52)	6	6.24 (1.53–25.37)	48 15 9	Sake 2.72 (1.22–6.08) Shochu 3.40 (1.33–8.68) Whisky 2.60 (0.91–7.41)

Table 2.19b Selected case-control studies of oesophageal cancer and consumption of different types of alcoholic beverages

Reference, location, name of study	Beer			Wine			Hard liquors		
	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)
Case-control studies									
Barra <i>et al.</i> (1990), northern Italy, 1986-90	≤55 drinks/week	6	1.8 (0.7-4.5)		61	1.7 (1.1-2.7)		27	1.8 (1.0-3.1)
	56-83 drinks/week	8	4.3 (1.6-11.3)		39	5.4 (3.1-9.3)		31	3.6 (2.0-6.4)
	≥84 drinks/week	6	4.3 (1.5-12.4)		7	15.0 (4.6-49.1)			10.0 (4.1-24.5)
Brown <i>et al.</i> (1994), USA, 1986-89	Never	60	1.0			1.0		64	1.0
	Drank	114	6 (0.4-0.9)			0.9 (0.6-1.4)		110	1.6 (1.1-2.4)
	<8 drinks/week	46	0.6 (0.4-1.0)	<3 drinks/week		0.9 (0.5-1.5)	<8 drinks/week	50	1.3 (1.0-3.2)
	8-15 drinks/week	26	0.7 (0.4-1.2)	3-13 drinks/week		0.8 (0.4-1.5)	8-15 drinks/week	24	0.8 (0.4-1.3)
	15-28 drinks/week	21	0.6 (0.3-1.1)	≥14 drinks/week		1.6 (0.7-3.8)	15-28 drinks/week	21	2.1 (1.1-4.0)
	≥29 drinks/week	50	0.6 (0.3-1.3)				≥29 drinks/week	13	2.8 (1.2-6.3)
Gammon <i>et al.</i> (1997), USA, 1993-95	Never	57	1.0		149	1.0		48	1.0
	Ever	164	2.2 (1.4-3.3)		72	0.6 (0.4-0.9)		173	3.1 (2.0-4.8)

Table 2.19b (continued)

Reference, location, name of study	Beer			Wine			Hard liquors		
	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Exposure categories	No. of exposed cases	Odds ratio (95% CI)
Lagergren <i>et al.</i> (2000), Sweden, 1995–97	Never	103	1.0	Strong beer				26	1.0
	Ever	64	1.3 (0.9–2.0)		68	1.0		141	1.0 (0.6–1.8)
	Grams of ethanol/week								
	1–5	21	1.3 (0.7–2.3)	1–5	26	0.8 (0.5–1.5)	1–7	26	0.6 (0.3–1.2)
	6–25	21	1.0 (0.6–1.9)	6–25	29	0.9 (0.5–1.7)	8–30	39	1.1 (0.5–2.2)
>25	22	1.2 (0.6–2.3)	>25	44	1.2 (0.7–2.1)	>30	76	2.3 (1.1–4.7)	
Wu <i>et al.</i> (2001), Los Angeles, USA, 1992–97	None	Not reported	1.0		Not reported	1.0		1.0	
	<7/week		0.44 (0.3–0.7)			0.86 (0.6–1.3)		0.93 (0.6–1.4)	
	7–14/week		0.30 (0.2–0.5)			0.72 (0.4–1.3)		1.35 (0.8–2.3)	
≥15/week		0.57 (0.3–1.0)			1.27 (0.6–2.8)		1.34 (0.8–2.3)		
Hashibe <i>et al.</i> (2007c), central and eastern Europe, 2000–02		12	0.87 (0.38–1.98)		4	0.50 (0.15–1.72)		19	Spirits 0.71 (0.39–1.29)

CI, confidence interval

Table 2.20 Case-control studies of oesophageal cancer and cessation of alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments			
Cheng <i>et al.</i> (1995), Hong Kong, China, 1989-90	400 consecutive patients during a 21-month period in 1989-90; histologically confirmed; response rate, 87%	1598 patients from the same surgical departments as the cases and from general practices from which the cases were originally referred; matched by age, sex; response rate, 95%	Interviewer-administered structured questionnaire	Never drinkers	53	1.0	Age, sex, education, smoking				
				1-199 g/week	103	1.1 (0.7-1.8)					
				200-599 g/week	92	3.3 (2.0-5.4)					
				≥600 g/week	130	9.2 (5.4-15.7)					
				<i>Duration</i>							
				Never drinkers	53	1.0					
				1-19 years	24	2.0 (1.0-3.8)					
				20-39 years	175	2.1 (1.4-3.2)					
				≥ 40 years	131	2.4 (1.6-3.8)					
				<i>Years since stopped drinking</i>							
				Current drinkers	207	1.0					
				0-1	47	2.5 (1.4-4.4)					
				1-4	36	1.5 (0.9-2.6)					
5-9	22	0.5 (0.3-0.9)									
10-14	20	0.8 (0.4-1.5)									
≥ 15	11	0.2 (0.1-0.6)									
Never drinkers	53	0.6 (0.4-1.0)									

Table 2.20 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Odds ratio (95% CI)	Adjustment factors	Comments
Bosetti <i>et al.</i> (2000), multicentre, 1992–99	404 squamous-cell cancer (356 men, 48 women), median age, 60 years (range, 34–77 years); newly diagnosed; histologically confirmed	1070 (878 men, 192 women), median age, 60 years (range, 32–77 years); patients admitted to the same hospitals for nonsmoking- or alcohol consumption-related non-neoplastic conditions	Interviewer-administered structured questionnaire	<i>Time since drinking cessation (years)</i> Current 1–9 ≥ 10		1 1.28 (0.67–2.43) 0.37 (0.14–0.99)	Age, sex, study centre, education, alcoholic beverage and tobacco consumption	Odds ratio represents the combined effect of time since smoking and drinking cessation on risk of oesophageal cancer.
Castellsagué <i>et al.</i> (2000), 1986–92	655 men with incident squamous-cell carcinoma	1408 men; individually matched to the cases on admitting hospital, age (±5 years)	Interviewer-administered structured questionnaire	<i>Years of drinking cessation</i> Current > 1–9 > 10 <i>p</i> for trend (two-sided)	348 176 34	1.0 0.9 0.5 0.02	Age group, hospital, years of schooling, average amount of pure ethanol consumed	Joint effect of years of smoking and drinking cessation on oesophageal cancer; reported odds ratios adjusted for years since quitting smoking.

CI, confidence interval

2.4.7 *Effect modification*

The combined effects of smoking and alcoholic beverage consumption on the development of cancer of the oesophagus have been examined in several studies (Tables 2.17 and 2.21), which varied in the methods and approaches used to assess effect modification, and ranged from being descriptive to giving a formal estimation of interaction terms in multivariate models. Eight case–control studies (Franceschi *et al.*, 1990; Negri *et al.*, 1992; Kabat *et al.*, 1993; Lagergren *et al.*, 2000; Gallus *et al.*, 2001; Znaor *et al.*, 2003; Wu *et al.*, 2006a; Hashibe *et al.*, 2007c) and two cohort studies (Kato *et al.*, 1992c; Sakata *et al.*, 2005) reported the joint effect of alcoholic beverage consumption and tobacco smoking on the risk for oesophageal cancer. Overall, the studies showed that the joint effects were multiplicative rather than additive, but, since multiple logistic regression models were used in the analyses in most of these studies, some also showed them to be additive rather than multiplicative.

Some studies investigated sex-specific effects (Table 2.22), and reported similar risks for both men and women (Negri *et al.*, 1992; Kabat *et al.*, 1993; Kinjo *et al.*, 1998). Most studies found non-significantly increased relative risks among women with oesophageal cancer, but a significant risk among men who were classified as heavy drinkers, after controlling for tobacco smoking (DeStefani *et al.*, 1990; Adami *et al.*, 1992b; Kinjo *et al.*, 1998). The studies from Japan and Italy found a significantly increased risk for oesophageal cancer among women (Gallus *et al.*, 2001; Yokoyama *et al.*, 2006).

2.5 **Cancer of the liver**

Hepatocellular carcinoma (HCC) is the third most common cause of mortality from cancer and the sixth most common cause of cancer incidence worldwide (Parkin *et al.*, 2005). Although it is relatively rare in developed countries compared to the developing world, the incidence of primary liver cancer has increased during the last few decades in the USA (Howe *et al.*, 2001) and in several European countries, although it has levelled off and subsequently declined in most of southern Europe over the last decade (La Vecchia *et al.*, 2000).

In 1988, the IARC Monograph on alcohol drinking concluded that there was “sufficient evidence for the carcinogenicity of alcoholic beverages” and that “the occurrence of malignant tumours of the liver is causally related to consumption of alcoholic beverages” (IARC, 1988). Since that time, further evidence has been presented on the risk of liver cancer associated with prolonged alcoholic beverage consumption, the increased risk of associated liver cancer among cirrhotics and the modifying effects of the infectious agents hepatitis B virus (HBV) and hepatitis C virus (HCV).

Table 2.21 Selected cohort and case–control studies of oesophageal cancer in nonsmokers and smokers by level of alcoholic beverage intake

Reference	Exposure categories	Nonsmokers		Smokers					
Cohort studies									
Kato <i>et al.</i> (1992c)		<i>Never smokers</i>		<i>Former and current smokers</i>					
		Cases	RR (95% CI)	Cases	RR (95% CI)				
	<30 mL/day	5	1.0	29	3.3 (1.3–8.4)				
	≥30 mL/day	3	8.6 (2.1–36.0)	34	17.3 (6.7–44.2)				
Sakata <i>et al.</i> (2005)		<i>Never smokers</i>		<i>Former smokers</i>		<i>Smokers</i>			
		Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)		
	Non-drinkers	4	1.0	1	0.34 (0.04–3.12)	4	0.74 (0.18–3.02)		
	Former drinkers	1	1.10 (0.12–10.24)	3	1.47 (0.31–7.08)	4	2.19 (0.51–9.40)		
	Drinkers	2	0.18 (0.03–1.02)	21	1.39 (0.47–4.10)	60	2.37 (0.85–6.58)		
Case–control studies									
Franceschi <i>et al.</i> (1990)		<i>Never smokers</i>		<i>Light smokers</i>		<i>Intermediate smokers</i>		<i>Heavy smokers</i>	
		Cases	Odds ratio	Cases	Odds ratio	Cases	Odds ratio	Cases	Odds ratio
		9	1.0	11	1.1	47	2.7	16	6.4
		3	0.8	19	7.9	78	8.8	14	11.0
		5	7.9	13	6.4	60	16.7	6	17.5
Negri <i>et al.</i> (1992)		<i>Never smokers</i>		<i>Ex/Moderate smokers</i>		<i>Heavy smokers</i>			
		Cases	Odds ratio	Cases	Odds ratio	Cases	Odds ratio		
	<4 drinks/day	7	1.0	10	2.8	11	4.3		
	4–6 drinks/day	2	1.6	4	4.5	6	6.9		
	>6 drinks/day	1	3.5	9	3.8	12	15.3		
Kabat <i>et al.</i> (1993)		<i>Never smokers</i>		<i>Ever smokers</i>					
			Odds ratio		Odds ratio				
	Non drinker/ occasional ≥1 oz WE/day		1.0 4.3 (1.4–12.5)		1.5 (0.5–4.2) 7.6 (3.1–18.6)				

Table 2.21 (continued)

Reference	Exposure categories	Nonsmokers		Smokers	
Gallus <i>et al.</i> (2001)		<i>Never and former smokers</i>		<i>Current smokers</i>	
		Cases	Odds ratio (95% CI)	Cases	Odds ratio (95% CI)
	<1 drink/day	18	1.0	11	2.25 (0.95–5.33)
	1–2 drinks/week	27	1.66 (0.85–3.25)	23	5.52 (2.57–11.85)
	≥3 drinks/week	16	5.79 (2.48–13.50)	19	12.75 (5.09–31.96)
Znaor <i>et al.</i> (2003)		<i>No smoking</i>		<i>Smoking</i>	
		Cases	Odds ratio (95% CI)	Cases	Odds ratio (95% CI)
	No drinking	45	1.00	155	3.57 (2.51–5.06)
	Drinking	7	3.41 (1.46–7.99)	164	7.33 (5.06–10.62)
Wu <i>et al.</i> (2006a)		<i>No smoking</i>		<i>Smoking</i>	
		Cases	Odds ratio (95% CI)	Cases	Odds ratio (95% CI)
	No alcohol	3	1.00	11	6.5 (1.9–29.8)
	Alcohol	4	23.3 (4.3–142.2)	54	108.0 (35.1–478.0)
Hashibe <i>et al.</i> (2007c)		<i>Nonsmokers</i>		<i>Smokers</i>	
		Cases	Odds ratio (95% CI)	Cases	Odds ratio (95% CI)
	Alcohol				
	No	4	1.0	1	0.71 (0.07–7.00)
	Yes	12	0.96 (0.28–3.28)	174	6.42 (2.03–20.30)

CI, confidence interval; HR, hazard risk; RR, relative risk; WE, whiskey-equivalent

Table 2.22 Selected cohort and case–control studies of oesophageal cancer in men and women by level of alcoholic beverage intake

Reference	Exposure categories	Men		Women	
		Cases/ deaths	Relative risk (95% CI)	Cases/ deaths	Relative risk (95% CI)
Cohort studies					
Adami <i>et al.</i> (1992b)	Alcoholics	26	6.9 (4.5–10.0)	1	5.9 (0.1–32.6)
Kinjo <i>et al.</i> (1998)	None	56	1.0	93	1.0
	1–3 times/month	24	0.8 (0.5–1.3)	7	0.6 (0.3–1.3)
	1–3 times/week	67	1.1 (0.7–1.6)	9	1.3 (0.6–2.5)
	≥4 times/week	181	2.4 (1.8–3.3)	3	2.0 (0.6–6.2)
Case–control studies					
		Odds ratio (95% CI)		Odds ratio (95% CI)	
DeStefani <i>et al.</i> (1990)	0 mL/day	26	1	38	1
	1–24 mL/day	16	0.85 (0.4–1.8)	12	1.04 (0.4–2.4)
	25–49 mL/day	12	0.71 (0.3–1.6)		
	50–149 mL/day	50	1.37 (0.8–2.4)		
	150–249 mL/day	46	3.57 (1.9–6.7)	12	1.89 (0.7–4.9)
Negri <i>et al.</i> (1992)	≥250 mL/day	49	5.27 (2.7–10.2)		
	<4 drinks/day	63	1	48	1
	4–6 drinks/day	50	1.5 (0.9–2.2)	8	2.2 (1.0–4.3)
	>6 drinks/day	131	3.5 (2.4–5.1)		$p=0.05$
			$p<0.001$		
Kabat <i>et al.</i> (1993)	Non-drinker	7	1.0	16	1.0
	Occasional	15	1.4 (0.6–3.5)	17	1.4 (0.7–2.9)
	1–3.9 oz WE/day	27	2.3 (1.0–5.4)	25	4.4 (2.2–8.7)
	≥4 oz WE/day	86	10.9 (4.9–24.4)	20	13.2 (6.1–28.8)
Gallus <i>et al.</i> (2001)	<1 drink/day			29	1.0
	1–2 drinks/day			50	1.99 (1.15–3.44)
	≥3 drinks/day			35	5.40 (2.70–10.80)
					$p<0.001$

Table 2.22 (continued)

Reference	Exposure categories	Men		Women	
		Cases/ deaths	Relative risk (95% CI)	Cases/ deaths	Relative risk (95% CI)
Yokoyama <i>et al.</i> (2006)	Never/rare			24	1.0
	Light			11	1.81 (0.81–4.05)
	Moderate			6	3.97 (1.40–11.26)
	Heavy			7	15.35 (4.85–48.62)
	Former drinker			4	4.58 (1.25–16.79)
					$p < 0.0001$
	<i>Strong alcoholic beverages</i>				
	Never			46	1.0
	Sometimes			4	2.58 (0.80– 8.33)
	Frequently			2	12.47 (0.97–160.06)
				$p = 0.012$	

CI, confidence interval; WE, whiskey-equivalent

2.5.1 Cohort studies

(a) Special populations (Table 2.23)

Most HCCs occur in cirrhotic livers, and cirrhosis is a pathogenic step in liver carcinogenesis (La Vecchia *et al.*, 1998). In alcoholics, prolonged, excessive alcohol consumption results in alcoholic cirrhosis. The risk of HCC has been examined among alcoholic and cirrhotic subjects. In western countries, a few cohort studies have provided information regarding these special populations. Results from these cohort studies are presented in Table 2.23. Since 1988, two cohort studies conducted in Sweden have assessed the risk of primary liver cancer. One cohort comprised alcoholic and cirrhotic subjects (Adami *et al.*, 1992a) and the other cohort included male and female alcoholics (Adami *et al.*, 1992b). An additional cohort study in Denmark was conducted among patients with cirrhosis (Sørensen *et al.*, 1998). The number of cases ranged from four to 182 within these three populations. Each of the three studies showed evidence of a strong association between alcoholism, cirrhosis and liver cancer. Two of these studies reported statistically significant SIRs greater than 35 among alcoholics and cirrhotics (Adami *et al.*, 1992a; Sørensen *et al.*, 1998). The Swedish cohort, which included alcoholics and cirrhotics, was based on a total of 83 cases and the Danish cohort of cirrhotics was based on a total of 245 cases. In contrast, a cohort study of 5332 Norwegian teetotallers reported a SIR for liver cancer of 0.31. However, this was based on only one observed case (Kjaerheim *et al.*, 1993).

(b) General population (Table 2.24)

Two cohort studies have been conducted among the general population since 1988 (Yuan *et al.*, 1997; Wang *et al.*, 2003b). Neither study observed an association between alcoholic beverage consumption and liver cancer. In a study of male residents from communities in Shanghai, Yuan *et al.* (1997) reported a non-statistically significant reduction in risk among moderate (relative risk 0.68) and heavy (relative risk 0.84) drinkers of alcohol compared with non-drinkers. Similarly, Wang *et al.* (2003b) found no significant associations with the risk for HCC among drinkers compared with non-drinkers in a study of male residents from Taiwan.

2.5.2 Case-control studies (Table 2.25)

Ten case-control studies published since the last evaluation (IARC, 1988) provide information related to alcoholic beverage consumption and liver cancer: four were conducted in Italy (La Vecchia *et al.*, 1998; Donato *et al.*, 2002; Gelatti *et al.*, 2005; Franceschi *et al.*, 2006), two in the USA (Yuan *et al.*, 2004; Marrero *et al.*, 2005), and one each in Greece (Kuper *et al.*, 2000a), Japan (Tanaka *et al.*, 1992), South Africa (Mohamed *et al.*, 1992) and Spain (Vall Mayans *et al.*, 1990). All of these studies, with the exception of Yuan *et al.* (2004), used hospital-based controls. Tanaka *et al.* (1992) used city residents who visited a local public health centre for a routine health

Table 2.23 Cohort studies of liver cancer and alcoholic beverage consumption in special populations

Reference, location, study name	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment	Comments
Adami <i>et al</i> (1992a), Sweden	Cohorts were selected from the in-patient registry containing diagnostic codes for alcoholism and/or liver cirrhosis; 12 942 patients included in the study. 8511 alcoholics (7609 men, 911 women), 3589 cirrhotics (1961 men, 1628 women), 836 alcoholics/cirrhotics (734 men, 102 women); follow-up 1965–1983; 90% histology confirmed	Hospital discharge-diagnosis	Liver (155.0, 155.1, 155.2, 155.3, 155.8, 155.9)	Alcoholics Cirrhotics Alcoholics and cirrhotics	13 59 11	SIR 3.1 (1.6–5.3) 35.1 (26.7–45.3) 34.3 (17.1–61.3)	Age, sex	Risk for liver cancer 10 times higher among cirrhotics than among alcoholics

Table 2.23 (continued)

Reference, location, study name	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment	Comments
Kjaerheim <i>et al.</i> (1993)	5332 members of the International Organization of Good Templars, Norwegian teetotalers; followed-up 1980–1989	Cancer Registry	Liver (155.0)	Teetotalers		SIR 0.31 (0.1–1.7)	Age, sex	
Adami <i>et al.</i> (1992b), Sweden	Population-based cohort of 9353 (8340 men; 1013 women) alcoholics diagnosed in 1965–1983, followed-up for 19 years; 90% diagnosed	Discharge diagnosis of alcoholism	Liver (ICD-7 307, 322; ICD-8 291, 303)	Alcoholics (men, women)	Men 23 Women 4	5.4 (3.4–8.1) 12.5 (3.4–32.0)	Age, years follow-up	No age related trends were seen with relation to liver cancer. Patients without a discharge diagnosis of cirrhosis experienced a 3-fold increase in risk for primary liver cancer.

Table 2.23 (continued)

Reference, location, study name	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment	Comments
Sørensen <i>et al.</i> (1998), Denmark	Danish National Registry of Patients; patients with a diagnosis of alcoholic cirrhosis, primary biliary cirrhosis, non-specified cirrhosis, chronic hepatitis or other type of cirrhosis, alcoholism not indicated between 1977 and 1989; 205 cases (182 men, 103 women); follow-up until 1993	Discharged diagnosis	Liver (ICD-8 571.09, 571.90, 571.92, 571.93, 571.99, 303)	Cirrhotics	Men 82 Women 63 Both 245	40.2 (NG) $p < 0.05$ 27.8 (NG) $p < 0.05$ 36 (31.6–40.8)	Age, sex	Excess risk for liver cancer observed among cirrhotics: 40-fold increase risk among men and 28-fold increase among women; risk further exaggerated among cases of hepatocellular carcinoma

CI, confidence interval; ICD, International Classification of Diseases; NG, not given; SIR, standardized incidence ratio

Table 2.24 Cohort studies of liver cancer and alcoholic beverage consumption

Reference, location, study name	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment	Comments
Yuan <i>et al.</i> (1997), Shanghai, China, 1986–1989	18 244 male residents living in 4 small communities in the city of Shanghai, aged 45–64 years; no history of cancer; follow-up until 1995	Structured questionnaire	Liver (ICD-9 155)	Non-drinkers	61	1.0	Age, level of education, cigarette smoking	No association between alcohol consumption and risk for liver cancer in men; CI not given, <i>p</i> values not given
				1–28 drinks/week	32	0.68		
				≥29 drinks/week	9	0.84		
Wang <i>et al.</i> (2003b); Taiwan 1990-2000	Residents of seven townships in Taiwan; 11 937 born between 1926 and 1960; follow-up until 2000	Personal interview; serum samples	Liver	Non-drinkers Drinkers	84 31	1.00 1.46 (0.97–2.21)	Age, residence, HBV, HCV markers	Elevated risk for HCC among users of alcohol although not significant

CI, confidence interval; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICD, International Classification of Diseases

Table 2.25 Case-control studies of liver cancer and alcoholic beverage consumption

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Mayans <i>et al.</i> (1990), Catalonia, Spain, 1986-88	96 hospital-based cases were diagnosed with primary liver cancer in 1986-88; 77% histologically confirmed as HCC	190 matched 2:1 on age (within 5 years), sex; selected from same hospital as cases	Structured interview	Non-drinker	3	1.00	Age, sex, HBV status	Alcohol consumption significantly associated with HCC; risk did not significantly change with HBV status; CI not given
				1-20 g/day	27	1.78		
				21-40 g/day	16	1.97		
				41-60 g/day	18	6.22		
				61-80 g/day	12	7.89		
>80 g/day	20	12.0	$p < 0.001$					
Yuan <i>et al.</i> (2004), Los Angeles County, CA, USA, 1984-2002	Population-based; 295 HCC cases, 18-74 years old; LA County Cancer Surveillance Program (1984-2002); 100% histologically confirmed	435 (age, gender, race) controls; Hispanic and non-Hispanic 2% match; age (within 5 years)	Personal interview; blood specimen	Non-drinker	91	1.00	Age, gender, race, level of education, smoking status, history of diabetes	Risk for HCC increased with increased drinking: reduction in risk for patients that consumed >2 drinks/day (40% reduction)
				>0-2 drinks/day	66	0.6 (0.4-0.9)		
				>2-4 drinks/day	43	1.4 (0.8-2.4)		
				>4 drinks/day	95	3.2 (1.9-5.3)		

Table 2.25 (continued)

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Gelatti <i>et al.</i> (2005), Brescia and Pordenone, Italy	200 cases of HCC, up to age 79 years; born in Italy; Caucasian	400 hospitalized for other reasons not related to liver disease, neoplasms, tobacco- or alcohol-related disease; frequency-matched with cases on age (± 5 years), sex, date of hospital admission	Interview; blood sample	0–60 g/day	86	1.00	Age, sex, HBV and HCV markers, area of recruitment	Heavy alcohol consumption related to increased risk for HCC; no other alcohol related findings reported
				61–100 g/day	48	1.2 (0.8–1.9)		
				>100 g/day	66	2.6 (1.7–4.0)		
Franceschi <i>et al.</i> (2006), Pordenone and Naples, Italy, 1999–2002	279 cases, aged 43–84 years; diagnosed with HCC without treatment; 78.2% histologically confirmed; enrolled from hospitals and cancer institutes in Naples and Pordenone (1999–2002)	431 hospital-based 40–83 years old; admitted for reasons other than alcohol- and tobacco-related use or hepatitis; distribution matched on age, sex	Questionnaire; HBV, HCV testing	Never	20	1	Gender, age, center, education, HBV, HCV markers	Significant increase in risk for HCC among heaviest drinkers
				<7 drinks/week	16	1.67 (0.55–5.13)		
				7–13 drinks/week	26	0.81 (0.35–2.38)		
				14–20 drinks/week	38	1.04 (0.41–2.65)		
				21–34 drinks/week	53	1.61 (0.61–4.29)		
≥ 35 drinks/week	76	5.94 (2.25–15.67)						

Table 2.25 (continued)

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Marrero <i>et al.</i> (2005), Michigan, USA, 2002–03	70 cases of HCC from liver or general medicine clinics; 81.4% histologically confirmed	70 with cirrhosis and 70 with no liver disease; 2:1 match on age (± 5 years) and sex: 80% histologically confirmed for cirrhosis controls	Validated questionnaire by trained interviewer	None <1500 g–years ≥ 1500 g–years	11 11 48	1.0 1.4 (0.8–1.9) 23.8 (7.3–79)	Body mass index, smoking, age	24-fold increased risk for HCC among heavy consumers of alcohol (HCC versus no liver disease); risk not as excessive in comparison with cirrhotics
Kuper <i>et al.</i> (2000a); Athens, Greece, 1995–98	333 cases enrolled from 3 teaching hospitals in Athens (283 men, 50 women); 99% confirmed diagnosis	360 (298 men, 62 women) hospital controls; matched 1:1 on gender, age (± 5 years)	Hospital interview; blood test	Non-drinkers <20 glasses/week 20–39 glasses/week ≥ 40 glasses/week	135 71 46 81	1.0 0.8 (0.4–1.4) 0.7 (0.3–1.5) 1.9 (0.9–3.9) $p=0.13$	Age, gender, years of education, HBV, HCV markers	Increased risk of HCC among heavy consumers of alcohol not significant.

Table 2.25 (continued)

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Mohamed <i>et al.</i> (1992), Johannesburg, South Africa	101 (77 men, 24 women) Southern African blacks with HCC, 20–87 years old; enrolled from a hospital outside Johannesburg;	101 controls; 1:1 matched on ethnic origin, sex, age (± 2 years); same hospital as cases with diagnosis other than HCC	Interview	<i>Men</i>			HBV status, smoking	Significant increased risk for HCC found only among men >40 years of age
				Non-drinkers	Not reported			
				Light/moderate	18	0.8 (0.2–2.6)		
				Heavy	39	4.4 (1.4–14.1) <i>p</i> =0.0005		
				<i>Women</i>				
				Non-drinkers	Not reported			
				Light/moderate	1	0.6 (0.0–8.8)		
				Heavy	7	1.4 (0.3–9.3) <i>p</i> =0.81		

Table 2.25 (continued)

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Tanaka <i>et al.</i> (1992), Fukuoka, Japan, 1985–89	204 HCC patients aged 40–69 (168 men, 36 women); residents of Fukuoka or Saga Prefecture, Japanese nationality, enrolled from Kyushu University Hospital; 40% histologically confirmed enrolled in 1985–89	410 residents (291 men, 119 women) of Fukuoka city who visited a public health center near Kyushu University Hospital between January 1986 and July 1989 for a health examination; matched on age, sex	In-person interview; blood sample	<i>Men</i>			Age, sex	History of heavy drinking significantly associated with increased risk for HCC
				Non-drinker	37	1.0 (reference)		
				0.1–33.9 drink–years	31	0.9 (0.5–1.6)		
				34.0–76.6 drink–years	36	0.9 (0.5–1.7)		
				>76.6 drink–years	64	1.7 (1.0–2.9)		
						<i>p</i> =0.03		
				<i>Women</i>				
				Non-drinkers	27	1.0 (reference)		
0.1–33.9 drink–years	5	2.1 (0.6–7.0)						
34.0–76.6 drink–years	2	–						
>76.6 drink–years	2	2.4 (0.6–9.1)						
		<i>p</i> =0.11						
La Vecchia <i>et al.</i> (1998), Milan, Italy, 1984–96	499 (276 men, 123 women) with HCC, aged 23–74 recruited from major teaching and general hospitals in the greater Milan area	1552 (1141 men, 411 women); aged 20–74 years; patients admitted to area hospitals; with no history of cancer	Interview	0 drink/day	26	13.4 (4.1–43.8)	Age, sex, tobacco smoking, hepatitis, diabetes, body mass index, family history	Association between heavy alcohol consumption and HCC among patients with a history of cirrhosis
				1–4 drinks/day	24	15.2 (3.2–72.9)		
				>4 drinks/day (cases with history of cirrhosis)	37	24.9 (8.2–76.0)		

Table 2.25 (continued)

Reference, location, study name	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment	Comments
Donato <i>et al.</i> (2002), Brescia, Italy, 1995–2000	464 (380 men, 84 women) patients with first diagnosis of HCC admitted between 1995–2000; aged <76 years; Italian, lived in province of Brescia	Hospital-based; 824 (686 men, 138 women), aged <76 years; no liver disease or cancer; frequency-matched with cases on age (± 5 years), sex, date or hospital admission; from Brescia, Italia	Questionnaire; blood sample	<i>Men</i>			Age, residence, HBV, HCV markers	For women, categories of alcohol consumption above 80 g/day were omitted; higher levels of alcohol consumption (>81 g/day) associated with HCC in men.
				Non-drinkers	8	1.0 (reference)		
				1–20 g/day	24	2.3 (0.7–7.2)		
				21–40 g/day	27	0.9 (0.3–2.7)		
				41–60 g/day	44	1.6 (0.5–4.6)		
				61–80 g/day	33	2.4 (0.8–7.1)		
				81–100 g/day	62	4.2 (1.5–11.7)		
				101–120 g/day	47	7.7 (2.7–22.7)		
				121–140 g/day	48	9.8 (3.3–29.1)		
				>140 g/day	87	11.0 (3.9–31.0)		
				<i>Women</i>				
				Non-drinkers	24	1.0 (reference)		
				1–20 g/day	22	0.6 (0.2–1.7)		
				21–40 g/day	15	1.4 (0.4–5.4)		
41–60 g/day	11	1.9 (0.4–8.1)						
61–80 g/day	4	3.1 (0.3–29.7)						
>80 g/day	8	16.5 (3.0–90.1)						

CI, confidence interval; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus

examination. Significantly higher relative risks were reported among heavy drinkers compared with non-, light or moderate drinkers in nine studies (Vall Mayans *et al.*, 1990; Mohamed *et al.*, 1992; Tanaka *et al.*, 1992; La Vecchia *et al.*, 1998; Donato *et al.*, 2002; Yuan *et al.*, 2004; Gelatti *et al.*, 2005; Marrero *et al.*, 2005; Franceschi *et al.*, 2006). In these studies, the magnitude of the association ranged from 2.6 for intake of more than 100 g/day compared with 60 g/day or less (Gelatti *et al.*, 2005); to 24.9 for those who consumed more than four drinks per day compared to those who consumed no drinks per day (La Vecchia *et al.*, 1998). Tanaka *et al.* (1992) found a significant 1.7-fold increase in risk among men whose cumulative alcohol consumption was greater than 76.6 drink-years. No significant associations were observed among women. However, despite the number of studies that have demonstrated evidence of an association between heavy alcoholic beverage consumption and liver cancer, a clear, consistent dose-response relationship between light or moderate drinking and HCC risk has not yet been established.

2.5.3 *Meta-analyses (Table 2.26)*

Two meta-analyses have examined the association between alcoholic beverage consumption and liver cancer. A meta-analysis of 229 studies that evaluated the association between alcohol drinking and risk for cancer included data from 17 case-control and three cohort studies and 2294 cases of HCC. These 20 studies reported a direct trend in risk for HCC with increasing alcoholic beverage consumption. The reported relative risks were 1.17 (95% CI, 1.11–1.23) for consumption of 25 g alcohol per day, 1.36 (95% CI, 1.23–1.51) for 50 g per day and 1.86 (95% CI, 1.53–2.27) for 100 g per day (Bagnardi *et al.*, 2001). An additional review of the Chinese literature included a meta-analysis of 55 case-control studies that investigated the risk factors for primary liver cancer in China. Twenty-two of these 55 studies assessed the effect of exposure to alcohol. A total of 3207 cases of primary liver cancer and 3983 controls were identified (Luo *et al.*, 2005). The combined odds ratio reported from these 22 studies was 1.88 (95% CI, 1.53–2.32) for alcoholic beverage drinkers versus non-drinkers. No information regarding the dose-risk relationship was given. [The Working Group could not determine whether there was possible overlap between the individual cohort and case-control studies listed and the studies included in the meta-analyses conducted by Bagnardi *et al.* (2001) and Luo *et al.* (2005), because the individual studies included in the meta-analyses were not identified.]

2.5.4 *Interaction with hepatitis viral infection (Table 2.27)*

The impact of alcohol on primary liver cancer is difficult to measure because of the existence of other factors, in particular chronic infection with HBV and HCV—which have already been shown to be important determinants for HCC worldwide, and may modify the relationship between alcoholic beverage consumption and liver cancer.

Table 2.26 Meta-analyses of liver cancer and alcoholic beverage consumption

Reference, description, study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment	Comments
Luo <i>et al.</i> (2005); meta-analysis of 55 case-control studies from China	Database search of Chinese biomedical literature database (1979–2003), China Hospital Knowledge Database (1999–2003) and Medline (1966–2003); inclusion criteria were: case-control studies investigating risk factors for PLC in Chinese population.	22 studies assessed exposure to alcohol	Non-drinkers Drinkers	Not reported 3207	1.0 1.88 (1.53–2.32) $p < 0.001$	Not reported	Studies of alcohol showed significant heterogeneity
Bagnardi <i>et al.</i> (2001); meta-analysis of 229 cohort and case-control studies	3 cohort and 16 case-control studies on liver cancer; total of 1961 cases	Exposure to alcohol	25 g/day 50 g/day 100 g/day		1.20 (1.13–1.27) 1.41 (1.26–1.56) 1.83 (1.53–2.19) p -trend < 0.01	Gender	A gender effect was also observed (p -trend < 0.05)

CI, confidence interval; PLC, primary liver cancer

Table 2.27 Selected cohort and case-control studies of liver cancer by alcoholic beverage consumption and infection with hepatitis B virus (HBV) and hepatitis C virus (HCV)

Study design	Odds ratio (95% CI) of risk for liver cancer by alcoholic beverage intake			
Cohort study				
Wang <i>et al.</i> (2003b)	<i>None</i>	<i>Light/moderate</i>		
HBV-negative	1	1.64 (0.74–3.64)		
HBV-positive	13.12 (7.82–22.01)	17.93 (9.58–33.68)		
Case-control studies				
Kuper <i>et al.</i> (2000a)	<i>None</i>	<i><20 drinks/week</i>	<i>20–39 drinks/week</i>	<i>≥40 drinks/week</i>
HBV/HCV	1	1.0 (0.2–4.1)	1.4 (0.3–7.9)	5.4 (0.6–50.3)
No infection	1	0.7 (0.3–1.3)	0.6 (0.2–1.4)	1.6 (0.8–3.4)
Donato <i>et al.</i> (2002)		<i><60 g/day</i>	<i>>60 g/day</i>	
No infection		1	7.0 (4.5–11.1)	
HCV		55.0 (29.9–101)	109 (50.9–233)	
HBV		22.8 (12.1–42.8)	48.6 (24.1–98.0)	
Yuan <i>et al.</i> (2004)		<i><4 drinks/day</i>	<i>>4 drinks/day</i>	
No infection		1	2.6 (1.3–5.1)	
HBV/HCV		8.1 (4.6–14.4)	48.3 (11.0–212.1)	
Franceschi <i>et al.</i> (2006)		<i><14 drinks/week</i>	<i>14–34 drinks/week</i>	<i>≥35 drinks/week</i>
No infection		1	0.68 (0.26–1.76)	4.96 (2.19–11.24)
HBV/HCV		28.82 (12.84–64.69)	47.6 (20.76–109)	74.36 (22.89–242)

CI, confidence interval

Chronic infections with HBV and HCV have been shown to increase the risk for HCC by approximately 20-fold (Parkin, 2006). Five studies examined the association between alcoholic beverage consumption and the risk for liver cancer among patients with chronic infection with HBV and HCV; one cohort study (Wang *et al.*, 2003b) and four case–control studies (Kuper *et al.*, 2000a; Donato *et al.*, 2002; Yuan *et al.*, 2004; Franceschi *et al.*, 2006). The cohort study reported a relative risk of 13.12 among non-drinkers with chronic HBV infection. Light to moderate drinking and heavy drinking further increased the relative risk to 17.93. All four case–control studies showed an increased risk for HCC with increased alcoholic beverage consumption among subjects infected with HBV or HCV. Three of these studies showed a significant increase in risk. However, the study by Kuper *et al.* (2000a), based on 333 cases of HCC and 360 controls, did not indicate the same significant trend in increased risk for HCC.

2.5.5 *Interaction with tobacco smoking*

The interaction between alcoholic beverage consumption and tobacco smoking—another recognized risk factor for HCC (IARC, 2004)—was considered in case–control studies in Greece (Kuper *et al.*, 2000a) and the USA (Yuan *et al.*, 2004; Marrero *et al.*, 2005). In the Greek study (Kuper *et al.*, 2000a), the relative risk was 5.6 (95% CI, 1.70–19.0) for heavy drinkers and heavy smokers compared with never smokers and non- and light drinkers. In a US dataset (Marrero *et al.*, 2005), the relative risk was 7.2 (95% CI, 2.2–14.1) for combined exposure to alcoholic beverages and tobacco compared with cirrhotic subjects. In another US dataset (Yuan *et al.*, 2004), the corresponding relative risk for exposure to both factors was 5.9 (95% CI, 3.3–10.4).

2.6 **Breast cancer**

Overall, more than 100 epidemiological studies—two thirds case–control and one third cohort—have evaluated the association between the consumption of alcoholic beverages and the risk for breast cancer. In addition, two pooled analyses, the largest of which included data from more than 50 studies, have been conducted. For ease of presentation, the data from the individual studies that were included in this pooled analysis are not presented in Tables 2.28 or 2.29, except for studies that examined detailed exposure effects, such as duration of alcoholic beverage consumption, that were not considered in the pooled analysis.

2.6.1 *Pooled and meta-analyses*

The pooling of data from many epidemiological studies permits the use of uniform definitions across studies and reduces the inevitable statistical variability in the findings from one study to another. This is particularly important when the associated risks are relatively small and individual studies lack statistical power. Hamajima *et al.*

(2002) (The Collaborative Group on Hormonal Factors on Breast Cancer) collated and re-analysed individual data from 53 studies on 58 515 women who had breast cancer, which constituted most of the evidence available worldwide at that time. Results from this pooled analysis showed a linear increase in risk for breast cancer with increasing levels of alcoholic beverage consumption, with a relative risk of 1.46 (95% CI, 1.34–1.60) for women who drank ≥ 45 g alcohol per day (median, 58 g per day) compared with non-drinkers. This corresponds to an increase of 7.1% (95% CI, 5.5–8.7%) per 10 g per day (Table 2.28; see Figure 2.1). The results were consistent across studies and between cohort and case–control studies included in the analysis (Figure 2.2).

A previous meta-analysis of 38 case–control and cohort studies (Longnecker, 1994), most of which were included in the Collaborative Group analysis, and a pooled analysis of six cohort studies, based on 4330 incident cases of breast cancer (Smith-Warner *et al.*, 1998), reported results consistent with the findings of the Collaborative Group (Hamajima *et al.*, 2002). The latter study showed a 9% increase in risk per 10 g intake of alcohol per day (8% after correction for measurement error), which was adjusted for a wide range of potential confounding factors (Smith-Warner *et al.*, 1998).

2.6.2 *Additional cohort studies*

Two cohort studies were conducted among women who had a high intake of alcoholic beverages; both were conducted in Sweden and reported a significant increase in incidence rates for breast cancer among alcoholics compared with national incidence rates (Sigvardsson *et al.*, 1996; Kuper *et al.*, 2000b) (Table 2.29). However, neither of these studies provided information on individual exposures, or adjusted for potential confounders.

The majority of the 21 additional cohort studies conducted in the general population also showed an increase in risk for breast cancer with increased alcoholic beverage consumption (Table 2.30). The largest of these studies, conducted by the European Prospective Investigation into Cancer and Nutrition (EPIC) and based on 4300 cases, reported a significant 13% increase in risk for breast cancer for intakes of ≥ 20 g alcohol per day, which corresponds to an increase in risk of 3% per 10 g intake of alcohol per day (95% CI, 1–5%) (Tjønneland *et al.*, 2007).

2.6.3 *Additional case–control studies*

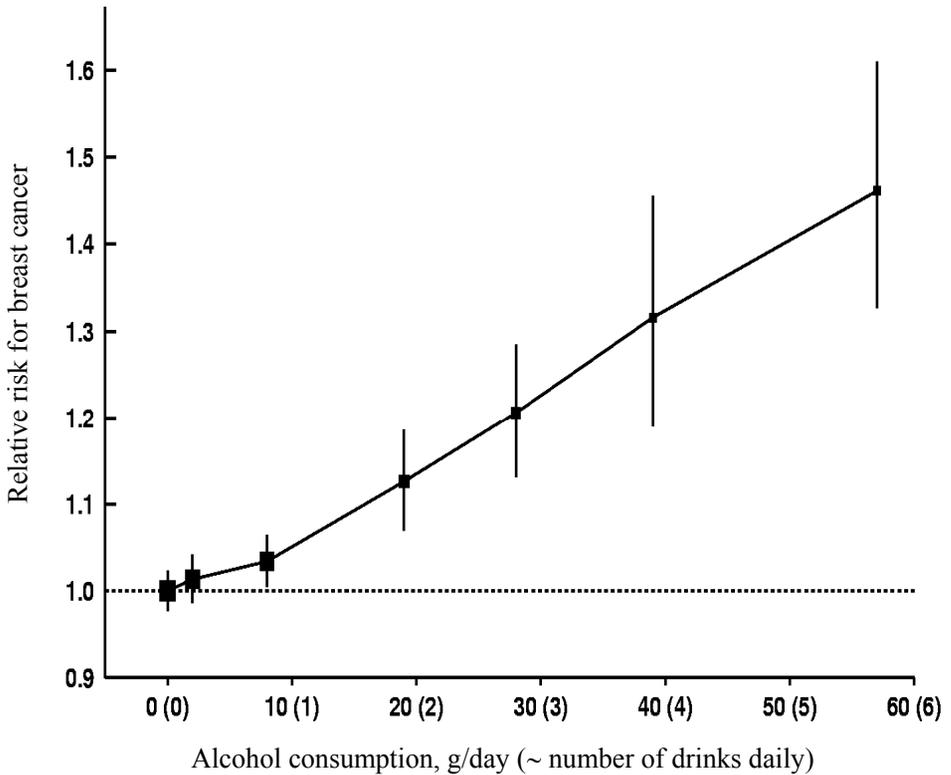
The majority of the 35 case–control studies that were not included in the pooled analyses have reported positive associations with increasing alcoholic beverage intake, which were statistically significant in 14 studies (Table 2.31).

2.6.4 *Measurements of alcoholic beverage intake*

Taken together, all of the results from these studies suggest that low to moderate alcoholic beverage intake (i.e. in the order of one drink per day) is associated with

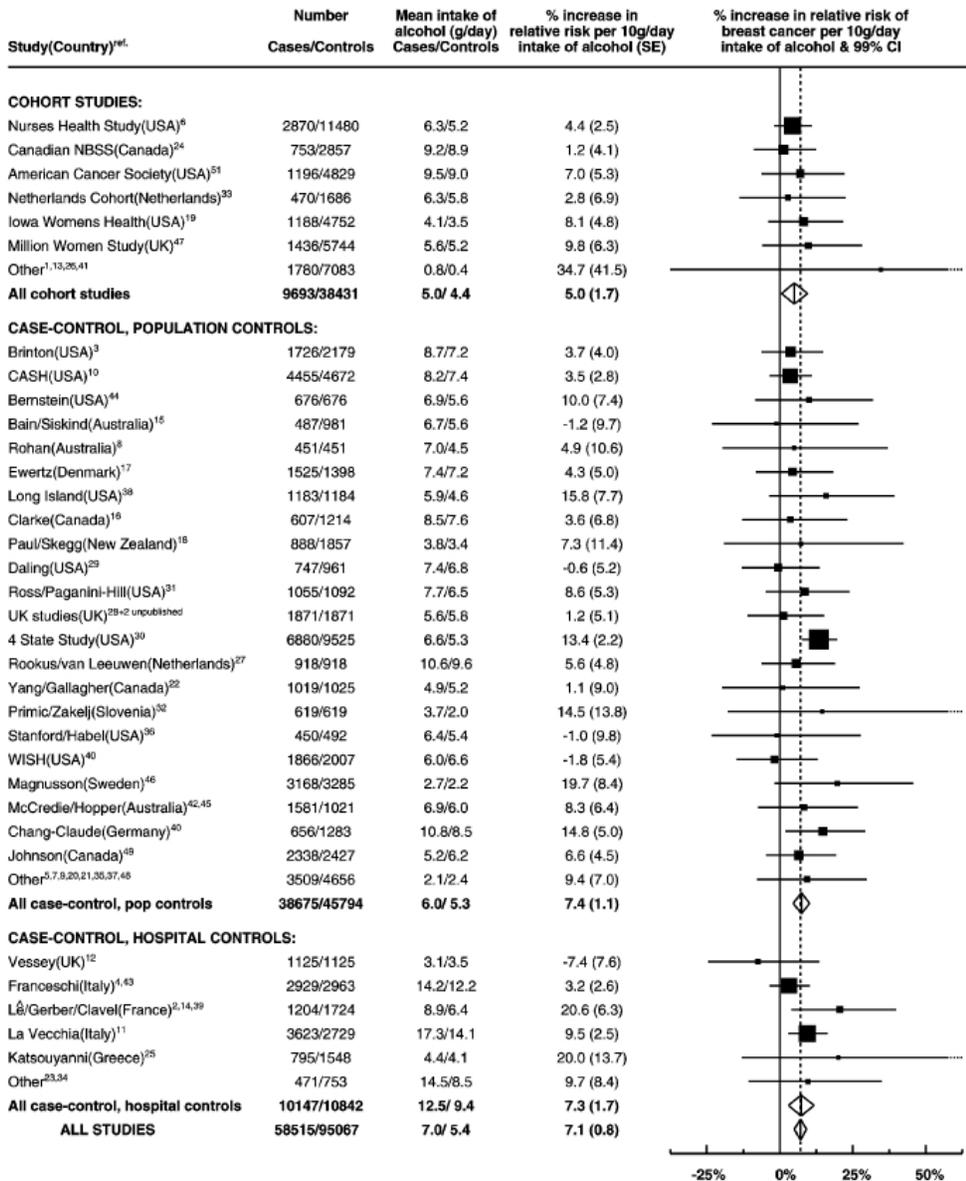
Figure 2.1. Relative risk for breast cancer in relation to reported alcoholic beverage consumption (adjusted by study, age, parity, age at first birth and tobacco smoking).

Pooled analysis of data from 53 studies that included 58 515 women with breast cancer



From Hamajima *et al.* (2002)

Figure 2.2. Details of and results from studies on the relation between alcohol consumption and breast cancer. Relative risks are stratified by age, parity, age at first birth and smoking history.



Reprinted by permission from Macmillan Publishers Ltd: British Journal of Cancer. Collaborative Group on Hormonal Factors in Breast Cancer (2002) Alcohol, tobacco and breast cancer – collaborative re-analysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. Br J Cancer, 87:1234–1245. Copyright 2002

Table 2.28 Pooled and meta-analyses of female breast cancer and alcoholic beverage consumption

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Longnecker (1994)	Meta-analysis of 38 case-control and cohort studies	Varied	<i>Alcohol intake (drinks/day)</i>	Not stated	1.0 1.11 (1.07–1.16) 1.24 (1.15–1.34) 1.38 (1.23–1.55)	As defined per study	Variation across studies found
			Non-drinker				
			1				
			2				
Smith-Warner <i>et al.</i> (1998), pooling project	Pooled analysis of six cohort studies; 322 647 women followed up for up to 11 years; 4335 cases of invasive breast cancer identified	Self-administered questionnaire	<i>Average intake (g/day)</i>	1462 680 882 727 360 194 30	1.0 1.07 (0.96–1.19) 0.99 (0.90–1.10) 1.06 (0.96–1.17) 1.16 (0.98–1.38) 1.41 (1.18–1.69) 1.31 (0.86–1.98)	Age at menarche, parity, age at first birth, menopausal status, history of benign breast disease, hormone replacement therapy use, oral contraceptive use, family history, smoking, education, body mass index, height, fat intake, fibre intake, energy intake	Correction for measurement error made little difference to the estimate; similar associations found for beer, wine and spirits; no difference by subgroup of menopausal status, family history, hormone-replacement therapy use or body mass index
			Non-drinker				
			>0–<1.5				
			1.5–4.9				
			5.0–14.9				
			15–29.9				
			30–59.9				
			≥60				
			<i>p</i> for trend				
			<i>Per 10 g/day</i>				
			Uncorrected				
Corrected							
Beer							
Wine							
Spirits							

Table 2.28 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Bagnardi <i>et al.</i> (2001)	Meta-analysis of 49 studies (12 cohort, 37 case-control, with a total of 44 033 cases)	Varied	<i>Alcohol intake (g/day)</i> 25 50 100	244 033	1.31 (1.27–1.36) 1.67 (1.56–1.78) 2.71 (2.33–3.08)	As per study	Significant heterogeneity between the studies
Hamajima <i>et al.</i> (2002), Collaborative Group on Hormonal Factors in Breast Cancer	Pooled analysis of 53 case-control and cohort studies; 58 515 invasive breast cancers; 95 067 controls	Varied	<i>Alcohol intake (g/day)</i> 0 <5 5–14 15–24 25–34 34–44 ≥45 Increase per 10 g/day	58 515	Relative risk (floated SE) 1.0 (0.012) 1.01 (0.014) 1.03 (0.015) 1.13 (0.028) 1.21 (0.036) 1.32 (0.059) 1.46 (0.060) 7.1% (SE, 0.8%)	Study, age, parity, age at first birth, smoking	No differences by subgroup of age at diagnosis, race, family history, menopausal status, parity, age at first birth, breastfeeding, education, age at menarche, height, weight, hormone replacement therapy use, oral contraceptive use, smoking
	Pooled analysis of 42 case-control studies		<i>Increase per 10 g/day</i> Population controls Hospital controls	38 675 10 147	7.4% (SE, 1.1%) 7.3% (SE, 1.7%)		
	Pooled analysis of 11 cohort studies		<i>Increase per 10 g/day</i>	9 693	5.0% (SE, 1.7%)		

CI, confidence interval; SE, standard error

Table 2.29 Cohort studies of breast cancer and alcoholic beverage consumption among special populations

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Standardized incidence ratio (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Alcoholics	Analytical cohort of 15 508 alcoholics (identified via Temperance Board records) in 1944–77; comparison group of 15 500 women, matched by age and region (identified via population register); follow-up not stated; 268 cases identified through cancer registry	Alcoholics	Comparison group (expected) Alcoholics (observed)	191	1.0	Age, region	Excluded ~6000 older women with no identification number; large changes in alcohol availability and attitudes during follow-up; not adjusted for potential confounders; no individual exposure data
				268	1.4 (1.2–1.7)		
Kuper <i>et al.</i> (2000b), Sweden, Hospital Discharge Records for Alcoholism	Analytical cohort of 36 856 women diagnosed with alcoholism from hospital discharge data, 1965–95; compared with national incidence rates; matched by age, sex, calendar time; excluding first year of follow-up; 514 cases identified through cancer registry	Hospital discharge related to alcoholism	National rates (expected) Alcoholics (observed)	Not stated 514	1.0 1.15 (1.05–1.25)	Age, sex, calendar time	No individual exposure information; no adjustment for potential confounders; no association found with age at diagnosis or menopausal status

CI, confidence interval

Table 2.30 Cohort and nested case–control studies of breast cancer and alcoholic beverage consumption in the general population

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Schatzkin <i>et al.</i> (1987), USA, NHANES I Epidemiologic Follow-up Study	Analytical cohort of 7188 women, aged 25–74 years; recruited 1971–75; median follow-up, 10 years; 121 cases identified through hospital records or death certificates	Interviewer-administered questionnaire	<i>Intake (g/day)</i> Non-drinker Any >0–1.2 1.3–4.9 ≥5	57 64 25 19 20	1.0 1.5 (1.1–2.2) 1.4 (0.9–2.3) 1.5 (0.9–2.6) 1.6 (1.0–2.7)	Age	Results presented for age-adjusted relative risks only; multivariate adjustment gave similar results, but based on fewer numbers (complete-case analysis); risk for any drinking versus none higher among younger versus older women, pre-versus post-menopausal women and lean versus overweight women; no differences in risk by subgroup of age at first birth, parity, age at menarche, family history, fat intake, smoking

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Dupont & Page (1985), USA, Nashville hospitals (retrospective cohort study)	Analytical cohort study of 3303 women with benign breast disease (100% histological confirmation); aged >20 years; recruited 1958-68 (response rate 84%); follow-up for a median of 17 years; 135 cases identified from death certificates and verified by pathology records	Self-administered questionnaire to patients or their next-of-kin; or via telephone interview.	<i>Alcohol</i>			Age, length of follow-up	Risk compared to women in the Third National Cancer Survey (Atlanta); mortality only; cohort of women with benign breast disease
			No	76	1.3 (1.1-1.7)		
Garfinkel <i>et al.</i> (1988), USA, American Cancer Society	Analytical cohort of 581 321 women across the USA, 1959-60, aged ≥ 30 years; mortality follow-up until 1972; 2933 deaths identified from death certificates	Self-administered questionnaire	<i>Intake (drinks/day)</i>			Age, education, age at first birth, family history, meat intake, smoking	Based on mortality only
			None	2334	1.00		
			Occasional	153	1.00 (0.82-1.13)		
			1	236	1.18 (1.03-1.36)		
			2	110	1.06 (0.86-1.30)		
			3	45	1.28 (0.95-1.74)		
			4	23	1.36 (0.90-2.07)		
			5	12	2.10 (1.18-3.72)		
≥ 6	20	1.60 (1.00-2.56)					

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Simon <i>et al.</i> (1991), USA, Tecumseh Community Health Study	Analytical cohort of 1954 women recruited in 1959–60, aged ≥ 21 years; follow-up for 28 years; 87 self-reported cases verified by pathology and medical records	Interviewer-administered questionnaire	Overall	87		Age, body mass index, subscapular and triceps skinfold measurements, education, smoking, family history, age at menarche, parity, age at first birth	No difference in risk by menopausal status (but low numbers)
			<i>No. of drinks/day</i>				
			Never		1.0		
			Former		0.93 (0.40–2.18)		
			0–<1		1.08 (0.64–1.82)		
1–1.9		1.23 (0.49–3.10)					
≥ 2		1.12 (0.25–5.01)					
Høyer & Engholm (1992), Denmark, Glostrup Population Study	Analytical cohort of 5207 women recruited 1964–86, aged 30–80 years; follow-up until 1989; 51 cases identified through registry	Self-administered questionnaire	<i>Intake (drinks/week)</i>	51		None stated	
			0		1.0		
			1–3		0.7 (0.3–1.6)		
			4–8		1.3 (0.7–2.5)		
			≥ 9		0.8 (0.3–2.0)		
			<i>p</i> for trend		0.2		

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Boice <i>et al.</i> (1995), USA, American Registry of Radiologic Technologists	Nested case-control study of 79 016 women recruited 1926–82, aged 23–90 years; follow-up for mean of 29 years; 528 cases matched with 2628 controls on age, year of diagnosis, follow-up time	Self-administered questionnaire	<i>Intake (drinks/week)</i> None <1 1–6 7–13 ≥14 Unknown	133 183 135 57 13 7	1.0 0.86 (0.67–1.10) 0.91 (0.69–1.20) 0.86 (0.61–1.22) 2.12 (1.06–4.27) 1.91 (0.74–4.92)	Age at menarche, age at menopause, age at first birth, family history, breast biopsy	

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Holmberg <i>et al.</i> (1995); Suzuki <i>et al.</i> (2005), Sweden, Swedish Mammography Cohort	Holmberg <i>et al.</i> (1995): nested case-control study of screening cohort, recruited 1987–90, aged 40–70 years; 380 cases ascertained through pathology departments and screening programme (response rate, 73%); 525 controls matched by age, date of diagnosis, region (response rate, 86%)	Self-administered questionnaire	Never Ever <i>Intake (g/day)</i> Never <0.76 0.76–2 ≥2	71 205 71 54 79 72	1.0 1.7 (0.2–2.4) 1.0 1.2 (0.8–1.8) 1.9 (1.2–2.9) 1.6 (1.0–2.4)	Family history, parity, age at first birth, education, body mass index	Stronger association for ever versus never drinking in women >50 versus <50 years; risk increased with increasing duration of drinking; no significant association with age at first started drinking

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Holmberg <i>et al.</i> (1995); Suzuki <i>et al.</i> (2005) (contd)	Suzuki <i>et al.</i> (2005): analytical cohort of 51 847 women, recruited 1987–90, aged 55–70 years;; follow-up until 2004 through cancer registry, verified by pathology and medical records; 1284 cases		<i>Intake in last 6 months (based on intake in 1987 and 1997; g/day)</i> None <3.4 3.4–9.9 ≥10 <i>p</i> for trend	314 476 343 151	1.0 1.08 (0.94–1.25) 1.10 (0.94–1.29) 1.43 (1.16–1.76) 0.012	Age, body mass index, height, education, parity, age at first birth, age at menarche, age at menopause, type of menopause, oral contraceptive use, hormone replacement use, family history, benign breast disease, energy intake, fibre and fat intake	Results also by receptor status (see accompanying table)

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Goodman <i>et al.</i> (1997a), Japan, Life Span Study	Analytical cohort of 22 000 residents of Hiroshima and Nagasaki in 1945, recruited 1979–1981, age range not stated; follow-up until 1989; 161 cases identified through cancer registry; 98% histologically confirmed	Self-administered questionnaire	<i>Alcohol use</i> Never Drinker	106 40	1.0 0.91 (0.61–1.31)	City, age, age at the time of the bombings, radiation dose to the breast	No association in women who drank beer, sake or other alcoholic beverages
Lucas <i>et al.</i> (1998), USA, Study of Osteoporotic Fractures	Analytical cohort of 7250 women recruited 1986–88, aged ≥ 65 years; follow-up 3 years after interview; 104 self-reported cases confirmed by medical records or through cancer registry	Self-administered questionnaire administered 1 year after recruitment; alcoholic beverage intake adjusted for atypical drinking (i.e. heavy drinking in past 30 days)	<i>Average no. of drinks per week</i> None <2 2–7 ≥ 8		<i>No family history of breast cancer</i> 21 1.0 38 1.13 (0.66–1.93) 17 1.41 (0.74–2.67) 8 1.70 (0.75–3.84)	No adjustment	Includes 4 cases with in-situ cancer; no association in women with a positive family history, but few cases ($n=20$)

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Zhang <i>et al.</i> (1999), USA, Framingham Study	Analytical cohort of 2764 women recruited in 1948, aged 28–62 years; plus 2284 recruited in 1971 in offspring cohort; follow-up until 1993; 287 cases (221 in original cohort, 66 in offspring cohort) identified through hospital admissions data and death certificates; verified from pathology and medical records (98% in original cohort and 100% in offspring cohort)	Self-administered questionnaire; intake assessed at several time points	<i>Average intake (g/day)</i> None 0.1–4.9 5–14.9 ≥15	69 110 55 53	1.0 0.8 (0.6–1.1) 0.7 (0.5–1.1) 0.7 (0.5–1.1)	Age, education, height, body mass index, physical activity, age at first birth, parity, age at menarche, age at menopause, smoking, hormone replacement therapy use	Similar risks for each cohort separately; no association with type of drink

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Vachon <i>et al.</i> (2001), USA, Minnesota Breast Cancer Family Study	Cohort of 426 families with breast cancer (probands, family members and their spouses; $n=9032$), recruited 1944–52, aged ≥ 18 years; follow-up until 1990; 558 cases identified from self-report and through death certificates	Telephone interviews (surrogate and self-reported)	Overall <i>Lifetime intake</i> Never < Weekly Weekly Daily	558	1.0 1.23 (1.00–1.51) 1.14 (0.86–1.51) 1.28 (0.85–1.91)	Age, birth cohort, familial clustering, type of respondent, smoking	Higher risk in first-degree relatives for daily versus never drinkers; validation study verified 136 of 138 breast cancers through medical and pathology records
Tjønneland <i>et al.</i> (2003, 2004), Denmark, Diet, Cancer and Health Study	Analytical cohort of 23 778 women, recruited 1993–97, aged 50–64 years; follow-up until 2000; 425 cases identified through registry	Self-administered questionnaire	<i>Intake (g/day)</i> None <6 6–12 13–24 25–60 ≥ 61 Occasional <i>Recent intake (per 10 g/day)</i>	10 122 9 93 93 9 9 423	1.21 (0.64–2.31) 1.0 0.97 (0.74–1.28) 1.18 (0.90–1.56) 1.45 (1.10–1.92) 1.35 (0.68–2.66) 1.32 (0.67–2.60) 1.09 (1.00–1.18)	Parity, age at first birth, benign breast disease, education, hormone replacement therapy use and duration, body mass index. As above plus intake earlier in life	No significant difference by beverage type or frequency of intake (days per week) for a given alcohol intake; association for 10 g/day intake similar by hormone replacement therapy use, although only significant in past users. No association with intake earlier in life or cumulative intake

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Dumeaux <i>et al.</i> (2004), Norway, Norwegian Women and Cancer Study	Analytical cohort of 86 948 women recruited 1991–97, aged 30–70 years; follow-up until 2001; 1130 cases identified through registries and death certificates	Self-administered questionnaire	<i>Intake in last year (g/day)</i> None 0.1–4.9 5–9.9 ≥10 <i>p</i> for trend	244 554 188 96	1.0 1.24 (1.06–1.44) 1.35 (1.11–1.64) 1.69 (0.32–2.15) <0.0001	Age, breast screening, age at menarche, parity, age at first birth, family history, menopausal status, hormone replacement therapy use, body mass index	Interaction with oral contraceptive use; increased risk among long-term users who consumed >10 g/day alcohol versus non-drinkers who had never used oral contraceptives; stronger association for high alcohol intake (≥10 g/day) in post- versus pre-menopausal women

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments		
Horn-Ross <i>et al.</i> (2004), USA, California Teachers Study	Analytical cohort of 103 460 women recruited 1995–96, aged 21–84 years; follow-up until 2001; 1742 invasive cases, ascertained through cancer registry and death certificates	Self-administered questionnaire	<i>Intake in past year (g/day)</i>	Non-drinkers	Pre-/perimenopausal	Age, race, energy intake, family history, age at menarche, parity, age at first birth, physical activity, body mass index, hormone replacement use and duration	Overall risk ≥ 20 g/day versus none, 1.28 (1.06–1.54); differences by menopausal status not significant; no clear pattern for age at started drinking; increased risk for ≥ 20 g/day among ever users of hormone replacement therapy versus non-drinkers who were never users; increased risk for ≥ 20 g/day among postmenopausal women who had a history of benign breast disease versus non-drinkers with no benign breast disease; no differences by subgroups of family history, body mass index, parity, physical activity		
				<5	95			1.0	
				5–9	53			0.93 (0.66–1.30)	
				10–14	55			1.05 (0.75–1.47)	
				15–19	42			1.09 (0.75–1.57)	
				≥ 20	27			1.28 (0.83–1.97)	
				Non-drinkers	Postmenopausal			physical activity, body mass index, hormone replacement use and duration	
				<5	311				1.0
				5–9	181				1.03 (0.86–1.24)
				10–14	150				1.04 (0.86–1.27)
15–19	126	1.08 (0.88–1.33)							
≥ 20	82	0.91 (0.71–1.16)							
	123	1.32 (1.06–1.63)							

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Mattisson <i>et al.</i> (2004), Sweden, Malmö Diet and Cancer Cohort	Analytical cohort of 11 726 women, recruited 1991–96, aged ≥ 50 years; follow-up until 2001; 342 cases (312 invasive; 30 <i>in situ</i>) identified through cancer registry	Interviewer-administered diet history (7-day diary)	<i>Intake (g/day)</i> None <15 15–29 ≥ 30	22 257 39 11	0.89 (0.57–1.39) 1.0 0.88 (0.62–1.24) 1.68 (0.91–3.12)	Interviewer, method version, season, age, energy, change in dietary habits, height, waist, hormone use, age at first birth, age at menarche, physical activity, smoking, education	Adjustment for energy from fat made little difference; association with high intake of wine (>20.8 cl/day versus <2.9 cl/day, relative risk for 2.1; 95% CI, 1.24–3.60)

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Petri <i>et al.</i> (2004), Denmark, Copenhagen City Heart Study and Glostrup Population Study (data for Glostrup Study also presented in Høyer & Engholm, 1992)	Analytical cohort of 13 074 women, aged 20–97 years; dates of recruitment not stated; followed-up until 1996; 473 cases identified through cancer registry	Self-administered questionnaire	<i>Average intake (drinks/week)</i>				Age, cohort, parity, hormone replacement therapy use	No difference by beverage type overall; stronger association for high intakes among premenopausal women, but based on very small numbers; positive association for spirits in postmenopausal women, but not for wine or beer (but again based on small numbers)
			<1	148	0.91 (0.73–1.13)			
			1–6	207	1.0			
			7–13	72	1.11 (0.85–1.45)			
			14–27	36	1.10 (0.77–1.57)			
			≥28	10	1.19 (0.58–2.41)			
			<i>Premenopausal</i>					
			<1	17	1.17 (0.66–2.07)			
			1–6	36	1.0			
			7–13	12	1.22 (0.66–2.25)			
			14–27	5	0.86 (0.33–2.21)			
			≥28	6	3.49 (1.36–8.99)			
			<i>Postmenopausal</i>					
<1	131	0.87 (0.69–1.10)						
1–6	171	1.0						
7–13	60	1.09 (0.81–1.47)						
14–27	31	1.15 (0.78–1.69)						
≥28	4	0.57 (0.18–1.78)						

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Baglietto <i>et al.</i> (2005), Australia, Melbourne Collaborative Cohort Study	Analytical cohort of 17 447 women recruited 1990–94, aged 40–69 years; follow-up until 2003; 537 cases identified through registries and histologically verified	Structured interview	<i>Intake in last year (g/day)</i>			Age, energy and folate intake	Adjustment for education, body mass index, age at menarche, parity, hormone replacement therapy, multivitamins had little effect; stronger association for high alcohol intake (≥ 40 g/day) among women with low folate intake; no association with alcoholic beverages at higher folate intake
			Never	171	1.0		
			Former	16	1.03 (0.62–1.73)		
			1–19	286	1.12 (0.93–1.36)		
			20–39	43	0.87 (0.62–1.22)		
≥ 40	21	1.41 (0.90–2.33)					
Lin <i>et al.</i> (2005), Japan, Japanese Collaborative Cohort	35 844 women recruited 1988–90, aged 40–79 years; follow-up until 1997; 151 cases ascertained through registries	Self-administered questionnaire	<i>Current intake (g/day)</i>	151		Age, body mass index, study area, family history, walking, hormone replacement therapy, age at menarche, parity, age at first birth, age at menopause	Significant association for binge drinking (> 23 g/day on one occasion); no association for age at started drinking or frequency of consumption
			Non-drinker	103	1.0		
			Former drinker	3	0.82 (0.20–3.33)		
			Current	45	1.27 (0.87–1.84)		
			0.1–4.9	13	1.07 (0.57–2.00)		
			5–14.9	5	0.83 (0.34–2.04)		
			≥ 15	11	2.93 (1.55–5.54)		
<i>p</i> for trend		0.01					

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hirvonen <i>et al.</i> (2006), France, Supplementation and Vitamins and Minerals Antioxidant Study	Analytical cohort of 4396 women recruited in 1994, aged 35–60 years; followed-up until 2002; 95 cases identified through clinical examination every 2 years and via self-report; validated through medical and pathology records	3 or more telephone-administered 24-hour recalls completed during the first year following recruitment	<i>Red wine (mL/day)</i>	0	39 1.0	Age, smoking, parity, oral contraceptive use, family history, menopausal status	
			1–149	25 1.06 (0.64–1.76)			
			≥150	31 1.24 (0.76–2.03)			
			<i>p</i> for trend	0.39			
			<i>White wine or rose (mL/day)</i>	0	62 1.0		
			1–149	14 0.87 (0.49–1.56)			
≥150	19 1.09 (0.64–1.84)						
			<i>p</i> for trend	0.88			
Stolzenberg-Solomon <i>et al.</i> (2006), USA, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial	Analytical cohort of 25 400 women, recruited 1993–2001 into screening arm, aged 55–74 years; follow-up until 2003; 691 self-reported cases (including 96 <i>in situ</i>), 72% verified by pathology and medical records, and through cancer registry	Self-administered questionnaire	<i>Intake (g/day)</i>	<0.01	104 1.0	Age, education (best fit model)	Stronger association for high alcohol intake (>7.62 g/day) among women with low folate intake; no association with alcoholic beverages at higher folate intake
			>0.01–0.43	138 1.23 (0.95–1.58)			
			>0.43–1.39	158 1.20 (0.94–1.54)			
			>1.39–7.62	118 0.97 (0.75–1.26)			
			>7.62	173 1.37 (1.08–1.76)			
<i>p</i> for trend	0.02						

Table 2.30 (continued)

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Tjønneland <i>et al.</i> (2007), European Prospective Investigation into Cancer and Nutrition	Analytical cohort of 274 688 women, recruited 1993–2000, aged 35–70 years; follow-up for 6.4 years; 4285 incident cases (all invasive) identified through registries and active follow-up	Self-administered questionnaire	<i>Recent intake (g/day)</i>				Height, weight, age at menarche, parity, oral contraceptive use, hormone replacement use, menopausal status, smoking, education	No differences by subgroups of body mass index or hormonal replacement therapy use; no association for age started drinking; similar association for wine, beer and spirits
			None	612	1.01 (0.91–1.13)			
			>0–1.5	701	1.0			
			1.6–4.7	723	0.98 (0.89–1.09)			
			4.8–10	731	0.97 (0.88–1.08)			
			10.1–19	759	1.07 (0.96–1.19)			
			≥20	765	1.13 (1.01–1.25)			
			20–23.6	211	1.08 (0.92–1.26)			
			23.7–29.9	154	1.03 (0.86–1.23)			
			30–37.1	194	1.36 (1.15–1.60)			
≥37.2	206	1.09 (0.93–1.28)						
Increase per 10 g/day		1.03 (1.01–1.05)						
<i>Lifetime alcohol</i>								
Increase per 10 g/day					1.02 (0.99–1.06)			

CI, confidence interval

Table 2.31 Case-control studies of breast cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Williams & Horm (1977), USA, Third National Cancer Survey, 1969-71	7518 (all sites, men and women), aged ≥ 35 years; histological confirmation not stated; 57% randomly selected	Randomly selected patients with cancer of other non-related sites	Interviewer-administered questionnaire	<i>Total alcohol (oz/year)</i>	1.0	Age, race, smoking	Increased risk for wine (low intake only) and hard liquor (low and high intake); no association with beer
				1	1.28 (significant)		
				2	1.55 (significant)		
Byers & Funch (1982), New York, USA, 1957-65	1314, aged 30-69 years; all admitted to hospital; response rate not stated	770 hospital-based (non-malignant); not matched; response rate not stated	Interviewer-administered questionnaire	<i>Drinks/month</i>	1.0	Age	No differences by type of drink; no association for lifetime alcoholic beverage intake; few heavy drinkers
				Never	0.59		
				Former	1.11		
				<3	1.02		
				3-8	1.09		
				9-25	1.13		
≥ 26	all non-significant						
Rosenberg <i>et al.</i> (1982), Canada, Israel, USA, 1976-80	1152, aged 30-69 years; verification by hospital discharge records or pathology records; response rate, 94% overall (cases and controls)	2702 hospital-based (519 endometrial/ovarian cancer; 2702 non-malignant); matching criteria not stated	Interviewer-administered questionnaire	<i>Intake in previous year (days/week)</i>	1.0	Age, region	Results presented using non-malignant controls; similar association using cancer controls; increased risk seen for beer, wine and spirits among regular drinkers
				Never	1.6 (1.1-2.4)		
				Former	1.9 (1.5-2.4)		
				<4	2.5 (1.9-3.4)		
				≥ 4			

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Begg <i>et al.</i> (1983), Canada, USA, 1982, survey of cancer patients	997 overall (cases and controls); response rate not stated	730 hospital-based (other cancers excluding head and neck and uncertain origin); matching criteria not stated	Interviewer-administered questionnaire	<i>Drinks/week</i> None 1–7 >7	1.0 0.9 (0.8–1.1) 1.4 (0.9–2.0)	Age, smoking	
O’Connell <i>et al.</i> (1987), North Carolina, USA, 1977–78	276, aged ≥ 30 years; 100% histologically confirmed; response rate, 93%	1519 population-based (selected from a stratified sample of households); response rate, 85%	Interviewer-administered questionnaire	<i>Usual intake (drinks/week)</i> None or <1 ≥ 1	1.0 1.45 (0.99–2.12)	Age, race, smoking, hormone replacement therapy use, oral contraceptive use	Higher risk in white versus black women, and in pre- versus postmenopausal women
Harris & Wynder (1988) 20 sites, USA, 1969–84	1467, ages not stated; verified by medical records and pathology reports; response rate not stated	10 178 hospital-based (non-malignant and not related to alcohol or tobacco); matched by age; response rate not stated	Interviewer-administered questionnaire	<i>Usual intake (g/day)</i> Never <5 5–15 >15	1.0 1.03 0.97 0.96	Education, occupation, marital status, smoking, age at diagnosis, year of interview	No association by subgroup of body mass index

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Cusimano <i>et al.</i> (1989a), Sicily, 1983–85	143, aged ≥ 30 years; 100% histologically confirmed; response rate, 68%	260 hospital-based (non-malignant); matched by age, health service; response rate, 91%	Interviewer-administered questionnaire	No Yes	1.0 1.68 (1.10–2.56)	Socioeconomic status	Stronger association in women with a family history of breast cancer
Kato <i>et al.</i> (1989), Japan, 1980–86	1740, aged ≥ 20 years; ascertained through registry; response rate not stated	8920 hospital-based (other cancers not related to alcohol); not matched; response rate not stated	Not stated; exposure information obtained at the hospital	<Daily Daily <i>p</i> for trend	1.0 1.35 (1.01–1.80) <0.01	Age, smoking, marital status, residence, occupation, family history	Higher risk for post- versus premenopausal women, and for beer versus sake or whisky
Iscoovich <i>et al.</i> (1989), Argentina, 1984–88	150, all ages; 100% histologically confirmed; response rate, 99%	150 population-based (same neighbourhood, not on a special diet) and hospital-based (in- and out patients); matched by age; response rate not stated	Interviewer-administered questionnaire	<i>Quartile of intake</i> 1 2 3 4	1.0 0.37 1.10 0.60		Results presented for population controls; similar results when using hospital-based controls

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Toniolo <i>et al.</i> (1989), Italy, 1983–86	250, aged 25–75 years; 100% histologically confirmed; response rate, 91%	499 population-based (electoral roll); matched by age; response rate, 79%	Interviewer-administered questionnaire	<i>Usual intake (g/day)</i> None >0–10 >10–20 >20–30 >30–40 >40 <i>p</i> for trend	1.0 0.9 (0.5–1.5) 1.2 (0.7–1.9) 1.0 (0.7–1.6) 1.2 (0.6–2.4) 1.6 (0.9–2.9) 0.17	Age, body mass index, menopausal status, non-alcohol energy intake	Increased risk also for wine-only drinkers; few women with high intakes (>30 g/day)
Van't Veer <i>et al.</i> (1989), Netherlands, 1985–87	120, aged 25–44 years (<i>n</i> =47) and 55–64 years (<i>n</i> =73); 96% histologically confirmed; response rate, 80%	164 population-based (population registry surrounding hospitals); matched by age; response rate, 55%	Interviewer-administered questionnaire	<i>Usual intake (g/day)</i> <i>Premenopausal</i> None 1–4 5–14 15–29 ≥30 ≥30 vs 1–4 <i>p</i> for trend <i>Postmenopausal</i> None 1–4 5–14 15–29 ≥30 30 vs 1–4 <i>p</i> for trend	1.0 0.3 (0.0–1.7) 0.5 (0.1–2.9) 0.8 (0.1–4.9) 2.3 (0.3–19.1) 8.5 (1.1–65.1) 0.04 1.0 0.8 (0.3–2.3) 1.0 (0.3–3.6) 1.1 (0.3–4.3) 0.9 (0.2–4.5) 1.1 (0.5–2.4) 0.37	Age, region, season, reproductive factors, education, family history, smoking, body mass index, fat intake	Increased risk if started drinking aged <25 years versus older ages, and in post- versus premenopausal women

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments	
Young (1989), Wisconsin, USA, 1981–82	277, aged 35–89 years; identified through hospital registry; response rate, 64%.	372 population-based (drivers' licence records); response rate, 57%; 433 hospital-based; (no alcohol-related disease); matched by age; response rate, 61%	Self-administered questionnaire	<i>Drinks/week aged 18–35 years</i>	None	1.0	None; adjustments made little difference	Results presented using population controls; weaker, but still significant association when cancer controls used; slightly stronger association if started drinking <35 years
				1–5	1.74 (1.37–2.21)			
				≥6	3.17 (2.20–4.57)			
				<i>Drinks/week aged >35 years</i>	None	1.0		
				1–5	1.13 (0.87–1.46)			
				≥6	2.67 (1.91–3.71)			
Nasca <i>et al.</i> (1990) NY State, USA, 1982–84	1617, aged 20–79 years; verified by pathology reports; response rate, 79%	1617 population-based (drivers' licence files); matched by age, region; response rate, 72%	Interviewer-administered questionnaire (telephone)	<i>Usual intake (g/day)</i>	None	1.0	Age, race, age at first birth, menopausal status, benign breast disease, family history	Increased risk for later age at starting (i.e. ≥31 years); no association for duration of use
				<1.5	1.07 (0.83–1.36)			
				1.5–4.9	1.04 (0.78–1.39)			
				5.0–14.9	1.10 (0.87–1.39)			
				≥15	1.26 (0.98–1.64)			

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zaridze <i>et al.</i> (1991), Moscow, 1987–89	139, aged <41–≥71 years; verification not stated; response rate, 99%	139 hospital-based (outpatients); matched by age, region; response rate, 94%	Interviewer-administered questionnaire	<i>Alcohol intake (g/week)</i>		Age at menarche, age at first birth	
				<i>Premenopausal</i>			
				0	1.0		
				<0.93	4.60 (0.46–46.14)		
				0.93–2.12	4.58 (0.38–55.89)		
				2.13–6.46	6.37 (0.72–56.34)		
				≥6.46	7.98 (0.79–80.47)		
				<i>p</i> for trend	0.08		
				<i>Postmenopausal</i>			
				0	1.0		
				<0.93	2.26 (0.66–7.76)		
				0.93–2.12	7.06 (1.70–29.40)		
2.13–6.46	3.10 (0.83–11.55)						
≥6.46	0.78 (0.06–8.89)						
<i>p</i> for trend	0.003						
Harris <i>et al.</i> (1992), New York, USA, 1987–89	604, all ages; verified by pathology and medical records; response rate not stated	520 hospital-based (unrelated to risk factors); matched by age, date of diagnosis, hospital; response rate not stated	Interviewer-administered questionnaire	<i>Premenopausal (n=192)</i>		Age, family history, age at menarche, parity, age at first birth, breastfeeding, smoking, oral contraceptive use	
				0 g/day			
				1–15 g/day	1.0		
				≥16 g/day	1.2 (0.7–1.9)		
				<i>Postmenopausal (n=412)</i>			
				0 g/day			
				1–15 g/day	0.7 (0.3–1.5)		
				≥16 g/day	1.0		
	1.1 (0.8–1.6)						
	0.8 (0.5–1.3)						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Kato <i>et al.</i> (1992d), Japan, 1990–91	908, aged ≥ 20 years; 100% histologically confirmed; response rate not stated	908 (244 breast cancer screening and 664 hospital-based [including benign breast disease and excluding hormone-related cancers]); matched by age; response rate not stated	Self-administered questionnaire	None Occasional Daily <i>p</i> for trend	1.0 0.99 (0.80–1.22) 0.97 (0.71–1.33) 0.64	None stated	~20% of controls had benign breast disease or gynaecological diseases
Pawlega (1992), Poland, 1987	127, aged ≥ 35 years; 100% histologically confirmed; response rate, 75%	250 population-based (electoral roll); matched by age, place of residence	Mailed self-administered questionnaire	Intake 20 years ago <i><50 years</i> Never vodka Ever vodka <i>≥ 50 years</i> Never vodka Ever vodka	1.0 4.4 (1.6–12.4) 1.0 1.2 (0.8–2.6)	Age, education, social class, marital status, no. of people in household, body mass index, smoking	

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Martin-Moreno <i>et al.</i> (1993), Spain, 1990–91	762, aged 18–75 years; 100% histologically confirmed; response rate, 89%	988 population-based (municipal rolls); matched by age; response rate, 82%	Interviewer-administered questionnaire	<i>Intake (g/day)</i> None <2.41 2.41–7.60 7.61–20.40 ≥20.41 <i>p</i> for trend	1.0 1.2 (0.9–1.6) 1.5 (1.1–2.1) 1.7 (1.2–2.3) 1.7 (1.3–2.3) 0.001	Age, region, socioeconomic status, body mass index, family history, age at menarche, menopausal status, age at menopause, age at first birth, energy intake	Increased risk for wine, sherry and spirits; no association with beer or liqueurs; slightly higher risk in post- versus premenopausal women

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Wakai <i>et al.</i> (1994), Japan, 1990-91	314, aged >25 years; 100% histologically confirmed; response rate not stated	900 hospital-based (outpatients at department of breast surgery; included women with benign breast disease); matched by age; response rate not stated	Self-administered questionnaire	<i>Current alcohol drinking</i> No Yes	1.0 1.04 (0.77–1.39)	Age, menopausal status, family history, history of benign breast disease, age at menarche, age at menopause, regularity of menstrual cycles, duration of menstrual cycles, age at first birth, parity, breastfeeding, smoking, height, weight	No significant association in pre- or postmenopausal women

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Freudenheim <i>et al.</i> (1995, 1999), New York, USA, 1986–91	740, aged 40–85 years; 100% histologically confirmed; response rate, 58%	810 population-based (drivers' licence and HCFA records); matched by age; response rate, 50%	Interviewer-administered questionnaire	<i>Total drink intake over 20 years</i>		Age, education, menopausal status, age at menarche, age at first birth, family history, benign breast disease, body mass index, energy intake, fat, carotenoids, vitamin C, α -tocopherol, folic acid, fibre	No association for cumulative intake by beverage type; no association for drinking 2, 10 or 20 years or at 16 years old; weak association with beer; Freudenheim <i>et al.</i> (1999) reported slight increased risk in premenopausal ($n=134$) versus postmenopausal ($n=181$), but not significant; results for alcohol intake 2, 10 and 20 years ago very similar
				0–479	1.0		
				480–1300	1.13 (0.84–1.53)		
				1301–4560	0.99 (0.73–1.35)		
				4561–6719	0.95 (0.59–1.52)		
≥ 6720	0.86 (0.61–1.21)						
<i>p</i> for trend	0.76						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gomes <i>et al.</i> (1995), Brazil, 1978–87	300, aged 25–75 years; 100% histologically confirmed	600 hospital-based (300 outpatients, 300 gynaecology patients); matched by age, date of diagnosis	Information from patient records	<i>Current intake</i> No Yes	1.0 1.16 (0.68–1.97)	No adjustment	
Longnecker <i>et al.</i> (1995), USA, 1988–91 [included in Collaborative Project, but incorporated here for details on lifetime exposure]	6662, aged <75 years; ascertained through cancer registry; response rate, 80%	9163 population-based (drivers' licence records and HCFA records); matched by age; response rate, 84%	Interviewer-administered questionnaire (via telephone) Lifetime intake (age 16 years to baseline [recent past])	<i>Most recent intake (g/day)</i> 0 >0–5 6–11 12–18 19–32 33–45 ≥46 per 13 g/day <i>p</i> for trend <i>Lifetime intake (g/day)</i> 0 >0–5 6–11 12–18 19–32 33–45 ≥46 per 13 g/day <i>p</i> for trend	1.0 1.08 (0.98–1.19) 1.09 (0.96–1.23) 1.17 (1.01–1.37) 1.49 (1.24–1.79) 1.95 (1.42–2.66) 1.96 (1.43–2.67) 1.24 (1.15–1.33) <0.0001 1.0 1.13 (1.01–1.26) 1.24 (1.08–1.42) 1.39 (1.16–1.67) 1.69 (1.36–2.10) 2.30 (1.51–3.51) 1.75 (1.16–2.64) 1.31 (1.20–1.43) <0.001	Age, state, age at first birth, parity, body mass index, age at menarche, education, benign breast cancer, family history	Slightly stronger association in post- versus premenopausal women (but both statistically significant); no association for intake when aged <30 years, especially among older women; similar association found for beer, wine and spirits

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Haile <i>et al.</i> (1996), Canada, USA, 1935–89 (Connecticut), 1970–89 (Los Angeles), 1975–89 (Canada)	144 premenopausal bilateral cases, aged <50 years; 100% histologically confirmed; response rate, 55%	232 sister controls; response rate, 55%	Mailed self-administered questionnaire	<i>Drinks/week</i> None 1–3 ≥3	1.0 1.2 (0.6–2.3) 1.8 (1.0–3.4)	Age, body mass index	Premenopausal bilateral breast cancer only; no difference according to family history of breast cancer
Royo-Bordonada <i>et al.</i> (1997), EURAMIC study, Europe (5 countries), 1991–92	315, aged 50–74 years; 100% histologically confirmed; response rate, 86%	364 population-based (population registries, GP records); matched by age, centre; response rate, 41%	Interviewer-administered questionnaire	<i>Alcohol intake (tertiles)</i> Never Former 1 2 3 <i>p</i> for trend	1.0 1.73 (1.07–2.79) 1.00 (0.60–1.67) 1.01 (0.60–1.73) 1.18 (0.69–2.03) 0.81	Age, centre, body mass index, smoking, parity, age at first birth, age at menopause, age at menarche, hormone replacement therapy, family history, benign breast disease	Higher risk for age started drinking <40 years versus ≥ 40 years; no difference by subgroup of body mass index

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Viel <i>et al.</i> (1997), France, 1986–89	154, aged 30–50 years; 100% histologically confirmed; response rate, 90%	154 population-based (women who attended a preventative health clinic); matched by age, socioeconomic status; response rate, 100%	Self-administered questionnaire; verified by interviewer	<i>Alcohol intake (kcal/day)</i> None 1–60 ≥60 <i>p</i> for trend	1.0 0.77 (0.41–1.47) 2.69 (1.40–5.17) 0.007	Parity, total energy intake	Premenopausal only; increased risk for amount of red wine and duration of red wine intake; no association with white wine, beer or fortified wine (but very low intake)
Tung <i>et al.</i> (1999), Japan, 1990–95	376, aged ≥29 years; histological confirmation not stated; response rate, 47%	430 hospital-based (non-malignant, non-endocrine, not related to nutritional or metabolic disease); matching criteria not stated; response rate, 77%	Self-administered questionnaire	<i>Drinking</i> None Former Current	1.0 0.42 (0.19–0.95) 0.86 (0.61–1.22)	Age at menarche, age at first birth, weight, height, smoking, education	No association in pre- or postmenopausal women

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments		
Huang <i>et al.</i> (2000); Kinney <i>et al.</i> (2000); Marcus <i>et al.</i> (2000), North Carolina Breast Cancer Study, 1993–96	Huang <i>et al.</i> (2000): 862, aged 20–74 years; 100% histologically confirmed; response rate, 77%	790 population-based (drivers' licence and HCFA records); matched by age, race; response rate, 68%	Interviewer-administered questionnaire	<i>Drank alcohol recently</i>	No	1.0	Age, race, sampling design	Results also by receptor status (see accompanying table)	
				Yes	1.0 (0.8–1.2)				
	Marcus <i>et al.</i> (2000): 864; recent intake	790			<i>Recent intake (drinks/week)</i>	None	1.0		No association with age at started drinking
					0.1–6.9	0.9 (0.8–1.2)			
					7–13.9	1.2 (0.8–1.8)			
					≥14	1.2 (0.8–1.8)			
	Kinney <i>et al.</i> (2000): 890; lifetime intake	841			<i>Lifetime intake (<25, 25–49, ≥50 years, g/week)</i>	Never	1.0	Age, race, family history, age at menarche, parity, previous breast biopsy, body mass index, education, smoking	No association for type of beverage; no significant association with binge drinking; no differences by race, age, menopausal status, use of hormone replacement therapy or body mass index
					<13	0.9 (0.7–1.2)			
					13–90.0	1.0 (0.7–1.3)			
					91–181.0	1.2 (0.8–1.9)			
≥182					0.8 (0.5–1.3)				
<i>p</i> for trend					0.96				

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Männistö <i>et al.</i> (2000), Finland, 1990–95	301 (113 pre-, 188 postmenopausal), aged 25–75 years; 100% histologically confirmed; response rate not stated	443 population-based (national register); matched by urban/rural residence, age; response rate, 72%	Interviewer-administered and self-administered questionnaire	<i>Intake (g/week)</i>		Age, area, age at menarche, age at first birth, oral contraceptive use, hormone replacement therapy use, family history, benign breast disease, education, smoking, physical activity, body mass index, waist-hip ratio	Results are presented for alcohol as measured from interviewer-administered questionnaire; no association from self-reported questionnaire either; no association with age at first use, or cumulative intake < age 30 years or over lifetime
				<i>Premenopausal</i>			
				Never	1.0		
				1–12	0.8 (0.4–1.9)		
				13–36	0.9 (0.4–1.9)		
				≥37	1.0 (0.4–2.2)		
				<i>Postmenopausal</i>			
				Never	1.0		
				1–12	0.9 (0.5–1.6)		
				13–29	0.6 (0.3–1.2)		
≥30	0.8 (0.4–1.6)						
Former	0.6 (0.2–1.7)						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Baumgartner <i>et al.</i> (2002), New Mexico, 1992–94	712 (332 Hispanic, 380 white), aged 30–74 years; ascertained through registry; response rate, 68% (Hispanics) and 77% (white)	844 population-based (random-digit dialling); matched by age, race, area; response rate, 76% (Hispanic) and 86% (white)	Interviewer-administered questionnaire	<i>Recent intake (g/week or drinks/week)</i>	<i>Hispanic</i>	Age, area, education, age at menarche, menopausal status, parity, age at first birth, breastfeeding, oral contraceptive use, benign breast disease, family history, smoking, body mass index, physical activity, energy intake, fat intake	Increased risks in postmenopausal women at high intakes (≥ 42 drinks) for both races (but not significant); no association for age at first use or duration of drinking; results also by receptor status (see accompanying table)
				Non-drinker	1.0		
				<8	1.21 (0.68–2.15)		
				8–20 (1 drink)	1.00 (0.54–1.85)		
				21–41 (2 drinks)	0.75 (0.37–1.53)		
				42–84 (2–4 drinks)	1.24 (0.52–2.93)		
				85–147 (5–7 drinks)	1.35 (0.63–2.93)		
					<i>White</i>		
				Non-drinker	1.0		
				<8	0.49 (0.28–0.85)		
				8–20 (1 drink)	0.46 (0.27–0.79)		
				21–41 (2 drinks)	0.44 (0.25–0.77)		
				42–84 (2–4 drinks)	0.60 (0.35–1.05)		
				85–147 (5–7 drinks)	0.49 (0.24–1.00)		
≥ 148 (≥ 8 drinks)	1.56 (0.85–2.86)						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gammon <i>et al.</i> (2002); Terry <i>et al.</i> (2006), Long Island Breast Cancer Study Project, 1996–97	Gammon <i>et al.</i> (2002): 1508 (<i>in situ</i> and invasive), aged 20–98 years; verified by medical records; response rate, 82% Terry <i>et al.</i> (2006) current alcohol (g/day)	1556 population-based (random-digit dialling and HCFA records); matched by age; response rate, 63%	Interviewer-administered questionnaire	<i>Intake</i>		Age Age, race, education, body mass index, lifetime intake Age, race, education, body mass index, current intake	No association when stratified by body mass index, menopausal status or hormone replacement therapy use; no association with drinking at specific ages; results also for receptor status (see accompanying table); no difference by subgroups of body mass index, menopausal status or hormone-replacement therapy use
				Never	1.0		
				Ever	1.00 (0.86–1.15)		
				<i>Current intake (g/day)</i>			
				None	1.0		
				<0.5	0.67 (0.50–0.91)		
				0.5–5	0.83 (0.63–1.11)		
				5–15	0.99 (0.75–1.31)		
				≥15	1.04 (0.74–1.45)		
				<i>p</i> for trend	0.2		
				<i>Lifetime intake (g/day)</i>			
				None	1.0		
				<15	1.12 (0.88–1.42)		
15–30	1.35 (0.96–1.91)						
≥30	0.81 (0.55–1.19)						
<i>p</i> for trend	0.5						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Lenz <i>et al.</i> (2002), Canada, 1996–97	556, aged 50–75; identified through pathology departments and cancer registry; 100% histologically confirmed; response rate, 81%	577 hospital-based (other cancers not related to alcohol); response rate, 76%	Interviewer-administered questionnaire	<i>Use</i> Never Ever Infrequent Regular Current regular (i.e. weekly or daily)	1.0 1.2 (0.9–1.7) 1.2 (0.8–1.8) 1.3 (0.9–1.8) 1.5 (1.0–2.2)	Age, family history, age at oophorectomy, education, marital status, race, age at menarche, oral contraceptive use, hormone replacement therapy use, breast feeding, smoking, body mass index, age at first birth, proxy respondent status	Similar association for type of drink (slightly higher for wine drinkers with long duration of intake); no association with age at first started drinking, duration of intake or lifetime alcoholic beverage intake

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments	
Althuis <i>et al.</i> (2003), USA (Atlanta, Seattle and New Jersey), 1990–92	1750 premenopausal women, aged 20–54 years; includes in-situ and invasive cancers identified through hospital records; response rate, 86%	1557 population-based (random-digit dialling); all premenopausal women; no matching criteria; response rate, 78%	Interviewer-administered questionnaire	Alcohol intake (drinks/week)			Study site, screening history, age, race, oral contraceptive use, parity, age at first birth, family history, age at menarche, body mass index	No significant difference by age group; overall relative risk for ≥ 14 drinks/week versus none, 2.06 (95% CI, 1.4–3.1)
				<i>Aged <35 years (n=265)</i>	None	1.0		
					<3	1.33 (0.8–2.2)		
					3–6.9	0.99 (0.6–1.7)		
					7–13.9	1.29 (0.6–2.7)		
					≥ 14	1.71 (0.7–4.0)		
				<i>Aged 35–44 years (n=1214)</i>	None	1.0		
					<3	1.04 (0.3–1.3)		
					3–6.9	1.00 (0.8–1.3)		
					7–13.9	1.04 (0.7–1.5)		
					≥ 14	1.95 (1.2–3.3)		
				<i>Aged 45–54 years (n=271)</i>	None	1.0		
					<3	1.98 (1.2–3.2)		
					3–6.9	1.95 (1.1–3.4)		
	7–13.9	1.84 (1.0–3.5)						
	≥ 14	4.24 (1.2–14.6)						

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Choi <i>et al.</i> (2003), Republic of Korea, 1995–2001	346, all ages; verification not stated; response rate not stated	332 hospital-based (non-malignant and no hormone-related or benign breast disease); response rate not stated	Interviewer-administered questionnaire	<i>Use</i> <1 month ≥1 month	1.0 1.4 (0.99–2.11)	Age, family history	Association stronger in post- versus premenopausal (no results stated)
Wrensch <i>et al.</i> (2003), Marin County, CA, USA, 1997–99	285, all ages; identified through cancer registry; verification not stated; response rate, 71%	286 population-based (random-digit dialling); matched by race, age; response rate, 87%	Interviewer-administered questionnaire	<i>Intake (aged ≥ 21, drinks/week)</i> <1 1–1.9 2 ≥3 <i>p</i> for trend	1.0 1.1 (0.7–1.8) 2.3 (1.2–4.4) 3.6 (1.2–11.5) 0.004	Smoking, socioeconomic status, religion, parity, breastfeeding, oral contraceptive use, hormone replacement therapy use, body mass index, screening history, family history, benign breast disease, radiation treatment, age at menarche, menopausal status	Stronger association for age started drinking >21 years versus <21 years; slightly stronger association in women aged <50 versus ≥50 years

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
McDonald <i>et al.</i> (2004), CARE Study, 5 centres in the USA, 1994–98	4575, aged 35–64 years; response rate, 77%	4682 population-based (random-digit dialling), matched by site, race, age; response rate, 65%	Interviewer-administered questionnaire	<i>Drinks/week 2 years ago</i> None <7 >7 7–<14 >14 Odds ratio for trend	1.0 1.0 (0.9–1.1) 1.2 (1.0–1.3) 1.2 (1.0–1.4) 1.2 (1.0–1.5) 1.1 (1.0–1.1)	Site, race, age, menopausal status, age at menarche, age at menopause, parity, age at first birth, body mass index, family history, oral contraceptive use, hormone replacement therapy use	Similar association for intake 1–10 years before recruitment; no significant difference by menopausal status; slightly stronger association for wine than for beer or spirits; stronger association for older women drinking >14 drinks/week

Table 2.31 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Ma <i>et al.</i> (2006), Los Angeles, USA, 2000–03	1725, aged 20–49 years; 100% histologically confirmed; response rate, 62%	440 population-based (neighbourhood walk algorithm); matched by age, race; response rate, 74%	Interviewer-administered questionnaire	<i>Drinks/week in last 5 years</i> Never <3 3–5 6–11 >12 <i>p</i> for trend	1.0 1.01 (0.76–1.35) 0.93 (0.63–1.37) 1.16 (0.75–1.81) 1.77 (1.01–3.08) 0.12	Age, race, education, family history, age at menarche, parity, body mass index, oral contraceptive use, menopausal status, hormone replacement use	Results also by receptor status (see accompanying table)

CI, confidence interval; HCFA, Health Care Finance and Administration

an increased risk for breast cancer, and that the risk increases with increasing intake (Figure 2.1). Hamajima *et al.* (2002) (The Collaborative Group on Hormonal Factors in Breast Cancer) found a significantly increased risk (relative risk, 1.13; 95% CI, 1.07–1.20) for an intake of 18 g alcohol per day. No single study was large enough to estimate reliably the risk for breast cancer at such low levels of intake.

Several studies have examined the effect of lifetime alcoholic beverage intake by total amount (Freudenheim *et al.*, 1995; Longnecker *et al.*, 1995; Kinney *et al.*, 2000; Gammon *et al.*, 2002) or by 10 g intake of alcohol per day (Longnecker *et al.*, 1995; Smith-Warner *et al.*, 1998; Hamajima *et al.* 2002; Tjønneland *et al.*, 2003) on the risk for breast cancer. One large case–control study, based on more than 6000 cases, reported an increase in risk of 31% per 13 g intake of alcohol per day (Longnecker *et al.*, 1995). In contrast, the EPIC cohort found no association with lifetime alcoholic beverage intake after adjustment was made for current alcoholic beverage intake (Tjønneland *et al.*, 2007).

Most studies that examined the age at which a woman started to drink in relation to risk for breast cancer reported no association (Freudenheim *et al.*, 1995; Holmberg *et al.*, 1995; Lenz *et al.*, 2002; Horn-Ross *et al.*, 2004; Tjønneland *et al.*, 2004; Lin *et al.*, 2005; Terry *et al.*, 2006; Tjønneland *et al.*, 2007).

One large case–control study found that, among women who had not recently consumed alcoholic beverages, consumption before the age of 30 years was positively associated with risk for breast cancer, which suggests a continuing increased risk with past consumption (Longnecker *et al.*, 1995). Overall, however, there is limited information on the association between cessation of drinking and subsequent risk for breast cancer, and therefore no firm conclusions can be drawn.

2.6.5 Tumour type

Three cohort (Table 2.32) and 12 case–control studies (Table 2.33) examined whether the association between alcoholic beverage intake and risk for breast cancer differed by estrogen receptor (ER) or progesterone receptor (PR) status.

Three cohort studies (Potter *et al.*, 1995; Colditz *et al.*, 2004; Suzuki *et al.*, 2005) (see Table 2.32) evaluated the association of alcoholic beverage intake according to receptor status. All three studies reported a significant association between alcoholic beverage consumption and risk for breast cancer for the most common subgroup of ER+ tumours; the small number of cases in the other subgroups may limit the power to detect significant differences between different subgroups of tumours. The Iowa Women's Health Study (Gapstur *et al.*, 1995; Potter *et al.*, 1995; Sellers *et al.*, 2002) reported a higher risk with increasing alcoholic beverage intake for ER–/PR– tumours and the Swedish Mammography Cohort Study found a higher risk for ER+/PR+ and ER+/PR– tumours (Suzuki *et al.*, 2005); both studies found stronger associations for users of hormone replacement therapy compared with non-users, although these were based on small numbers of cases and should be interpreted with caution.

Table 2.32 Cohort studies of alcoholic beverage intake and breast cancer by hormone-receptor status

Reference, name of study	Cohort description	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gapstur <i>et al.</i> (1995); Potter <i>et al.</i> (1995); Sellers <i>et al.</i> (2002), Iowa Women's Health Study	37 105 women, aged 55–69 years; recruited in 1986; follow-up until 1992 through registry; 939 cases identified through cancer registry (610 had receptor status)	<i>Intake in last year</i>	<i>ER+/PR+ (414)</i>	Age at menopause, hormone replacement	Gapstur <i>et al.</i> (1995) found higher risk for women who consumed ≥ 4 g/day and had ever used hormone replacement therapy versus non-drinkers who had never used hormone replacement therapy for ER+/PR+ and ER-/PR- tumours; no association with other tumour subtypes; also interaction by family history and body mass index. Sellers <i>et al.</i> (2002) reported higher risk for women who consumed ≥ 4 g/day and had a low folate intake for ER- tumours; no association with other tumour subtypes
		None	1.0	therapy use, current	
		Any	1.17 (0.95–1.44)	body mass index and at	
		None	1.0	age 18 years, waist:hip	
		Any	1.23 (0.81–1.87)	ratio, age at menarche,	
		None	1.0	type of menopause,	
Any	1.37 (0.86–2.18)	family history, parity, age at first birth, oral contraceptive use			

Table 2.32 (continued)

Reference, name of study	Cohort description	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Colditz <i>et al.</i> (2004), Nurses Health Study	66 145 women; aged 30–55 years; recruited in 1976; follow-up from 1980 until 2000; 2096 self-reported invasive cancers verified through medical and pathology records with ER/PR status	<i>Cumulative intake before menopause</i>	<i>ER+/PR+ (1281)</i>	Not clearly stated	No strong association with alcoholic beverage intake after menopause for any tumour subgroup; no difference by hormone replacement therapy use for any tumour subgroup
		β coefficient (SE)	0.0003 (0.00009)		
		<i>p</i> for trend	0.001		
		<i>ER+/PR- (318)</i>			
		β coefficient (SE)	0.0002 (0.0002)		
		<i>p</i> for trend	0.20		
		β coefficient (SE)	<i>ER-/PR- (417)</i>		
		<i>p</i> for trend	-0.00003 (0.0002)		
		β coefficient (SE)	0.86		
		<i>p</i> for trend	<i>ER-/PR+ (80)</i>		
		β coefficient (SE)	0.0002 (0.0004)		
		<i>p</i> for trend	0.68		

Table 2.32 (continued)

Reference, name of study	Cohort description	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments	
Suzuki <i>et al.</i> (2005), Swedish Mammography Cohort	51 847 women, aged 55–70 years; recruited 1987–90; follow-up until 2004 through cancer registry; verified by pathology and medical records; 1188 invasive cases with ER/PR status	<i>Intake in last 6 months (1987 and 1997; g/day)</i>			Age, body mass index, height, education, parity, age at first birth, age at menarche, age at menopause, type of menopause, oral contraceptive use, hormone replacement therapy use, family history, benign breast disease, energy intake, fibre and fat intake	Stronger association with increasing alcohol intake in hormone replacement therapy users versus never users for ER+/PR+ tumours; no difference for other tumour subtypes
		None	ER+/PR+ (716)	1.0		
		<3.4	1.07 (0.89–1.30)			
		3.4–9.9	1.09 (0.88–1.35)			
		≥10	1.35 (1.02–1.80)			
		<i>p</i> for trend	0.05			
		None	ER+/PR– (279)	1.0		
		<3.4	1.10 (0.78–1.55)			
		3.4–9.9	1.30 (0.91–1.87)			
		≥10	2.36 (1.56–3.56)			
		<i>p</i> for trend	<0.01			
		None	ER–/PR– (143)	1.0		
		<3.4	1.11 (0.72–1.71)			
		3.4–9.9	1.09 (0.68–1.75)			
≥10	0.80 (0.38–1.67)					
<i>p</i> for trend	0.45					
None	ER–/PR+ (50)	1.0				
<3.4	1.27 (0.63–2.57)					
3.4–9.9	1.30 (0.58–2.89)					
≥10	0.62 (0.13–2.90)					
<i>p</i> for trend	0.57					

CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor; SE, standard error; +, positive; –, negative

Table 2.33 Case-control studies of alcoholic beverage intake and breast cancer by hormone-receptor status

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
McTiernan <i>et al.</i> (1986), Cancer and Steroid Hormone Study, Washington, USA, 1981-82	329 (240 with receptor status) identified through cancer registry, aged 25-54 years; 100% histologically confirmed; response rate, 79%	332 population-based (random-digit dialling); matched by age, all in same region; response rate, 87%	Interviewer-administered questionnaire	<i>No. of drinks/week</i>	<i>ER+</i> (143)	Adjusted for age, age at menarche, benign breast disease, age at first birth, parity
				Never/rarely	1.0	
				1-6	1.2 (0.7-1.9)	
				≥7	1.7 (1.1-2.8)	
					<i>ER-</i> (97)	
				Never/rarely	1.0	
1-6	1.1 (0.6-2.0)					
≥7	2.1 (1.1-3.6)					
Nasca <i>et al.</i> (1994) NY State, USA, 1982-84	1152, aged 20-79 years; verified by pathology reports; response rate, 79%	1617 population-based (drivers' licence records); matched by age, region; response rate, 72%	Interviewer-administered questionnaire (telephone)	<i>Intake (g/day)</i>	<i>ER+</i> (794)	Unadjusted results shown; adjustment for age, menopausal status, smoking, race, age at menopause, age at first birth, history of benign breast disease and family history made no difference to the risk estimates.
				None	1.0	
				<1.5	1.18 (0.88-1.57)	
				1.5-4.9	1.28 (0.91-1.80)	
				5.0-14.9	1.28 (0.96-1.70)	
				≥15	1.35 (0.99-1.85)	
				<i>p</i> for trend	0.07	
					<i>ER-</i> (358)	
				None	1.0	
				<1.5	0.92 (0.62-1.36)	
1.5-4.9	1.19 (0.77-1.83)					
5.0-14.9	0.94 (0.64-1.35)					
≥15	1.05 (0.70-1.59)					
<i>p</i> for trend	0.73					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Yoo <i>et al.</i> (1997), Japan, 1988–92	1154 (455 had receptor status), aged ≥ 25 years; 100% histologically confirmed; response rate not stated	21 714 hospital-based (non-malignant); response rate not stated	Self-administered questionnaire	<i>Intake</i>	<i>ER+/PR+ (176)</i>	Adjusted for age, occupation, family history, age at menarche, menstrual regularity, age at menopause, parity, age at first birth, breastfeeding, smoking
				Never	1.0	
				Ever	1.0 (0.71–1.41)	
				<i>ER+/PR- (114)</i>	1.0	
				Never	0.96 (0.60–1.52)	
				Ever	0.96 (0.60–1.52)	
<i>ER-/PR- (141)</i>	1.0					
Never	0.68 (0.44–1.05)					
Ever	0.68 (0.44–1.05)					
<i>ER-/PR+ (24)</i>	1.0					
Never	0.80 (0.32–2.02)					
Ever	0.80 (0.32–2.02)					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Enger <i>et al.</i> (1999), 2 studies in Los Angeles, USA, 1983–89	424 premenopausal, aged <41 years; response rate, 77%; 760 postmenopausal, aged 55–64 years; response rate, 67%; 100% histologically confirmed; included invasive and in-situ cancers	760 premenopausal population-based; matched by region, parity, age; response rate, 79%; 1506 postmenopausal; response rate, 80%; all controls identified through a neighbourhood walk algorithm	Interviewer-administered questionnaire	Intake (g/day)		Adjusted for age, socioeconomic status, education, age at menarche, age at first birth, parity, breastfeeding, physical activity, family history (premenopausal, also oral contraceptive use); insufficient data for ER–/PR+; no differences by subgroup of body mass index or hormone replacement therapy use among ER+/PR+ cases
				<i>Premenopausal</i>	<i>ER+/PR+ (205)</i>	
				0	1.0	
				1–5	0.73 (0.46–1.15)	
				6–13	1.07 (0.69–1.65)	
				≥14	1.10 (0.67–1.80)	
				<i>p</i> for trend	0.56	
				Increase per 13 g/day	1.10 (0.91–1.32)	
					<i>ER+/PR- (52)</i>	
				0	1.0	
				1–5	0.45 (0.18–1.10)	
				6–13	0.16 (0.04–0.69)	
				≥14	0.71 (0.30–1.68)	
				<i>p</i> for trend	0.21	
Increase per 13 g/day	0.88 (0.59–1.30)					
	<i>ER–/PR- (149)</i>					
0	1.0					
1–5	0.68 (0.40–1.16)					
6–13	0.90 (0.53–1.51)					
≥14	1.04 (0.60–1.81)					
<i>p</i> for trend	0.84					
Increase per 13 g/day	1.08 (0.89–1.31)					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Enger <i>et al.</i> (1999) (contd)				<i>Postmenopausal</i>	<i>ER+/PR+ (450)</i>	
				0	1.0	
				1–13	0.97 (0.74–1.27)	
				14–26	1.18 (0.80–1.75)	
				≥27	1.76 (1.14–2.71)	
				<i>p</i> for trend	0.03	
					<i>ER+/PR- (159)</i>	
				0	1.0	
				1–13	0.75 (0.49–1.14)	
				14–26	1.36 (0.80–2.33)	
				≥27	1.10 (0.53–2.26)	
				<i>p</i> for trend	0.65	
				Increase per 13 g/day	1.05 (0.90–1.24)	
					<i>ER-/PR- (127)</i>	
				0	1.0	
				1–13	0.81 (0.52–1.26)	
				14–26	0.91 (0.47–1.75)	
				≥27	1.37 (0.68–2.76)	
			<i>p</i> for trend	0.77		

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Gammon <i>et al.</i> (1999), USA, New Jersey, 1990–92 [data also reported in Althuis <i>et al.</i> (2003)]	509 in-situ and invasive cancers, aged 20–44 years; identified through hospital records; 401 had tissue blood material for assessment of HER-2 amplification; response rate, 83%	462 population-based (random-digit dialling); matched by age; response rate, 77%	Interviewer-administered questionnaire	<i>Alcohol intake (drinks/week)</i>	<i>HER2+ (159)</i>	Adjusted for age; premenopausal women only
				None	1.0	
				<7	0.95 (0.65–1.40)	
				≥7	1.24 (0.65–2.36)	
				None	<i>HER2- (212)</i>	
				<7	1.0	
≥7	1.43 (1.00–2.04)					
Huang <i>et al.</i> (2000), North Carolina Breast Cancer Study, 1993–96	862, aged 20–74 years; 100% histologically confirmed; response rate, 77%	790 population-based (drivers' licence and HCFA records), matched by age, race; response rate, 68%	Interviewer-administered questionnaire	<i>Most recent intake</i>	<i>ER+/PR+ (381)</i>	Adjusted for age, race, age at menarche, parity/age at first birth, breastfeeding, abortion/miscarriage, body mass index, waist:hip ratio, oral contraceptive use, hormone replacement therapy use, family history, chest X-ray, smoking, education; no significant difference by menopausal status
				No	1.0	
				Yes	0.8 (0.6–1.1)	
				No	<i>ER+/PR- (78)</i>	
				Yes	1.0	
				Yes	1.5 (0.9–2.8)	
				No	<i>ER-/PR- (262)</i>	
				Yes	1.0	
Yes	0.9 (0.6–1.2)					
No	<i>ER-/PR+ (64)</i>					
Yes	1.0					
Yes	1.5 (0.8–2.8)					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Baumgartner <i>et al.</i> (2002), New Mexico, 1992–94	281 (128 Hispanic, 153 white), aged 30–74 years; response rate, 68% (Hispanics) and 77% (white); ascertained through registry	532 population-based (random digit dialling); matched by age, race, area; response rate, 76% (Hispanic) and 86% (white)	Interviewer-administered questionnaire	<i>Recent intake (g/week)</i>	ER+/PR+	Adjusted for age, area, education, age at menarche, menopausal status, parity, age at first birth, breastfeeding, oral contraceptive use, benign breast disease, family history, smoking, body mass index, physical activity, energy intake, fat intake; too few cases for ER+/PR– and ER–/PR+
				Non-drinker	<i>Hispanic</i>	
				<8	1.0	
				8–41 (1–2 drinks)	0.83 (0.35–1.98)	
				≥42 (≥3 drinks)	0.97 (0.49–1.91)	
					<i>White</i>	
				Non-drinker	1.0	
				<148 (<8 drinks)	0.46 (0.28–0.74)	
				≥148 (≥8 drinks)	2.13 (1.03–4.43)	
					ER–/PR–	
	<i>Hispanic</i>					
Non-drinker	1.0					
<8	1.04 (0.39–2.79)					
8–41 (1–2 drinks)	0.39 (0.17–1.08)					
≥42 (≥3 drinks)	1.43 (0.55–3.74)					
	<i>White</i>					
Non-drinker	1.0					
<148 (<8 drinks)	0.37 (0.19–0.73)					
≥148 (≥8 drinks)	1.62 (0.51–5.18)					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Britton <i>et al.</i> (2002), Women's Interview Study of Health, multi-site USA, 1990–92	1556 (1212 had receptor status); aged 20–44 years; identified through registry and medical records; response rate, 86%	1397 population-based (random-digit dialling); matched by age, region; response rate, 79%	Interviewer-administered questionnaire	<i>Usual intake (drinks/week)</i>	<i>ER+/PR+ (615)</i>	Adjusted for site, age, race, education, body mass index, waist:hip ratio, parity, age at first birth, breastfeeding, oral contraceptive use, smoking, physical activity, age at menarche, family history, menopausal status
				None	1.0	
				<7	1.11 (0.88–1.41)	
				≥7	1.33 (0.94–1.87)	
				<i>ER+/PR– (117)</i>	1.0	
				<7	0.86 (0.55–1.35)	
				≥7	0.94 (0.47–1.86)	
				<i>ER–/PR– (360)</i>	1.0	
				<7	1.08 (0.81–1.43)	
				≥7	1.38 (0.93–2.06)	
				<i>ER–/PR+ (118)</i>	1.0	
				<7	0.87 (0.55–1.39)	
≥7	1.64 (0.90–2.98)					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments	
Cotterchio <i>et al.</i> (2003), 2 studies in Canada (ECSS, WHS), 1995–98	3748 (2638 had receptor status), aged 25–74 years; confirmed by pathology reports; response rate, 86% for ECSS, 73% for WHS	373 population (Ministry of Finance rolls); matched by age, all in same region; response rate, 80% for ECSS, 61% for WHS	Self-administered questionnaire	Drinks/week			Adjusted for age at menarche, parity, age at first birth, oral contraceptive use, age at menopause, hormone replacement therapy use, body mass index, smoking, breastfeeding, benign breast disease, family history, age, oophorectomy; significant difference for ER+/PR+ versus ER-/PR- in premenopausal women; no significant differences for postmenopausal women
				<i>Premenopausal</i>	ER+/PR+ (479)		
				0	1.0		
				≤1	1.08 (0.72–1.60)		
				1.5–3	0.84 (0.55–1.28)		
				≥3.5	1.38 (0.91–2.10)		
				<i>Postmenopausal</i>	(1332)		
				0	1.0		
				≤1	1.03 (0.23–1.30)		
				1.5–3	0.90 (0.69–1.15)		
				≥3.5	1.27 (1.00–1.64)		
				<i>Premenopausal</i>	ER-/PR- (256)		
				0	1.0		
				≤1	1.31 (0.78–2.19)		
1.5–3	1.36 (0.81–2.28)						
≥3.5	0.92 (0.51–1.68)						
<i>Postmenopausal</i>	(442)						
0	1.0						
≤1	1.06 (0.75–1.50)						
1.5–3	0.90 (0.62–1.32)						
≥3.5	1.13 (0.79–1.64)						

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Li <i>et al.</i> (2003), 3 sites in Seattle, USA, 1997–99	975; aged 65–79 years; cases identified through cancer registry and verified by medical and pathology records; response rate, 81%	998 population-based (HCFA records); matched by date; response rate, 74%	Interviewer-administered questionnaire	<i>Intake in last 20 years (g/day)</i>	<i>ER+</i> (789)	Adjusted for age, family history, body mass index; no significant association with alcohol intake overall
				Never	1.0	
				Ever	1.3 (1.0–1.6)	
				<1.5	1.2 (0.8–1.8)	
				1.5–4.9	1.6 (1.0–1.8)	
				5–14.0	1.2 (0.9–1.6)	
				15–29.9	1.2 (0.9–1.8)	
				≥30	1.7 (1.1–2.7)	
				<i>p</i> for trend	0.71	
				<i>PR+</i> (648)		
				Never	1.0	
				Ever	1.3 (1.1–1.7)	
				<1.5	1.2 (0.8–1.9)	
				1.5–4.9	1.4 (1.0–2.0)	
				5–14.0	1.2 (0.9–1.6)	
				15–29.9	1.3 (0.9–1.9)	
				≥30	1.8 (1.1–2.8)	
				<i>p</i> for trend	1.0	
				<i>ER-</i> (106)		
				Never	1.0	
				Ever	1.1 (0.7–1.7)	
<1.5	1.1 (0.4–2.7)					
1.5–4.9	1.1 (0.5–2.1)					
5–14.0	1.0 (0.6–1.9)					
15–29.9	1.4 (0.7–2.7)					
≥30	1.2 (0.5–3.2)					
<i>p</i> for trend	0.54					

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Li <i>et al.</i> (2003) (contd)				Never	<i>PR-</i> (244) 1.0	
				Ever	1.1 (0.8–1.4)	
				<1.5	1.0 (0.5–1.9)	
				1.5–4.9	1.0 (0.6–1.6)	
				5–14.0	1.1 (0.7–1.6)	
				15–29.9	1.1 (0.6–1.8)	
				≥30	1.4 (0.7–2.7)	
				<i>p</i> for trend	0.71	
McDonald <i>et al.</i> (2004), CARE Study, multisite, USA, 1994–98	4575, aged 35–64 years; response rate, 77%	4685 population-based (random-digit dialling); matched by site, race, age; response rate, 65%	Interviewer-administered questionnaire	<i>Drinks/week</i>	<i>ER+/PR+</i> (2155)	Adjusted for site, race, age, menopausal status, age at menarche, age at menopause, parity, age at first birth, body mass index, family history, hormone replacement therapy use, oral contraceptive use; slightly stronger association in postmenopausal women across all subtypes, except for <i>ER-/PR-</i>
				None	1.0	
				<7	1.0 (0.9–1.1)	
				≥7	1.2 (1.0–1.4)	
					<i>ER+/PR-</i> (370)	
				None	1.0	
				<7	1.3 (1.04–1.70)	
				≥7	1.6 (1.2–2.3)	
					<i>ER-/PR-</i> (1071)	
				None	1.0	
				<7	0.9 (0.8–1.1)	
				≥7	1.0 (0.8–1.2)	
					<i>ER-/PR+</i> (202)	
				None	1.0	
				<7	0.8 (0.5–1.1)	
				≥7	1.4 (0.98–2.1)	

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Ma <i>et al.</i> (2006), Los Angeles, USA, 2000–03	1725 (1419 had receptor status), aged 20–49 years; 100% histologically confirmed; response rate, 62%	440 population-based (neighbourhood walk algorithm); matched by age, race; response rate, 74%	Interviewer-administered questionnaire	<i>Intake in last 5 years (drinks/week)</i> Never <3 3–5 6–11 >12 <i>p</i> for trend Never <3 3–5 6–11 >12 <i>p</i> for trend	<i>ER+/PR+ (739)</i> 1.0 1.11 (0.81–1.53) 1.01 (0.66–1.54) 1.26 (0.78–2.03) 2.10 (1.17–3.79) 0.03 <i>ER-/PR- (334)</i> 1.0 0.89 (0.61–1.30) 0.76 (0.45–1.28) 1.06 (0.60–1.86) 1.71 (0.87–3.38) 0.42	Adjusted for age, race, education, family history, age at menarche, parity, body mass index, oral contraceptive use, menopausal status, hormone replacement therapy use; differences not statistically significant between ER-/PR- and ER+/PR+; data not shown for ER-/PR+ or ER+/PR-

Table 2.33 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors and comments
Terry <i>et al.</i> (2006), Long Island Breast Cancer Study Project, 1996–97	1508 (ER status for 66%), aged 20–98 years; verified by pathology reports; response rate, 82%; included in-situ and invasive cancers	1556 population-based (HCFA records and random-digit dialling); matched by age; response rate, 63%	Interviewer-administered questionnaire	<i>Lifetime intake (g/day)</i>		Adjusted for age, race, education, body mass index; alcohol not associated with risk overall; stronger association for ≥ 15 g/day intake for ER+ cases among lean women (body mass index <25); no association among overweight women
				None	<i>ER+</i> (730)	
				<15	1.0	
				≥ 15	1.04 (0.85–1.27)	
				None	<i>PR+</i> (636)	
				<15	1.0	
				≥ 15	1.08 (0.89–1.33)	
				None	<i>ER+/PR+</i> (583)	
				<15	1.0	
				≥ 15	1.06 (0.86–1.32)	
				None	<i>ER-</i> (265)	
				<15	1.0	
≥ 15	1.03 (0.77–1.39)					
None	<i>PR-</i> (355)					
<15	1.0					
≥ 15	1.27 (0.85–1.90)					
None	<i>ER-/PR-</i> (212)					
<15	1.0					
≥ 15	0.97 (0.75–1.27)					
None	<i>ER+/PR-</i> (212)					
<15	1.0					
≥ 15	1.52 (1.08–2.14)					
None	<i>ER-/PR+</i> (212)					
<15	1.0					
≥ 15	0.99 (0.71–1.37)					
None	<i>ER+/PR+</i> (212)					
<15	1.0					
≥ 15	1.41 (0.92–2.16)					

CI, confidence interval; ECSS, Enhanced Cancer Surveillance Study; ER, estrogen receptor; HCFA, Health Care Finance and Administration records; PR, progesterone receptor; WHS, Women Health Study ;+, positive; –, negative

Of the case–control studies, only one reported a stronger association for ER+/PR+ tumours than for ER–/PR– tumours in premenopausal women (relative risks, 1.4 and 0.9, respectively, for ≥ 3.5 drinks per week versus non-drinkers), although no significant difference was found in postmenopausal women (Cotterchio *et al.*, 2003).

2.6.6 *Types of alcoholic beverage*

Results from studies that have looked at the type of alcoholic beverage consumed and risk for breast cancer have suggested an increased risk with increasing alcoholic beverage consumption regardless of the beverage type. Estimates from a pooled analysis of six cohort studies showed risks of 11%, 5% and 5% per 10 g intake of beer, wine and spirits per day, respectively (Smith-Warner *et al.*, 1998), which suggests that the effect is principally due to the presence of alcohol.

2.6.7 *Subgroups of women*

Evidence of whether the association of alcoholic beverage intake and risk for breast cancer varied by lifestyle and other factors was available in the study of Hamajima *et al.* (2002) (Collaborative Group on Hormonal Factors in Breast Cancer). This pooled analysis indicated that the association of alcoholic beverages with the risk for breast cancer was not modified by tobacco smoking, age at diagnosis, reproductive factors, having a mother or sister with a history of breast cancer, use of oral contraceptives or use of hormone replacement therapy (see Fig. 2.3).

2.6.8 *Male breast cancer*

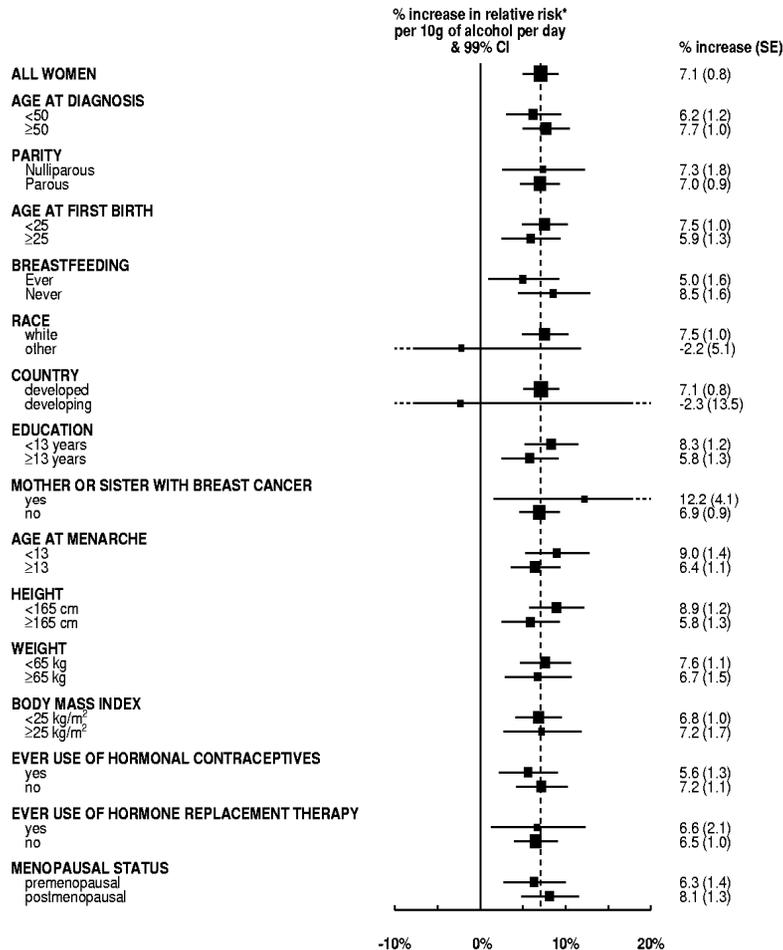
Overall, one cohort study (Table 2.34) and eight case–control studies (Table 2.35) have evaluated the association between consumption of alcoholic beverages and the risk for male breast cancer.

One cohort study of male alcoholics in Sweden has reported on the relationship with male breast cancer; this study found no difference in the rates of male breast cancer between alcoholics and the general population, based on 13 cases (Weiderpass *et al.*, 2001c; Table 2.34).

Two case–control studies were based on a population of alcoholics as reported from hospital records. One study reported a significant twofold increased risk for alcoholics (Olsson & Ranstam, 1988) and the other found no association (Keller, 1967). [Both studies included small numbers of exposed cases, had a high proportion of cases for whom data were missing and, in Olsson and Ranstam (1988), different risk estimates were produced when different groups of controls were used.] A European case–control study, based on 74 cases, found a sixfold increase in risk in the highest category of alcoholic beverage consumption (>90 g alcohol per day) compared with light drinkers and non-drinkers, corresponding to an increase in risk per 10 g intake of alcohol per day of 17% for beer and wine, but not spirits (Guénel *et al.*, 2004). All other studies

Figure 2.3. Percentage increase in the relative risk for breast cancer per 10 g of alcoholic beverage consumption per day in various subgroups of women (adjusted by study, age, parity, age at first birth and tobacco smoking).

Pooled analysis of data from 53 studies that included 58 515 women with breast cancer



* stratified by study, age, parity, age at first birth and tobacco consumption.

From Hamajima et al. (2002)

Table 2.34 Cohort study of male breast cancer and alcoholic beverage consumption

Reference, location, name of study	Cohort description (no. in analysis)	Exposure assessment	Exposure categories	No. of cases	Standardized incidence ratio (95% CI)	Adjustment factors	Comments
Weiderpass <i>et al.</i> (2001c), Cohort of Alcoholics (hospital discharge records)	145 811 men diagnosed as alcoholics in hospital records; recruited 1965–95; follow-up through linkage with cancer registry; comparison with national incidence rates; matched by age, sex, calendar time	Incidence rates in alcoholics compared with national rates	Comparison group Alcoholics	13	1.0 1.1 (0.6–2.0)	Age, calendar time	No individual exposure information; no adjustment factor

CI, confidence interval

Table 2.35 Case-control studies of male breast cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Keller (1967), Veterans Administration hospitals, USA, 1958-63	181 (adenocarcinoma), aged 26-88 years	Group 1: 181 hospital-based (discharge lists of medical procedures); matched by age, place of residence; Group 2: 181 hospital-based (bladder or kidney cancer); matched by age, place of residence, hospital characteristics	Indication of alcoholism abstracted from medical records	<i>Chronic alcoholism</i> No Yes	No data, but similar proportions of cases and controls were alcoholics.		14 cases, 10 group 1 controls and 9 group 2 controls were alcoholics; information on alcoholic beverage intake was missing for >50%.
Mabuchi <i>et al.</i> (1985a), New York, USA, 1972-75	52 identified through hospital medical and pathology records; 100% histologically confirmed; response rate, 81%	52 hospital-based; matched by age, sex, race, marital status (selected from hospital lists); response rate not stated	Interviewer-administered questionnaire	Usual intake of ≥ 1 glass/day	No relative risk reported (no association with wine, beer, mixed drink, whisky)		

Table 2.35 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Casagrande <i>et al.</i> (1988), Los Angeles, USA, 1978–85	75, aged 20–74 years; 100% histologically confirmed; response rate, 61%	75 population-based (neighbourhood survey); matched by age, race; response rate not stated	Interviewer-administered questionnaire	Alcohol drinks intake (oz/week)	No relative risk reported; 12.2 oz/wk in cases and 12.8 oz/wk in controls; $p=0.81$		No significant difference by wine, beer and spirits
Olsson & Ranstam (1988), Sweden, 1970–86	95 identified through registry, aged 21–99 years; verified through medical records	383 hospital-based (lung cancer and non-Hodgkin lymphoma); matched on hospital	Indication of alcoholism abstracted from medical records	<i>Chronic alcoholism</i> No Yes	1.0 2.3 (not significant; using lung cancer controls) 13.5 (significant; using non-Hodgkin lymphoma controls)		Only 8 cases were alcoholics

Table 2.35 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Thomas <i>et al.</i> (1992); Rosenblatt <i>et al.</i> (1999), 10 states, USA, 1983–86	227 identified through registry, all ages; 100% histologically confirmed; response rate, 75%	300 population-based (random-digit dialling and HCFA records); matched by age, cancer registry area; response rate, 45%	Interviewer-administered questionnaire	<i>Lifetime intake (no. of drinks)</i> None 1–2314 2315–7774 7775–20 878 ≥20 879	1.0 0.6 (0.3–1.3) 1.2 (0.6–2.2) 1.0 (0.6–1.9) 0.9 (0.5–1.7)	Matching factors	Thomas <i>et al.</i> (1992): No association with current intake or intake during period of life when one drank the most, or with age at which one started drinking
Hsing <i>et al.</i> (1998b), USA, 1985–86. National (US) Mortality Followback Survey	178 identified from death certificates, aged 25–74 years; response rate, 88%	512 decedants of other causes, excluding smoking- or alcohol-related causes; matched by age, race; response rate not stated	Questionnaire completed by next of kin	<i>Intake (drinks/day)</i> None Ever 1 2 3–4 ≥5	1.0 0.9 (0.6–1.6) 0.8 (0.5–1.6) 1.1 (0.6–2.0) 0.9 (0.5–1.8) 0.9 (0.5–1.8)	Age at death, socioeconomic status	Exposure information taken from next of kin; drinking could be overascertained in the controls.
Petridou <i>et al.</i> (2000), Greece, 1996–97	23 identified in 2 hospitals; 100% histologically confirmed; response rate not stated	76 hospital-based, matched by age, sex (visitors and patients of trauma unit); response rate not stated	Interviewer-administered questionnaire	<i>Drinks/week</i> None <7 ≥7 <i>p</i> for trend	1.0 1.15 (0.26–6.07) 0.44 (0.09–2.48) 0.12	None	

Table 2.35 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Johnson <i>et al.</i> (2002), Canada, National Cancer Surveillance System 1994–98	81 identified through cancer registry, aged 42–74 years; 100% histologically confirmed; response rate, 68%	1905 population-based (health insurance records and random-digit dialling); matched by age, sex; response rate, 65%	Self-administered questionnaire	<i>Intake (servings/week)</i> None < 3 3–9 ≥10 <i>p</i> for trend	1.0 0.66 (0.35–1.26) 0.91 (0.50–1.65) 0.63 (0.33–1.23) 0.3	Age, marital status, coffee, physical activity, body mass index, area	
Guénel <i>et al.</i> (2004), multisite, Europe, 1995–97	74 identified through pathology and clinical departments; aged 35–70 years; 100% histologically verified; response rate, 87%	1432 population (population registers and electoral roll); matched by age, sex, region; response rate, 52%–78% by region	Interviewer-administered questionnaire	<i>Intake 5 years ago (g/day)</i> 0–15 16–30 31–45 46–60 61–75 76–90 >90 Per 10 g/day	1.0 0.87 (0.30–2.47) 1.37 (0.46–4.08) 2.28 (0.73–7.11) 4.45 (1.12–17.7) 4.68 (1.07–20.6) 5.62 (1.54–20.6) 1.17 (1.05–1.30)	Age, region, smoking, gynaecomastia, diabetes, fertility problems, head injury, body mass index	Increased risk for wine and beer, but not spirits; similar results found when using hospital-based controls (rare cancers); adjustment for confounders made little difference to the estimates.

CI, confidence interval; HCFA, Health Care Finance and Administration

have found no association (Mabuchi *et al.*, 1985a; Casagrande *et al.*, 1988; Hsing *et al.*, 1998b; Rosenblatt *et al.*, 1999; Petridou *et al.*, 2000; Johnson *et al.*, 2002).

2.7 Cancer of the stomach

A possible relationship between alcoholic beverage consumption and risk for stomach cancer has long been hypothesized, but epidemiological evidence has been considered uncertain (IARC, 1988). This section evaluates the human evidence related to the risk for stomach cancer based on relevant publications from cohort and case-control studies published since 1988. Because a large proportion of cases of stomach cancer occur in China (accounting for 38% throughout the world), papers published in the Chinese literature are also included in this review.

The effects of total alcoholic beverage consumption on the risk for stomach cancer are summarized in Table 2.36 (cohort studies), Table 2.37 (cohort studies in the Chinese literature), Table 2.38 (case-control studies) and Table 2.39 (case-control studies in the Chinese literature). The effects of alcoholic beverage consumption and risk for stomach cancer by anatomic subtypes (cardia and distal cancer) are shown in Table 2.40, the effects of alcoholic beverage types are presented in Table 2.41 and the effects of alcoholic beverage consumption and the risk for stomach cancer stratified by gender are given in Table 2.42.

2.7.1 Cohort studies

(a) Special populations (Table 2.36)

In the Danish cohort study of 18 368 alcohol abusers conducted in Copenhagen in 1954–87, 64 cases of stomach cancers occurred during follow-up (Tønnesen *et al.*, 1994). The SIR for stomach cancer was slightly increased and marginally significant (SIR, 1.3; 95% CI, 1.0–1.7). In the Swedish cohort of alcoholics (Adami *et al.*, 1992a), a total of 25 cases resulted in a null association and an SIR of 0.9 (95% CI, 0.6–1.4) for men and 0.7 (95% CI, 0.0–4.0) for women.

(b) General population (Tables 2.36 and 2.37)

A total of 12 cohort studies of the general population that were conducted in Japan, the USA, Sweden, China, Denmark and the United Kingdom have examined the association between alcoholic beverage consumption and stomach cancer; three studies reported a significant association. Two cohort studies reported a statistically significant association between alcoholic beverage consumption and the risk for stomach cancer (Kato *et al.*, 1992b; Fan *et al.*, 1996) and one study with a large sample size reported an inverse relationship (Tran *et al.*, 2005). Nine studies reported either a non-statistically significant association or no association.

Table 2.36 Cohort studies of stomach cancer and alcoholic beverage consumption

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
<i>Special populations</i>								
Kono <i>et al.</i> (1987), Japan, Japanese Physicians' Study	5130 male Japanese physicians, aged 27–89 years; followed up for 19 years; 1965–	Self-administered questionnaire	ICD-8 (155) Primary liver cancer ICD-8 (151)	Never Occasional Daily (<2 g/day) Daily (≥2 g/day)	Total: 116 deaths	1.00 1.11 (0.69–1.79) 1.30 (0.79–2.12) 1.17 (0.66–2.07)	Age, smoking	Daily consumption of alcohol (1'go' sake) 1'go' =180 mL; 1'go' sake ≈ 27 mL alcohol
Adami <i>et al.</i> (1992a), Sweden, Uppsala Alcoholics Study	9353 (8340 men, 1013 women) selected from the Uppsala Inpatients Register with a discharge diagnosis containing a diagnostic code for alcoholism during 1965–83; follow-up, 19 years (mean, 7.7)	Follow-up was by record linkage to the nationwide Cause of Death Registry and the Swedish Cancer registry.	ICD-7 (155.0) Liver cancer; ICD-7 (307,322) ICD-8 (291,303)		Total, 24 cases 23 men 1 woman	SIR 0.9 (0.6–1.4) 0.7 (0.0–4.0)	-	Expected numbers of cancers computed from cancer incidence in the study population (Uppsala health care region) to compare with the observed

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Tønnesen <i>et al.</i> (1994), Denmark, Alcohol Abusers Study	18 368 alcoholics from Copenhagen who entered a public outpatient clinic for free treatment in 1954–87; 15 214 men observed for 12.9 years on average and 3093 women observed for an average of 9.4 years	Records of cohort members linked to the Danish Cancer Registry to obtain cancer morbidity information		Alcohol abuse (male, female alcoholics)	64 cases 60 men 4 women	SIR 1.3 (1.0–1.6) $p \leq 0.05$ 1.8 (0.5–4.6) $p \leq 0.05$	Age, sex	Observed cancer incidence compared with that expected in the Danish population

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Nomura <i>et al.</i> (1995), Hawaii, USA, American Men of Japanese Ancestry Study	8006 men born in 1900–19, and residing on the Hawaiian island of Oahu; followed up for 25 years examined between 1965–1968 at all hospitals on Oahu and the Hawaiian Tumor Registry	Interviewed; surveillance to identify incident cases		Non-drinker <5 oz/month 5–14 oz/month 15–39 oz/month ≥40 oz/month	86 cases 43 41 39 36	1.0 0.9 (0.6–1.3) 1.1 (0.8–1.6) 1.0 (0.7–1.5) 1.2 (0.8–1.8) <i>p</i> =0.20	Age, smoking history	

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
<i>General population</i>								
Kneller <i>et al.</i> (1991), USA	17 633 white American men insurance policy holders, largely of Scandinavian and German descent, aged ≥ 35 years; follow-up, 1966–86	Mailed questionnaire		Alcoholic beverage consumption (data not presented)	75 deaths	No association	-	Data regarding alcohol use and risk for stomach cancer not presented
Kato <i>et al.</i> (1992a), Japan	3914 subjects who underwent gastroscopic examination; 4.4 years of follow-up on average (1985–89)	Self-recorded questionnaire, cancer registry and death certificate	Organ site (ICD code)	None Past Occasional Daily	12 cases 6 11 16 Total: 45 (35 men, 10 women)	1.00 2.19 (0.78–6.19) 1.10 (0.47–2.60) 1.51 (0.65–3.54)	Sex, age, residence	Non-significant increase in risk for stomach cancer among past and daily drinkers

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kato <i>et al.</i> (1992b), Japan	9753 Japanese men and women, aged ≥ 40 and ≥ 30 years, respectively; follow-up, 1986–91; response rate, 85.9%	Baseline survey using a mailed questionnaire; death certificate		None Occasional Daily <50 mL Daily ≥ 50 mL	26 cases 12 7 12 Total: 57 (33 men, 22 women)	1.0 1.75 (0.84–3.61) 1.20 (0.48–3.00) 3.05 (1.35–6.91)	Sex, age	Association between alcohol intake and stomach cancer slightly weakened when smoking status, diet and family history of stomach cancer were included in the multivariate analysis.

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Guo <i>et al.</i> (1994), China, Lin Xian Nutrition Intervention Trial	Nested case-control study; 29 584 adults who participated in a randomized intervention trial, aged 40–69 years; follow-up, 1986–91; 539 cases, 2695 controls, 5 controls per case; matched by age, sex	Structured interview		Lifetime consumption of alcoholic beverages (data not presented)	539 cases			Drinking alcoholic beverages was relatively uncommon in this area, but was reported by 22% of the cancer patients; no significant association (data not presented)

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Murata <i>et al.</i> (1996), Japan, Chiba Center Association Study	Nested case-control study; 887 cases and 1774 controls, selected from a cohort of 17 200 male participants of a gastric mass survey in 1984; followed up for 9 years; 2 controls per case; matched by sex, birth year, first digit of the address code	Self-administered questionnaire		0 (cup/day) 0.1–1.0 (cups/day) 1.1–2.0 (cups/day) ≥2.1 (cups/day)	101 cases 82 51 12	1.0 1.1; $p>0.05$ 1.1; $p>0.05$ 0.5; $p>0.05$	Smoking	No 95% CI provided; a cup of 180 mL Japanese sake contains 27 mL ethanol.

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Yuan <i>et al.</i> (1997), China, Shanghai Men's Study	18 244 male residents of Shanghai, enrolled between 1986 and 1989 (80% of eligible subjects); only 50 subjects lost to follow-up until 1993	Structured interviewed; cancer incidence ascertained through the population-based Shanghai Cancer Registry and vital status ascertained by inspection of the Shanghai death certificate records		Non-drinkers 1–28 drinks/week ≥29 drinks/week	48 deaths 33 10	1.0 0.98 1.37	Age, education, smoking	95% CI not given; non-significant 30–40% increase in risks of death from cancers of the stomach observed in heavy drinkers.

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Terry <i>et al.</i> (1998), Sweden, Swedish Twin Registry Study	11 546 individuals born in 1886–1925 in the Swedish Twin Registry, and both still living in Sweden in 1961; followed up, 1967–92; 98% follow-up	Mailed questionnaire, record linkage to the National Cancer and Death Registers.	Organ site (ICD code)	None Light Moderate	116 cases	1.00 1.51 (0.89–2.55) 1.36 (0.83–2.24)	Fruit and vegetable intake, age, gender, body mass index, socioeconomic status, smoking	Alcoholic beverage consumption was assessed as number of drinks per week (data not presented); no. of cases per drinking category not given.
Sasazuki <i>et al.</i> (2002), Japan, The Japan Public Health Center Study Cohort I	19 657 men, born in 1930–49, aged 40–59 years at baseline; followed up, 1990–99; response rate: men, 76%; women, 82%	Self-administered questionnaire, death certificates, cancer registry	ICD-9 (151)	0–3 days/month 0–161.0 g/week 162.0–322.0 g/week 322.5 g/week	68 deaths 54 77 74	1.0 0.8 (0.6–1.2) 1.1 (0.8–1.5) 1.1 (0.8–1.6)	Age, area, smoking habit, consumption of fruit, green or yellow vegetables, salted cod roe or fish gut, body mass index	Reference group (0–3 days/month) included drinkers; data for women collected but not presented

Table 2.36 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Tran <i>et al.</i> (2005), China, Linxian General Population Trial	29 584 adults who participated in the Linxian General Population Trial, 40–69 years of age at baseline; follow-up, 15 years (1984–98)	Structured interview; case ascertainment considered complete and loss to follow-up minimal (176 or 1%)		Alcoholic beverage consumption (data not presented)	1089 363	Gastric cardia cancer 0.84 (0.72–0.97); Gastric non-cardia cancer 0.79 (0.61–1.02)	Age, sex	Alcoholic beverage drinking defined as any in previous 12 months

CI, confidence interval; ICD, International Classification of Diseases; SIR, standardized incidence ratio

Table 2.37 Cohort studies of stomach cancer and alcoholic beverage consumption published in the Chinese literature^a

Reference, study location, period	Characteristics of cases	Characteristics of cohort	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Fan <i>et al.</i> (1996), Sifang County, Shichuan, 1985–90	128 digestive tract cancers identified from the Disease Surveillance Spot, including stomach, liver, colorectal and oesophageal cancer; 97% diagnosed by county level hospitals	29 929 farmers, aged >35 years; age and sex distribution not provided; loss to follow-up not described	Interviewer-administered questionnaire (once a year)	<i>Cumulative alcohol consumption (kg)</i> Non-drinkers <i>Men</i> 1–125 125–500 ≥500 <i>Women</i> 1–125 125–500 ≥500	(Stomach cancer only) 1.0 2.53 (0.74–8.70) 3.89 (1.55–9.74) 6.28 (1.11–12.97) 0.69 (0.17–2.73) 1.67 (0.34–8.20) 1.81 (0.70–4.68)	Not mentioned	Relative risk for death from stomach cancer
Wang <i>et al.</i> (2005a), Shanghai, 1986–2002	18 244 cancer-free men followed from 1986 to 2002		Interview	<i>Alcoholic beverages (g/day)</i> 0 <30 30–70 >70	1.00 1.00 1.16 1.42 (<i>p</i> -value>0.05)	Age, smoking, education	

CI, confidence interval

There was evidence of an association between alcohol consumption and an increased risk stomach cancer in the two cohort studies conducted in Japan (57 cases; Kato *et al.*, 1992b) and China (128 cases; Fan *et al.*, 1996). The relative risks for stomach cancer were 3.05 (95% CI, 1.35–6.91) for 50 mL or more alcohol per day (three or more drinks per day) when adjusted for age and gender (Kato *et al.*, 1992b) and 6.28 (95% CI, 1.11–12.97) for men who had a cumulative alcoholic beverage consumption of 500 kg or more (Fan *et al.*, 1996). One cohort study in China with a large sample size (1089 cardia cancer and 363 non-cardia cancer) reported inverse associations with alcoholic beverage consumption, with relative risks of 0.84 (95% CI, 0.72–0.97) for cardia cancer and 0.79 (95% CI, 0.61–1.02) for non-cardia cancer (Tran *et al.*, 2005). The two studies that reported a positive association (Kato *et al.*, 1992b; Fan *et al.*, 1996) adjusted for age and gender, but it is not clear what confounding factors were adjusted for in the study by Tran *et al.*, (2005).

A positive, but not statistically significant, association was observed in five studies (Kono *et al.*, 1987; Kato *et al.*, 1992a; Yuan *et al.*, 1997; Terry *et al.*, 1998; Wang *et al.*, 2005a) and null results were reported in three studies with relatively large sample sizes ranging from 75 to 493 cases (Kneller *et al.*, 1991; Nomura *et al.*, 1995; Murata *et al.*, 1996; Sasazuki *et al.*, 2002).

2.7.2 Case-control studies (Tables 2.38 and 2.39)

Several case-control studies have reported results on the influence of alcoholic beverage consumption on the risk for stomach cancer. More than 50% of the studies reported a positive association between alcoholic beverage consumption and stomach cancer: 60% of the studies that adjusted for confounding factors and 52% of the studies that did not also report a positive association. The proportion of positive associations was 71% in the Chinese literature and 44% in the English literature.

In more than half of the studies, the odds ratios were adjusted for variables such as sex, age, residence, education, diet, socioeconomic status and cigarette smoking. Odds ratios were adjusted for *Helicobacter pylori* status in one study (Kikuchi *et al.*, 2002). In 25 case-control studies, of which 11 were published in English (Lee *et al.*, 1990; Boeing *et al.*, 1991; Jedrychowski *et al.*, 1993; Falcao *et al.*, 1994; Inoue *et al.*, 1994; Ji *et al.*, 1996; De Stefani *et al.*, 1998a; Zaridze *et al.*, 2000; Muñoz *et al.*, 2001; Kikuchi *et al.*, 2002; Shen *et al.*, 2004), an association was found between stomach cancer and alcoholic beverage consumption. The point estimates of adjusted odds ratios for an association between alcoholic beverage consumption and the risk for stomach cancer were between 2.4 and 2.8 for 2–3 drinks per day.

2.7.3 Anatomic subsite and histological type (Table 2.40)

Among 12 case-control studies of both cardia cancer and distal stomach cancer, eight demonstrated a stronger association for cardia cancer than for distal stomach

Table 2.38 Case-control studies of stomach cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Lee <i>et al.</i> (1990), Taiwan, China, 1954–88	210 (123 men, 87 women); histologically confirmed; adenocarcinoma, 97.7%; other type of carcinoma, 2.3%; participation rate, 90%; death certificate from Taiwan Provincial Department of Health	810 (478 men, 332 women) from ophthalmic service in four major hospitals in Taipei; matched with cases on hospital, age, sex; participation rate, 96%	Interviewer-administered structured questionnaire		<i>Days/week</i> None 1–3 ≥4	150 21 39	1.0 0.93 1.51; $p < 0.05$	Smoking; green tea drinking, salted meat consumption, fried food consumption, fermented bean consumption, milk consumption	Frequency and duration of alcoholic beverage drinking both associated with stomach cancer; dose-response relationship
Boeing <i>et al.</i> (1991), Germany, 1985–88	143 incident, almost equal number of men and women, aged 32–80 years; histologically confirmed; patients from 5 hospitals in Germany	579 hospital patients and visitors; matched by 2:1 match by age (± 3 years), sex	Interviewer-administered standardized questionnaire		<i>Beer</i> None <100 g/day 100–500 g/day >500 g/day <i>Wine</i> None <20 g/day >20 g/day <i>Liquor</i> None <2 g/day >2 g/day	37 24 50 32 69 53 21 107 22 14	1.0 1.12 (0.62–2.01) 2.22 (1.30–3.77) 1.82 (0.95–3.50) $p < 0.05$ 1.0 0.94 (0.61–1.45) 0.52 (0.30–0.93) $p < 0.05$ 1.0 0.75 (0.43–1.29) 0.52 (0.27–1.00) $p < 0.05$	Age, sex, hospital	Beer is the dominant alcoholic beverage in the study area.

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hoshiyama & Sasaba (1992a,b), Saitama, Japan, 1984–90	216 single and 35 multiple, newly diagnosed stomach adenocarcinomas (men); participation rate, 73%	483 randomly selected from electoral roll; stratification by sex, age; participation rate, 28%	Interviewer-administered standardized questionnaire		Single stomach cancer			Age, smoking status	No association between single and multiple stomach cancer risk and alcoholic beverage consumption
					Never	33	1.0		
					Past	11	1.0 (0.4–2.2)		
					Occasional	48	1.0 (0.6–1.7)		
					Daily	124	1.0 (0.6–1.6)		
							<i>p</i> =0.56		
					<i>Total alcohol consumption (mL/lifetime)</i>				
					Non-drinker		1.0		
					<500 000		0.9 (0.6–1.6)		
					≥500 000		1.1 (0.7–1.9)		
					Multiple stomach cancer				
					Never		1.0		
					Past		4.7 (1.0–21.6)		
					Occasional		2.6 (0.7–9.6)		
Daily		1.4 (0.4–5.2)							
<i>Total alcohol consumption (mL/lifetime)</i>									
Non-drinker		1.0							
<500 000		1.7 (0.4–6.4)							
≥500 000		2.5 (0.7–9.3)							

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Jedrychowski <i>et al.</i> (1993), Poland, 1986–90	520 men, aged <75 years; histologically confirmed, classified according to the Lauren criteria; 137 cardia (58% intestinal, 20% diffuse type), 383 non-cardia (51.2% intestinal, 36% diffuse type); participation rate, 100%	520 men from nine university hospitals in Poland admitted mostly for accidents, orthopaedic problems or general surgery; matched by age (± 5 years); disease of gastrointestinal tract and other cancers excluded; participation rate, 100%	Interviewer-administered standardized questionnaire		<i>Average quantity of vodka per occasion</i>			Hospital, age, sex, occupation, education, sausage consumption, fruit/vegetable consumption, smoking	Non-drinkers: abstainers or who reported drinking vodka occasionally but less than 100 g at a time; those who drank vodka before breakfast had a nearly threefold elevated risk; findings on alcoholic beverages other than vodka not reported.
					Non-drinker	68	1.0		
					100 g	85	1.99 (1.23–3.23)		
					250 g	208	2.01 (1.33–3.05)		
					>250 g	159	2.43 (1.57–3.75)		
							<i>p</i> <0.001		
					<i>Frequency of vodka drinking</i>				
					Non-drinker	68	1.0		
					Very rare (<1/month)	132	1.83 (1.18–2.83)		
					1–3/month	205	2.09 (1.38–3.16)		
≥ 1 /week	115	3.06 (1.90–4.95)							
		<i>p</i> <0.001							
<i>Vodka drinking on an empty stomach</i>									
Non-drinker	68	1.0							
Not drinking before breakfast	401	2.09 (1.42–3.08)							
Drinking before breakfast	51	2.98 (1.60–5.53)							
		<i>p</i> <0.001							

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Kabat <i>et al.</i> (1993), USA, 1981–90	Adenocarcinoma of the oesophagus/cardia (160 men, 21 women), squamous-cell carcinoma of the oesophagus (122 men, 78 women), adenocarcinoma of distal stomach (113 men, 30 women); newly diagnosed, histologically confirmed	Hospitalized patients with disease not related to smoking and of organ systems other than the gastrointestinal tract (4162 men, 2222 women); matched by age (± 5 years), sex, race, hospital	Interviewer-administered structured questionnaire; all subjects were interviewed in 28 hospitals in eight cities in the USA between 1981 and 1990	ICD-9 (150, 151.0, 151.1–151.9)	Adenocarcinoma of distal stomach <i>Men</i> Non-drinker Occasional 1–3.9 oz WE/day ≥ 4 WE/day <i>Women</i> Non-drinker Occasional 1–3.9 oz WE/day ≥ 4 WE/day		1.0 1.0 (0.6–1.7) 0.5 (0.3–0.9) 0.7 (0.4–1.3) 1.0 0.6 (0.3–1.4) 0.6 (0.2–1.8) 0.9 (0.3–3.1)	Age education, smoking, hospital, time period (1981–84, 1985–90)	Non-drinker: less than 1 drink per week; occasional: ≥ 1 drink per week but < 1 drink per day; WE: whiskey-equivalent; analysis limited to whites; joint effect of smoking and drinking (analysis limited to men), 0.9 (0.5–1.5) for adenocarcinoma of distal stomach and 2.4 (1.3–4.2) for oesophagus/cardia
D'Avanzo <i>et al.</i> (1994), Milan, Italy, 1985–93	746 (457 men, 289 women), aged 19–74 years; histologically confirmed incident; refusal rate, 5%; admitted to National Cancer Institute; 5 major hospitals in Milan	2053 hospitalized (1205 men, 848 women) for acute non-neoplastic non-digestive tract disease, aged 19–74; >90% from Italy; refusal rate, 5%;	Interviewer-administered standardized questionnaire		Non-drinkers <2 drinks/day 2<4 drinks/day 4<6 drinks/day 6<8 drinks/day ≥ 8 drinks/day <i>Duration (years)</i> Non-drinkers <30 ≥ 30	187 115 199 109 52 84 187 132 427	1.0 1.1 (0.9–1.5) 1.1 (0.9–1.4) 1.1 (0.8–1.5) 1.3 (0.9–1.9) 1.6 (1.1–2.2) $p < 0.05$ 1.0 1.1 (0.9–1.4) 1.2 (1.0–1.6) $p < 0.05$	Sex, age, education	Conditions of controls: traumatic diseases, 47%; non-traumatic orthopaedic, 20%; acute surgical, 19%; other miscellaneous disorders, 14%

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Falcao <i>et al.</i> (1994), Portugal	74 selected from patients undergoing gastroscopy; histologically confirmed	193 patients undergoing gastroscopy or colonoscopy or other recto-sigmoidal procedure; patients accompanying patients; matched for age (± 5 years), sex	Interviewer-administered structured questionnaire		<i>Red wine consumed per week (g of alcohol)</i>		1.0		
					<187	1.36 (0.64–2.93)			
					187–372	1.77 (0.63–4.98)			
					373–559	3.67 (1.42–9.49)			
Hansson <i>et al.</i> (1994), central and northern Sweden, 1989–92	338 (218 men, 120 women), aged 40–79 years; histologically confirmed; 74.1% of original sample	679 randomly selected from population registers; mean age, 67 years; 1:2 frequency-matched by age strata, sex; participation rate, 77.3%	Interviewer-administered structured questionnaire		<i>Total alcohol consumption (mL 100% alcohol/month)</i>			Age, gender, socioeconomic status	High alcohol intake tended to increase the risk associated with tobacco use; among non-drinkers, odds ratio for tobacco use was 0.53 (0.25–1.12) and, among drinkers, was 1.77 (1.22–2.57) ($p=0.0073$)
					Non-drinkers	83	1.0		
					1–35	95	1.17 (0.81–1.70)		
					36–160	87	1.11 (0.75–1.64)		
					>160	73	0.92 (0.60–1.42) $p=0.64$		

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Inoue <i>et al.</i> (1994), Nagoya, Japan, 1988–91	668 (420 men, 248 women); histologically confirmed; 123 cardia, 218 middle (body), 256 antrum, 71 unclassified	668 (420 men, 248 women) with no history of cancer or any other specific disease, randomly selected from outpatients at same hospital; matched by sex, age (\pm 2 years), time of hospital visit	Common self-administered questionnaire	ICD-9 (151.0–151.9)	Drinker (versus non-drinker)		1.23 (0.92–1.65)	Sex	Joint effect of smoking and drinking: 1.97 (1.14–3.42); especially in the development of cardia cancer, 4.70 (1.10–20.2); drinkers included 'ex-drinkers'; only data for men were presented.
					Current drinker		1.16 (0.86–1.56)		
					Former drinker		1.87 (1.11–3.15)		
					<1 year after quitting		2.60 (1.09–6.19)		
					$p < 0.05$				
					≥ 1 year after quitting		1.60 (0.87–2.94)		

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Gajalakshmi & Shanta (1996), India, 1988–90	388 incident (287 men, 101 women); 75% confirmed histologically, 25% by barium meal, exploratory surgery or endoscopy	287 men and 101 women cancer patients from Cancer Institute, diagnosed in 1988–90; site of cancer: penis, 23.5%; bone and connective tissue, 15.2%; skin, 13.1%; cervix, 11.9%; leukaemia, 6.2%; prostate, 6.2%; breast, 5.2%; other sites, 18.7%; 1:1 matched by age (\pm 5 years), sex, religion, mother tongue; cancers of gastrointestinal tract, bladder and pancreas and smoking-related cancers excluded	Interviewer-administered standardized questionnaire		Non-drinkers Former drinkers Current drinkers Former and current	285 37 66 103	1.0 1.4 (0.54–3.40) 0.8 (0.41–1.77) 1.1 (0.58–1.95)	Chewing habit, income group, education, residence (multivariate model)	Controls were cancer patients.

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Ji <i>et al.</i> (1996), Shanghai, China, 1988–89	1124 (770 men, 354 women), aged 20–69 years; 52.1% confirmed histologically, 48% by surgery, endoscopy, X-rays or ultrasound as cancer of cardia (16%), distal stomach (70%) or unclassified (14%); participation rate, 65.5%	1451 (819 men, 632 women) randomly selected permanent residents in Shanghai; frequency-matched for age, sex; participation rate, 85.8%	Interviewer-administered structured questionnaire	ICD-9 (151.0, 151.1–151.8, 151.9)	<i>Ethanol intake (g/week)</i>				Age, income, education, smoking	Risk for distal cancer among men increased more than twofold (odds ratio, 2.21; 95% CI, 1.28–3.82) for users of both tobacco and alcohol relative to non-users but no statistically significant interaction between lifetime amounts of smoking and alcoholic beverage drinking; data for women not presented.
					<175	75	1.02 (0.71–1.49)	<i>Men</i>		
					175–349	80	1.00 (0.70–1.43)			
					350–524	79	1.08 (0.75–1.53)			
					≥525	79	1.19 (0.84–1.68)	<i>p</i> =0.36		
					Non-drinker	483	1.0			
					Former drinker	27	1.91 (1.16–3.15)			
					Current drinker	307	1.04 (0.84–1.30)			
					<i>Duration (years)</i>					
					<15	100	0.80 (0.57–1.13)			
					15–< 34	113	1.21 (0.90–1.63)			
					≥35	121	1.30 (0.96–1.75)	<i>p</i> =0.06		
					<i>Lifetime ethanol intake (g/week × years)</i>					
<2450	76	0.68 (0.46–1.02)								
2450–7462	79	1.37 (0.98–1.93)								
7463–15 399	79	0.87 (0.60–1.25)								
≥15 400	78	1.39 (0.99–1.95)	<i>p</i> =0.12							

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Zhang <i>et al.</i> (1996), USA, 1992–94	95 (79 men, 16 women) incident with pathological diagnosis of adenocarcinomas of oesophagus and gastric cardia, 67 (43 men, 24 women) with adenocarcinoma of the distal stomach; participation rate, 81%	132 (62 men, 70 women) consecutive patients scheduled to have an upper gastrointestinal endoscopy in the cancer centre and later classified as cancer-free; participation rate, 81%	Self-administered modified National Cancer Institute Health Habits History Questionnaire	ICD-0 (150.0–150.9; 151.0, 151.1–151.9)	<i>ACDS</i>	20	1.00	Age, sex, race, education, pack-years of smoking, body mass index, total dietary intake of calories	Frequency of self-reported alcohol use multiplied by 0.5 if patient's portion size was small; by 1 if the portion size was medium; and by 1.5 if the portion size was large.
					No	20	1.60 (0.65–3.93)		
					≤ 1 /week	27	0.98 (0.43–2.27)		
					> 1 /week		$p=0.93$		
					<i>ACOGC</i>	14	1.0		
No	26	3.02 (1.14–8.02)							
	55	2.02 (0.85–4.82)		$p=0.19$					
Gammon <i>et al.</i> (1997), Connecticut, USA, 1993–95	Gastric cardia adenocarcinomas (223 men, 38 women), other gastric adenocarcinomas (254 men, 114 women); aged 30–79 years; histologically confirmed, newly diagnosed; all identified by use of established rapid-reporting systems	695 (555 men, 140 women) identified by Waksberg's random-digit dialling, aged 30–64 years; frequency-matched by age, sex; overall response rate, 70.2%	Structured questionnaire administered by trained interviewers		<i>Any intake</i>		<i>Gastric adenocarcinoma</i>	Age, sex, geographical centre, race, body mass index, income, cigarette smoking, all other types of alcohol use	Interviews administered directly to the study subject, rather than to the closest next of kin (usually the spouse) for more than 67% of cases and 96% of controls
					Never	125	1.0		
					Ever	238	0.8 (0.6–1.1)		
					< 5 drinks/week	74	0.7 (0.5–1.1)		
					5–11 drinks/week	68	0.9 (0.6–1.3)		
					12–30 drinks/week	55	0.7 (0.4–1.0)		
					> 30 drinks/week	41	0.6 (0.4–1.0)		

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Muñoz <i>et al.</i> (1997), northern Italy, 1985–92	88, aged <75 years (median age, 62 years) reported a family history of stomach cancer in first degree relatives; refusal rate <3%	103 hospital controls (median age, 57 years) reported a family history of stomach cancer in first degree relatives; 80% of cases and controls resided in the same region and >90% in northern Italy.	Structured interview		<1 day/week 1–3 days/week ≥4 days/week	26 31 31	1.0 0.61 (0.34–1.42) 0.73 (0.27–1.98)	Sex, age, residence, education	88 cases and 103 controls reported a family history of stomach cancer in first degree relatives.
DeStefani <i>et al.</i> (1998a), Montevideo, Uruguay, 1992–96	331 men, aged 25–84 years; admitted to any of four major hospitals in Montevideo; 311 microscopically confirmed adenocarcinoma of stomach; 77.2% located in the antrum and pylorus; response rate, 92.8%	622 hospitalized men; frequency-matched by age, residence; response rate, 92.6%	Interviewer-administered standardized questionnaire		<i>Total alcohol consumption</i> Non-drinkers 1–60 g 61–120 g >120	64 70 65 112	1.0 1.0 (0.7–1.5) 1.5 (0.9–2.3) 2.4 (1.6–3.7) <i>p</i> <0.001	Age, residence, smoking, vegetable intake	Pure alcohol content was calculated according to concentrations specific to Uruguay: 6% for beer; 12% for wine and 46% for spirits.

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
López-Carrillo <i>et al.</i> (1998), Mexico (no study dates given)	220 (44.5% women 55.4% men), aged 24–88 years; histologically confirmed adenocarcinoma of the stomach from 15 large hospitals	752 (60.6% women, 39.4% men) population-based, aged 20–98 years; surrogate responders, 7%	Structured interview		<i>Ethanol (g/day)</i> Abstainers <1.5 1.5–4.9 ≥5.0	91 23 59 47	1.0 1.01 (0.52–1.96) 1.27 (0.76–2.11) 1.93 (1.00–3.71) <i>p</i> =0.068	Age, sex, total calorie intake, chili pepper, history of peptic ulcer, socioeconomic status, cigarette smoking, fruit, vegetables, salt, processed meats	One drink (1 oz or 30 mL) of tequila = 14.03 g ethanol; one drink (200 mL can/bottle) of beer = 12.96 g; one drink (60 mL) of wine = 9.58 g; and one drink of rum or brandy (30 mL) = 14.03 g ethanol; cases represented 80% of stomach cancer cases reported to the Mexican National Cancer Registry

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Chow <i>et al.</i> (1999), Warsaw, Poland, 1994–97	464 (302 men, 162 women) from 22 hospitals in Warsaw, aged 21–79 years; confirmed histologically mainly as intestinal (67%) or diffuse (14%); participation rate, 90%	480 (314 men, 166 women) Warsaw residents randomly selected from a computerized registry of all legal residents in Poland; frequency-matched by age, sex; participation rate, 82%	Interviewer-administered standardized questionnaire; a 30-mL blood sample collected	(ICD-0; I51 ICD-0-2 C16)	Current non-drinker	170	1.0	Age, education, years lived on a farm, pack-years of cigarette smoking, history of cancer	Current drinking of beer, wine or liquor was inversely related to risk for stomach cancer among men but not women.
					<1 drink/week	41	0.7 (0.4–1.2)		
					1–<3 drinks/week	42	0.5 (0.3–0.9)		
					3–<7 drinks/week	32	0.4 (0.2–0.7)		
					≥7 drinks/week	79	1.2 (0.7–2.0)		
					<i>Age started (years)</i>				
					<20	81	0.5 (0.3–0.8)		
					20–24	66	0.5 (0.3–0.9)		
					≥25	44	1.0 (0.6–1.7)		
					<i>Drink-years</i>				
					<10	72	0.6 (0.4–0.9)		
					10–19	29	0.5 (0.3–0.9)		
					20–29	20	0.6 (0.3–1.3)		
30–39	12	0.5 (0.2–1.3)							
40–79	32	1.3 (0.6–2.6)							
≥80	27	1.0 (0.5–2.0)							
Ye <i>et al.</i> (1999), northern and central Sweden, 1989–95	90 (71 men, 19 women) gastric cardia cancer, 260 (190 men, 70 women) and 164 (87 men, 77 women) distal gastric cancer of intestinal and diffuse types, aged 40–79 years; histologically confirmed; participation rate, 62%	1164 (779 men, 385 women) randomly selected from population registers, aged 40–79 years; frequency-matched by age, sex; participation rate, 76%	Interviewer-administered structured questionnaire		<i>Total alcohol consumption (mL 100% alcohol/month)</i>			Age, gender, residence area, body mass index, socioeconomic status, smoking, use of smokeless tobacco, use of different kinds of alcoholic beverages	Interviewed about lifetime smoking, use of smokeless tobacco and use of alcohol 20 years ago
					Non-drinkers	52	<i>Intestinal type</i> 1.0		
					1–35	64	1.2 (0.8–1.9)		
					36–160	73	1.2 (0.8–1.9)		
					>160	66	1.2 (0.7–1.9) <i>p</i> =0.56		
					<i>Diffuse type</i>				
					Non-drinkers	36	1.0		
					1–35	50	1.3 (0.8–2.1)		
					36–160	42	1.0 (0.6–1.7)		
					>160	34	1.0 (0.5–1.8) <i>p</i> =0.73		

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Zaridze <i>et al.</i> (2000), Moscow, Russia, 1996–97	448 (248 men, 200 women), aged <75 years; confirmed histologically as cancer of cardia (92) or non-cardia (356); lived in Moscow city; participation rate, 98%	610 (292 men, 318 women) patients restricted to Moscow city residents; conditions included respiratory (10%) and heart (10%) diseases, diseases of the nervous system (10%) and hypertension and stroke (9%); cancer and/or gastrointestinal diseases excluded; participation rate, 97%	Self-administered questionnaire; blood samples		<i>Gastric cardia</i>		<i>Men</i>	Age, education, smoking	There was an effect of interaction between smoking and vodka consumption on the risk for cardia cancer.
					Never	4	1.0		
					Ever	56	2.7 (0.9–8.3)		
					<i>Women</i>				
					Never	14	1.0		
					Ever	18	0.8 (0.4–1.9)		
					<i>Non-gastric</i>				
					Never	20	1.0		
Ever	168	1.7 (1.1–3.2)							
<i>Women</i>									
Never		1.0							
Ever		1.3 (0.8–1.9)							

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Muñoz <i>et al.</i> (2001), Venezuela, 1991–97	292, aged >35 years; histologically confirmed; non-epithelial tumours of the stomach excluded	485 (119 hospital, 366 neighbourhood); 1:2 matched by age (± 5 years), sex	Structured interview		Never/occasional Current Former	89 76 42	<i>Men</i> 1.0 2.9 (1.9–4.3) 3.5 (2.0–6.0)	Age, socioeconomic status	Only 1/143 female controls reported being an ever drinker; analysis of alcoholic beverage consumption therefore confined to men; most common forms of alcohol consumed were beer and aguardiente (sugar cane spirit): 69% of men who were current or former drinkers drank beer, 52% drank aguardiente and 28% drank other alcoholic drinks.

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Wu <i>et al.</i> (2001), Los Angeles, USA, 1992–97	277 cancer of cardia (231 men, 46 women), 443 distal stomach (261 men, 182 women), aged 30–74 years; histologically confirmed; participation rate, 56%	1356 whites, latinos, African-Americans and Asian Americans (999 men, 357 women); matched by sex, race, date of birth, ethnicity; neighbourhood control subject was sought by use of a systematic algorithm based on the address of the case patient; diagnosis of stomach or oesophageal cancer excluded	Interviewer-administered structured questionnaire, completed by 55% of those identified and 77% of those approached		<i>Gastric cardia</i>			Age, sex, smoking, race, birth place, education	Race: whites, African-Americans, latinos and Asian Americans
					Never	48	1.0		
					Former	118	0.91 (0.6–1.4)		
					Current	109	0.98 (0.7–1.5)		
					<i>Distal</i>				
					Never	148	1.0		
					Former	150	0.85 (0.6–1.2)		
					Current	194	0.96 (0.7–1.3)		

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Hamada <i>et al.</i> (2002), Sao Paulo, Brazil, Japanese ancestry, 1991–94	96 (60 men, 36 women) of Japanese ancestry; aged 38–89 years; histologically confirmed; among 87 cases with known location, 80 tumours (92%) were in the lower portion (body or antrum); no patients refused the interview	192 (120 men, 72 women) patients; 80 of 192 patients recruited voluntarily from the Japanese community in Sao Paulo; matched by age (± 5 years), sex	Interviewer-administered standardized questionnaire; 15-mL blood sample		<i>Consumption frequency</i>			Country of birth	Alcohol consumption not associated with risk for stomach cancer	
					<1/month	68	1.0			
					1 day/month–4 days/week	17	1.7 (0.8–3.9)			
					Daily	11	1.8 (0.7–4.7) <i>p</i> = 0.16			
					<i>Lifetime alcohol consumption</i>					
					<1000 g	84	1.0			
1000–2000 g	2	0.5 (0.1–2.7)								
>2000 g	8	2.0 (0.6–2.5) <i>p</i> = 0.38								
Kikuchi <i>et al.</i> (2002), Tokyo, Japan, 1993–95	718 (494 men, 224 women), aged <70 years; histologically confirmed; classified by type (intestinal or diffuse), stage (early or advanced) and subsite of the lesions (proximal, middle or distal)	883 (448 men, 435 women) recruited from several health check programmes in a hospital in the same area between June 1993 and November 1994	Self-administered questionnaire; sera provided		<i>Alcohol–years^a</i>			<i>Men</i>	Age, smoking, <i>Helicobacter pylori</i> status	Alcohol–years (mL intake of pure alcohol per day multiplied by years of drinking); a J- or U-shaped effect on risk for stomach cancer; models designated ‘occasional’ drinker as reference or ‘never’ drinker as reference
					0 (never drinker)	34	1.89 (0.97–3.69)			
					Occasional (1–134.9)	31	1.0			
					135–1349.9	90	2.82 (1.63–4.86)			
					≥ 1350	138	2.84 (1.97–4.83)			
					<i>Women</i>					
					0 (never drinker)	57	1.54 (0.90–2.63)			
					Occasional (0.1–134.9)	29	1.0			
≥ 135.0	15	1.39 (0.66–2.93)								

Table 2.38 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Nishimoto <i>et al.</i> (2002), Sao Paulo, non-Japanese Brazilians, 1991–94	236 (170 men, 66 women) with no Asian background, aged 40–79 years; 78% white; no refusal to be interviewed	236 (170 men, 66 women) hospital-based; matched by age (± 5 years), sex; 86.4% white; refusal rate, 8.4%	Interviewer-administered standardized questionnaire; 15-mL blood sample		<i>Consumption frequency</i>			Race (white or non-white), education, fruit and vegetable intake	Alcohol consumption not associated with risk for stomach cancer; the association did not change when analysis restricted to men.
					<1/month	158	1.0		
					1 day/month–4 days/week	29	0.4 (0.2–0.8)		
					Daily	49	1.1 (0.7–1.9) $p=0.93$		
					<i>Lifetime alcohol consumption</i>				
<1000 g	173	1.0							
1000–2000 g	10	1.9 (0.6–5.9)							
>2000 g	41	1.0 (0.6–1.6) $p=0.88$							
Shen <i>et al.</i> (2004), China, 1997–98	165 (110 men, 55 women), aged 34–81 years; 108 intestinal-type gastric cancer, 57 gastric cardia cancer; identified by endoscopic and pathological diagnosis	295 (190 men, 105 women) healthy cancer-free subjects living in the same community, either siblings of cases or non-blood relatives (spouses and spouses' siblings of same gender as cases), aged 30–78 years	Interviewer-administered structured questionnaire; blood sample		Never	97	1.00	Age, gender	Possible recruitment bias in the selection of controls including cases' siblings
					Current	18	0.18 (0.10–0.35)		
					Past	50	1.80 (1.06–3.08) $p<0.01$		

ACDS, adenocarcinoma of distal stomach; ACOGC, adenocarcinoma of oesophagus and gastric cardia; CI, confidence interval; ICD, International Classification of Diseases Odds ratio when risk of the second category is defined as 1.0

Table 2.39 Case-control studies of stomach cancer and alcoholic beverage consumption in China (published in the Chinese literature)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Hu <i>et al.</i> (1989), Heilungjiang, Harbin, 1985–86	241; age and sex distribution not given; 100% histologically confirmed; response rate not given	Hospital patients from surgery department (non-cancer); matched to cases on age, sex, residence; response rate not given	Interviewer-administered questionnaire	Salty food intake + alcoholic beverage drinking Alcoholic beverage drinking + years of having chronic gastritis	<i>Odds ratios</i> 1.80 5.53	Hardness of food, average vegetable intake, smoking index, salty food intake, years of having chronic gastritis	95% CI not provided [<i>p</i> -value <0.05]
Wu & Yao (1994), Shanshi, 1990	200 incident (178 men, 22 women), aged 30–79 years; 100% histologically confirmed; response rate not given	200 population; matched to cases on residence, sex, race, occupation, age	Interviewer-administered questionnaire	<i>Intake</i> >1 time/week	<i>Odds ratio</i> 2.87	Logistic models	

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Ye <i>et al.</i> (1998), Changle and Fuqing cities of Fujian Province, 1994–95	272 (233 men, 39 women), aged 30–78 years; lived in that area for more than 20 years; histologically or surgically confirmed; response rate not given	1:2 population; matched to cases by age, race, residence; not diagnosed with stomach diseases for past 3 years	Interviewer-administered questionnaire	Hard liquor Liquor Wine Beer	<i>Odds ratios</i> 1.41 (0.63–3.1) 1.12 (0.86–1.47) 1.09 (0.89–1.33) 1.33 (0.93–1.88)		
Qiu <i>et al.</i> (1999), Guangxi, 1992–97	319 hospitalized (226 men, 93 women), aged 18–76 years; 100% histologically confirmed; response rate not given	1:1 population, aged 17–78 years; matched to cases by sex, age, residence; not diagnosed with any malignancy; response rate not given	Interviewer-administered questionnaire	Alcohol drinking	<i>Odds ratio</i> 6.22 (3.08–10.92)	Multivariate logistic regression modeling	

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Sun <i>et al.</i> (1999), Harbin, 1995–96	361 hospitalized (264 men, 97 women); aged 30–74 years; mean age: men (58.3), women (57.4); 100% histologically confirmed; response rate not given	1525 randomly selected healthy population; age similar to cases; mean age: men (48.5); women (48.6)	Interviewer-administered questionnaire	Intake No Yes	1.0 1.82 (1.37–2.41)	Age, sex, education, occupation, smoking	Odds ratio for smoking + drinking white wine + having chronic stomach diseases, 62.55 (18.44–212.18)
Sun <i>et al.</i> (2000), Harbin, 1996–99	201 (146 men, 55 women); mean age, 60.14 years; diagnosed by city hospitals; response rate not given	1818 (1560 men, 558 women) randomly selected from Harbin; mean age, 59.53 years; matched on sex, age; response rate not given	Interviewer-administered questionnaire	Alcohol drinking Smoking and drinking	1.29 (0.89–1.86) 2.34 (1.52–2.60)	Not listed	Categorization of each variable not listed

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Ding <i>et al.</i> (2001a,b) Taixing, Jiungsu, 1998–99	591 oesophageal cancer, 360 liver cancer, 430 stomach cancer (921 men, 460 women), aged 21–89 years; not histologically confirmed; response rate not given	1:1 population; matched on age, sex, residential area; response rate not given	Interviewer-administered questionnaire	Drinking white wine	<i>Odds ratio</i> 2.76	Results from multivariate logistic regression models	95% CIs not provided; categorization of variable not clear
Shen <i>et al.</i> (2001), Yangzhong, Jiangsu, 1997–98	265 with endoscopy and pathology diagnosis (117 from higher incidence area; 148 from lower incidence area); sex and age distribution not described, but percentage of men and mean age significantly higher in cases than in controls	2066 (850 from higher incidence area; 1216 from lower incidence area) selected from the spouse and siblings of cases or the sibling-in-law	Interviewer-administered questionnaire	Men ever drinking alcohol in higher incidence area Men ever drinking alcohol in lower incidence area	<i>Odds ratio</i> 3.6 3.7 (1.3–10.8)	Results from multivariate logistic regression model	CI not clear

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Tong <i>et al.</i> (2001), Tongliao, Inner Mongolia, 1999	76 oesophageal cancer (71 men, 5 women), aged 39–80 years; mean age, 58.5 years; 44 stomach cancer (35 men, 9 women), aged 35–78 years; mean age, 58.6 years; 100% histologically confirmed; response rate not given	1:3 hospital patients, aged 33–82 years; mean age, 58.2 years; matched on age, sex, residence area, time of diagnosis; response rate not given	Interviewer-administered questionnaire	Oesophagus and stomach combined Alcohol drinking (Yes/No)	<i>Odds ratio</i> 4.15 (1.71–15.92)	Results from multiple logistic regression model	

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zheng <i>et al.</i> (2001), Fujian, 2000	251 (93 cardia, 85 non-cardia gastric cancer, 73 non-digestive tract cancer), aged 30–79 years; sex ratio (men/women), 6; lived in Fujian for more than 20 years; answered questions clearly; diagnosis confirmed by pathology, surgery, or endoscopy; response rate, 98.1%	97 hospital patients selected from orthopaedics and urinary departments, aged 30–79 years; lived in Fujian for more than 20 years; answered questions clearly; response rate, 98.1%	Interviewer-administered questionnaire	Hard liquor (Yes/No)	Cardia 3.25 (0.90–8.41) Non-cardia 2.08 (0.88–4.96)		
Chen <i>et al.</i> (2002b), Changle, Fujian, 1999	310, mean age, 60.8 years; sex ratio (male/female), 5; 95% histologically confirmed	1:1 selected from neighbours or colleagues of cases; matched to cases by age	Interviewer-administered questionnaire				No significant association between alcohol drinking and the use of refrigerator and the risk for stomach cancer.

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gao <i>et al.</i> (2002a,b), Huaian, Jiangsu, 1997–2000	153 stomach cancer (118 men, 35 women); mean age, 61.1 years for men, 59.8 years for women; 141 oesophageal cancer (78 men, 63 women); mean age, 60.9 years for men, 60.7 years for women; 100% histologically confirmed; response rate not given	223 randomly selected population (149 men, 74 women); mean age, 58.9 years for men, 57.6 years for women; matched to cases on age; response rate not given	Questionnaire; blood samples	Alcohol drinking (frequently versus not)	1.76 (1.01–3.07)	Sex, age, vegetable intake, fruit intake, pickled vegetables, meat intake, soya product intake	Alcohol drinking increased the risk for stomach cancer among GSTM1 non-null people.

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mu <i>et al.</i> (2003), Taixing, Jiangsu, 2000	206 stomach cancer, 204 liver cancer, 218 oesophageal cancer; sex ratio (male/female), 2 for stomach, 3.5 for liver, 2 for oesophageal cancer; aged >50 years, 88.1% for stomach cancer, 59.8% for liver cancer, 85.8% for oesophageal cancer	415 healthy population from Taixing; selected according to age and sex distributions of three case series; lived in Taixing for more than 10 years; sex ratio (male/female), 2.15; aged ≥ 50 years, 75.8%	Interviewer-administered questionnaire; blood samples	<i>Green tea drinkers</i>		Age, sex, education level	
				Alcohol drinking			
				Not frequent	1.0		
				Frequent	0.44 (0.23–0.86)		
				<i>Green tea non-drinkers</i>			
				Alcohol drinking			
				Not frequent	1.0		
				Frequent	2.32 (1.23–4.38)		

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Fei & Xiao (2004), Shanghai	189 hospitalized, aged 29–91 years; mean age, 63.6 years; sex ratio (male/female), 1.4; 100% histologically confirmed; response rate not given	567 selected from the same hospital (medical check-up patients, non-digestive tract disease, non-cancer patients) as cases or from neighbours of cases; no difference between case and control groups on age, sex, ethnic group, residential area; response rate not given	Interviewer-administered questionnaire	Alcohol drinking (yes vs no)	<i>Odds ratio</i> 2.38 (1.48–3.82)		Univariate logistic regression analysis

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Yang <i>et al.</i> (2004), Jintan, Huaian, Jiangsu, 1998–2003	285 (212 men, 73 women), aged 31–84 years; mean age, 61.4 years; % of histologically confirmed not given; response rate not given	265 (191 men, 74 women) aged 30–87 years; mean age, 61.5 years; selected and matched 1:1 to cases on residency, ethnic group, sex, age; residents with cancer and digestive tract diseases and those who did not answer questions clearly excluded; response rate not given	Questionnaire; blood sample	Alcohol drinking (yes/no)	<i>p</i> -value, 0.84	Crude analysis	

Table 2.39 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Luo (2005), Luoyang, Henan, 2003–2004	153 (117 men, 36 women), aged 38–74 years; lived in Luoyang for at least 15 years	153 healthy selected randomly from Luoyang; matched to cases on age, sex, ethnicity; lived in Luoyang for more than 15 years	Interviewer-administered questionnaire	Alcohol drinking (yes versus no)	2.14 (1.42–3.21)	Not described	Variables not well defined

CI, confidence interval; GSTM1, glutathione *S*-transferase M1

Table 2.40 Selected cohort and case-control studies of cancer in subsites of the stomach and intake of alcoholic beverage

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Cohort studies									
Sasazuki <i>et al.</i> (2002), Japan, Japan Public Health Cohort Study		Cardia and upper third gastric		Distal gastric cancer					
		<i>All histological types</i>		<i>Differentiated type</i>		<i>Undifferentiated type</i>			
	0–3 times/month	3	1.0	32	1.0	17	1.0		
	0–161.0 g/week	8	2.5 (0.7–9.5)	27	0.9 (0.5–1.5)	11	0.7 (0.3–1.4)		
	162.0–322.0 g/week	13	3.3 (0.9–11.6)	38	1.1 (0.7–1.8)	15	0.9 (0.5–1.9)		
≥322.5 g/week	11	3.0 (0.8–11.1)	27	0.9 (0.5–1.5)	20	1.3 (0.7–2.6)			
		<i>p</i> =0.66		<i>p</i> =1.00		<i>p</i> =0.07			
Lindblad <i>et al.</i> (2005), United Kingdom, General Practitioner Research Database (nested case-control study)		<i>Gastric cardia</i>		<i>Non-cardia gastric</i>		<i>Unknown subsite of gastric adenocarcinoma</i>			
		Odds ratio		Odds ratio					
	Units/day								
	0–2	55	1.00	124	1.00	172	1.00		
	3–15	33	1.08 (0.70–1.69)	61	0.99 (0.72–1.36)	72	0.82 (0.61–1.09)		
	16–34	14	1.22 (0.67–2.24)	19	0.91 (0.55–1.51)	25	0.79 (0.51–1.22)		
>34	4	1.04 (0.37–2.93)	2	0.29 (0.07–1.18)	10	0.96 (0.49–1.87)			
Unknown use	89	1.38 (0.84–2.26)	121	0.57 (0.38–0.87)	222	1.20 (0.89–1.62)			

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	
Case-control studies										
Jedrychowski <i>et al.</i> (1993), Poland, 1986-90	Average vodka per occasion	Cardia				Non-cardia				
		<i>Intestinalis</i>		<i>Diffusum</i>		<i>Intestinalis</i>		<i>Diffusum</i>		
	Non-drinker	6	1.0	6	1.0	26	1.0	20	1.0	
	100 g	13	2.12 (0.69-6.50)	5	1.22 (0.28-5.35)	38	2.48 (1.28-4.82)	17	1.10 (0.48-2.50)	
	250 g	36	2.28 (0.83-6.31)	9	1.16 (0.31-4.40)	77	2.06 (1.14-3.71)	57	1.70 (0.87-3.34)	
	>250 g	24	3.04 (1.11-8.28)	8	1.64 (0.46-5.83)	58	2.47 (1.35-4.51)	44	1.81 (0.91-3.58)	
		<i>p</i> =0.03		<i>p</i> =0.47						
Kabat <i>et al.</i> (1993), USA, 1981-90	<i>Men</i>	<i>Distal oesophagus/cardia adenocarcinoma</i>				<i>Distal stomach adenocarcinoma</i>				
		Non-drinker	NR		NR		NR		NR	
		Occasional	2.0 (1.1-3.5)		1.0 (0.6-1.7)					
		1-3.9 oz WE/day	2.1 (1.2-3.6)		0.5 (0.3-0.9)					
		≥4 oz WE/day	2.3 (1.3-4.3)		0.7 (0.4-1.3)					
	<i>Women</i>	NR				NR				
		Non-drinker	1.0		1.0					
		Occasional	0.6 (0.2-1.9)		0.6 (0.3-1.4)					
		1-3.9 oz WE/day	0.9 (0.2-3.5)		0.6 (0.2-1.8)					
		≥4 oz WE/day	3.8 (0.9-16.6)		0.9 (0.3-3.1)					

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Inoue <i>et al.</i> (1994), Nagoya, Japan, 1988–91		<i>Cardia</i>		<i>Middle</i>		<i>Antrum</i>			
	Drinker (versus non-drinker)	NR	1.60 (0.92–2.78)	NR	1.47 (0.94–2.28)	NR	1.00 (0.69–1.46)		
	Current drinker		1.45 (0.82–2.57)		1.38 (0.88–2.16)		0.96 (0.65–1.41)		
	Former drinker		2.81 (1.21–6.54)		2.29 (1.12–4.68)		1.36 (0.69–2.70)		
	<1 year after quitting		3.71 (1.02–13.5)		3.63 (1.23–10.7)		2.16 (0.75–6.25)		
≥1 year after quitting		2.47 (0.93–6.59)		1.78 (0.75–4.23)		1.06 (0.46–2.45)			
Ji <i>et al.</i> (1996), Shanghai, China, 1988–89	Men	<i>Cardia</i>		<i>Distal</i>					
	<i>Ethanol (g/week)</i>								
	<175	8	0.55 (0.25–1.21)	51	1.14 (0.76–1.71)				
	175–349	14	0.75 (0.40–1.43)	54	1.08 (0.73–1.61)				
	350–524	23	1.37 (0.78–2.41)	57	1.07 (0.72–1.58)				
	≥525	16	0.81 (0.44–1.50)	80	1.36 (0.93–1.97)				
			<i>p</i> =0.93		<i>p</i> =0.17				
Non-drinker	80	1.0	272	1.0					
Former drinker	6	1.03 (0.40–2.67)	43	2.16 (1.27–3.69)					
Current drinker	57	0.86 (0.58–1.28)	218	1.11 (0.87–1.38)					

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Ji <i>et al.</i> (1996), (contd)	<i>Duration (years)</i>								
	<15	10	0.52 (0.26–1.06)	54	0.92 (0.63–1.34)				
	15–<24	27	1.19 (0.72–1.98)	89	1.23 (0.88–1.72)				
	≥35	26	0.88 (0.52–1.48)	115	1.40 (1.01–1.94)				
			<i>p</i> =0.88		<i>p</i> =0.03				
	<i>Lifetime ethanol (g/week × years)</i>								
	<2450	6	0.37 (0.15–0.88)	37	0.83 (0.54–1.28)				
	2450–7462	20	1.27 (0.71–2.26)	71	1.45 (1.00–2.11)				
	7463–15 399	18	1.01 (0.55–1.83)	46	0.83 (0.55–1.26)				
	≥15 400	17	0.84 (0.45–1.56)	88	1.55 (1.07–2.26)				
		<i>p</i> =0.91		<i>p</i> =0.06					
Zhang <i>et al.</i> (1996), USA, 1992–94	<i>Oesophagus and gastric cardia adenocarcinoma</i>								
	No	14	1.00	20	1.00	<i>Distal stomach adenocarcinoma</i>			
	≤1/week	26	3.02 (1.14–8.02)	20	1.60 (0.65–3.93)				
	>1/week	55	2.02 (0.85–4.82)	27	0.98 (0.43–2.27)				
		<i>p</i> =0.19		<i>p</i> =0.93					

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Gammon <i>et al.</i> (1997), USA, 1993–95	<i>Any</i>	<i>Gastric cardia adenocarcinoma</i>		<i>Other gastric adenocarcinoma</i>					
	Never	63	1.0	125	1.0				
	Ever	196	0.7 (0.5–1.1)	238	0.8 (0.6–1.1)				
	<5 drinks/week	46	0.6 (0.4–1.0)	74	0.7 (0.5–1.1)				
	5–11 drinks/week	59	0.8 (0.5–1.3)	68	0.9 (0.6–1.3)				
	12–30 drinks/week	52	0.7 (0.4–1.1)	55	0.7 (0.4–1.0)				
>30 drinks/week	39	0.7 (0.4–1.2)	41	0.6 (0.4–1.0)					
DeStefani <i>et al.</i> (1998a), Montevideo, Uruguay, 1992–96	<i>Total</i>	<i>Cardia</i>		<i>Fundus</i>		<i>Antrum</i>			
	1–60 g	8	1.0	7	1.0	49	1.0		
	61–120 g	6	0.6 (0.2–1.9)	7	1.1 (0.4–3.2)	78	1.5 (1.0–2.3)		
>120 g	10	1.0 (0.4–2.7)	11	1.8 (0.6–5.1)	113	2.6 (1.7–3.9)			
			<i>p</i> =0.93		<i>p</i> =0.25		<i>p</i> <0.001		
Ye <i>et al.</i> (1999), Sweden, 1989–95	<i>Total (mL 100% alcohol/month)</i>	Cardia cancer <i>All histological types</i>		Distal stomach cancer <i>Intestinal type</i>		<i>Diffuse type</i>			
	Non-drinker	18	1.0	52	1.0	36	1.0		
	1–35	20	0.9 (0.4–1.9)	64	1.2 (0.8–1.9)	50	1.3 (0.8–2.1)		
	36–160	27	0.8 (0.4–1.7)	73	1.2 (0.8–1.9)	42	1.0 (0.6–1.7)		
	>160	22	0.7 (0.3–1.5)	66	1.2 (0.7–1.9)	34	1.0 (0.5–1.8)		
			<i>p</i> =0.30		<i>p</i> =0.56		<i>p</i> =0.73		

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Lagergren <i>et al.</i> (2000), Sweden	Any	<i>Gastric cardia adenocarcinoma</i>							
	Never	34	1.0						
	Ever	228	0.8 (0.5–1.2)						
	<i>Ethanol (g)/week</i>								
	1–15	73	0.9 (0.5–1.5)						
	16–70	79	0.6 (0.4–1.1)						
	>70	76	0.9 (0.5–1.5)						
Zaridze <i>et al.</i> (2000), Moscow, Russia, 1996–97	<i>Vodka (L/year)</i>	<i>Cardia (men)</i>		<i>Other subsites (men)</i>					
	Never	4	1.0	24	1.0				
	Low <2.6	16	2.8 (0.9–9.2)	62	2.0 (1.0–3.8)				
	Medium 2.6–10.4	19	3.6 (1.1–11.8)	62	2.2 (1.1–4.1)				
	High >10.4	21	3.9 (1.2–12.3) <i>p</i> =0.03	40	1.3 (0.7–2.5) <i>p</i> =0.77				
Wu <i>et al.</i> (2001), Los Angeles, USA, 1992–97		<i>Gastric cardia adenocarcinoma</i>		<i>Distal gastric adenocarcinoma</i>					
	1–7 drinks/week	1.00 (0.7–1.5)		0.83 (0.6–1.2)					
	8–21 drinks/week	0.70 (0.4–1.1)		0.68 (0.5–1.0)					
	22–35 drinks/week	1.09 (0.7–1.8)		1.10 (0.7–1.7)					
	≥36 drinks/week	1.35 (0.8–2.3)		1.35 (0.8–2.2)					
		<i>p</i> =0.42		<i>p</i> =0.29					

Table 2.40 (continued)

Reference, study location, period	Alcoholic beverage consumption	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Kikuchi <i>et al.</i> (2002), Tokyo, Japan, 1993–95	Men	NR	Proximal	Distal	0	2.72 (1.13–6.53)	1.28 (0.60–2.76)		
					0.1–134.9	1.0	1.0		
					135–1349.9	2.24 (1.01–4.96)	1.85 (1.00–3.41)		
					≥1350	2.46 (1.17–5.17) <i>p</i> =0.06	1.56 (0.86–2.84) <i>p</i> =0.25		
	Women	NR	Proximal	Distal	0 (never drinker)	1.50 (0.70–3.21)	1.69 (0.85–3.35)		
					0.1–134.9	1.0	1.0		
					135–1349.9	0.43 (0.10–2.05)	1.78 (0.67–4.71)		
					≥1350	0.43 (0.10–2.05) <i>p</i> =0.21	1.78 (0.67–4.71) <i>p</i> =0.28		

CI, confidence interval; NR, not reported

cancer. In two studies of histological types, the intestinal type seemed to be more strongly associated with alcoholic beverage consumption (Jedrychowski *et al.*, 1993).

(a) *Gastric cardia cancer*

Prospective cohort studies have reported an association between alcoholic beverage consumption and the risk for adenocarcinoma of the gastric cardia and distal stomach (Sasazuki *et al.*, 2002; Lindblad *et al.*, 2005; Tran *et al.*, 2005). Sasazuki *et al.* (2002) reported an elevated risk for cardia cancer of all histological types with alcoholic beverage consumption, although the relationship failed to reach significance. Tran *et al.* (2005) reported inverse associations for cardia and non-cardia cancer with alcoholic beverage consumption. The relative risks were 0.84 (95% CI, 0.72–0.97) for cardia cancer and 0.79 (95% CI, 0.61–1.02) for non-cardia cancer.

Among 12 case–control studies that reported an association between alcoholic beverage consumption and cardia cancer, five studies reported a statistically significant association (Jedrychowski *et al.*, 1993; Kabat *et al.*, 1993; Inoue *et al.*, 1994; Zaridze *et al.*, 2000; Kikuchi *et al.*, 2002). The adjusted odds ratios were between 2.3 and 3.9 for heavy drinkers and a strong dose–response relationship was demonstrated in four of the five studies.

Zaridze *et al.* (2000) reported that the effect of hard liquor (vodka) consumption was stronger for cancer of the cardia in men. Compared with non-drinkers, the adjusted odds ratios in men were 2.8 (95% CI, 0.9–9.2) for light drinkers, 3.6 (95% CI, 1.1–11.8) for medium drinkers and 3.9 (95% CI, 1.2–10.2) for heavy drinkers.

An elevated risk for cardia cancer was observed among heavy drinkers in two case–control studies, but the results were not statistically significant (Zhang *et al.*, 1996; Wu *et al.*, 2001). Five studies observed no association between alcoholic beverage consumption and cardia cancer (Ji *et al.*, 1996; Gammon *et al.*, 1997; De Stefani *et al.*, 1998a; Ye *et al.*, 1999; Lagergren *et al.*, 2000). In a population-based case–control study of 90 cases of gastric cardia cancer, 260 and 164 cases of intestinal and diffuse types of distal gastric cancer, respectively, results from Ye *et al.*, (1999) showed that intake of alcoholic beverages was not associated with an increased risk for any type of cardia or gastric cancer. In a case–control study in Shanghai, China, Ji *et al.* (1996) examined the role of alcoholic beverage drinking as a risk factor for carcinoma by anatomic subsite of the stomach. Alcoholic beverage consumption was associated with a moderately excess risk for distal stomach cancer (odds ratio, 1.55; 95% CI, 1.07–2.26), but was not related to the risk for cardia cancer.

(b) *Distal stomach cancer*

Among 11 studies of distal stomach cancer, six observed a positive association (Jedrychowski *et al.*, 1993; Inoue *et al.*, 1994; Ji *et al.*, 1996; De Stefani *et al.*, 1998a; Zaridze *et al.*, 2000; Kikuchi *et al.*, 2002). The relationship was not as strong as that for cardia cancer, but the dose–response relationship was just as clear.

2.7.4 *Type of alcoholic beverage (Table 2.41)*

Some investigators considered the role of different types of alcoholic beverage and reported that the consumption of beer, spirits or wine did not affect the incidence of stomach cancer (Hansson *et al.*, 1994; Zhang *et al.*, 1996; Ye *et al.*, 1999; Wu *et al.*, 2001). In northern Italy, where wine was the most frequently consumed alcoholic beverage and accounted for approximately 90% of all alcoholic beverage consumption in the population, D'Avanzo *et al.* (1994) reported that the risk estimates adjusted for age and sex were 1.1 for light-to-moderate wine drinkers, 1.3 for intermediate drinkers, 1.6 for heavy drinkers and 1.4 for very heavy drinkers (≥ 8 drinks per day). López-Carrillo *et al.* (1998) reported an assessment of alcoholic beverage consumption in Mexico, including the popular Mexican liquor tequila, in relation to the incidence of stomach cancer. After adjustment for known risk factors, wine consumption was positively associated with the risk for developing stomach cancer (odds ratio, 2.93; 95% CI, 1.27–6.75) in the highest category of wine consumption, which corresponded to at least 10 glasses of wine per month, with a significant trend ($P=0.005$).

In a multicentric hospital-based case–control study carried out in Poland, the relative risk for stomach cancer increased as the frequency and amount of vodka drunk increased. People who drank vodka at least once a week had an threefold higher risk compared with non-drinkers (relative risk, 3.06; 95% CI, 1.90–4.95) (Jedrychowski *et al.*, 1993). Alcoholic beverage consumption, particularly that of vodka, was found to increase the risk for gastric cancer in a Russian study (Zaridze *et al.*, 2000). A case–control study that included 331 cases and 622 controls conducted in Montevideo, Uruguay, found that alcoholic beverage consumption (particularly that of hard liquor and beer) was associated with an odds ratio of 2.4 (95% CI, 1.5–3.9), after controlling for the effect of tobacco, vegetables and other types of beverage (De Stefani *et al.*, 1998a). In another multicentric, hospital-based case–control study conducted in Germany, increased consumption of beer showed a positive association with risk whereas increased consumption of wine and liquor showed a significantly negative association (Boeing *et al.*, 1991).

2.7.5 *Effect modification (Table 2.42)*

Several studies reported on the joint effects of alcoholic beverage consumption and tobacco smoking (Kabat *et al.*, 1993; Hansson *et al.*, 1994; Inoue *et al.*, 1994; Ji *et al.*, 1996; De Stefani *et al.*, 1998a; Zaridze *et al.*, 2000). The results of a case–control study in Nagoya, Japan, showed that the joint effect of drinking and smoking may play an important role in the development of stomach cancer, especially that of cardia cancer (odds ratio, 4.7; 95% CI, 1.1–20.2) (Inoue *et al.*, 1994). However, most studies did not evaluate potential effect modification between alcoholic beverage consumption and tobacco smoking.

Table 2.41 Selected cohort and case-control studies of stomach cancer and different types of alcoholic beverage

Reference, location, period	Cohort/cases and controls	Beer			Wine			Hard liquor		
		Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)
Cohort study										
Nomura <i>et al.</i> (1990), USA, Hawaii, American Men of Japanese Ancestry Study	7990 American men of Japanese ancestry, born 1990–19, residing on the Hawaiian island of Oahu; follow-up, 19 years	Non-drinker	64	1.0	Non-drinker	124	1.0	Non-drinker	86	1.0
		<10 oz/month	10	0.7 (0.4–1.4)	1 oz/month	13	1.1 (0.6–1.9)	<5 oz/month	29	0.9 (0.6–1.4)
		10–99 oz/month	17	1.2 (0.7–2.1)	≥2 oz/month	11	0.7 (0.4–1.3)	5–49 oz/month	26	1.5 (1.0–2.2)
		100–499 oz/month	28	1.1 (0.7–1.8)				≥50 oz/month	8	1.0 (0.5–2.1)
		≥500 oz/month	28	1.1 (0.7–1.7)						
Case-control studies										
D'Avanzo <i>et al.</i> (1994), Milan, Italy, 1985–93	746 cases of histologically confirmed stomach cancer; 2053 hospital controls	Non-drinker	672	1.0	Non-drinker	197	1.0	Non-drinker	650	1.0
		<1 drink/day	35	0.9 (0.6–1.4)	<2 drinks/day	108	1.1 (0.8–1.4)	<1 drink/day	45	0.7 (0.5–0.9)
		1–2 drinks/day	15	1.6 (0.9–3.1)	2–<4 drinks/day	201	1.1 (0.9–1.4)	1–<2 drinks/day	31	1.0 (0.7–1.6)
		≥2 drinks/day	24	1.1 (0.7–1.9)	4–6 drinks/day	121	1.3 (1.0–1.7)	≥2 drinks/day	20	0.9 (0.5–1.5)
					6–<8 drinks/day	56	1.6 (1.1–2.4)			
					≥8 drinks/day	63	1.4 (1.0–2.0)			

Table 2.41 (continued)

Reference, location, period	Cohort/cases and controls	Beer			Wine			Hard liquor		
		Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)
Hansson <i>et al.</i> (1994), Sweden, 1989–92	338 histologically confirmed cases of gastric cancer; 679 controls	Non-drinker	278	1.0	Non-drinker	154	1.0	Non-drinker	123	1.0
		Drinkers	60	0.95 (0.68–1.37)	1–59 mL/month	86	1.35 (0.97–1.88)	1–79 mL/month	98	1.23 (0.87–1.76)
					60–199 mL/month	31	0.70 (0.44–1.13)	80–319 mL/month	57	0.91 (0.61–1.38)
					200–599 mL/month	51	0.21 (0.80–1.83)	≥320 mL/month	60	1.27 (0.83–1.96)
					≥600 mL/month	16	0.57 (0.31–1.04)			<i>p</i> =0.61
Zhang <i>et al.</i> (1996), USA, 1992–94	95 adenocarcinomas of oesophagus and gastric cardia, 67 adenocarcinomas of the distal stomach; 132 cancer-free controls	No	20	1.00	No	20	1.00	No	20	1.00
		≤1/week	17	1.13 (0.46–2.76)	≤1/week	21	1.21 (0.51–2.83)	≤1/week	19	1.91 (0.76–4.79)
		>1/week	11	1.43 (0.45–4.58)	>1/week	12	0.97 (0.36–2.58)	>1/week	12	0.66 (0.22–1.99)
				<i>p</i> =0.55			<i>p</i> =0.99			<i>p</i> =0.73
Gammon <i>et al.</i> (1997), USA, 1993–95	368 gastric adenocarcinoma and 695 other gastric	Never	200	1.0	Never	258	1.0	Never	188	1.0
		Ever	166	0.8 (0.6–1.1)	Ever	108	0.7 (0.5–0.9)	Ever	177	1.0 (0.8–1.4)

Table 2.41 (continued)

Reference, location, period	Cohort/cases and controls	Beer			Wine			Hard liquor				
		Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)		
DeStefani <i>et al.</i> (1998a), Montevideo, Uruguay, 1992–96	331 cases; 622 controls (men only)	Non-drinker	265	1.0	Non-drinker	97	1.0	Non-drinker	166	1.0		
		1–60 g/day	18	1.1 (0.6–2.1)	1–60 g/day	106	1.1 (0.7–1.5)	1–60 g/day	62	1.0 (0.7–1.5)		
		61–120 g/day	20	1.9 (0.9–3.7)	61–120 g/day	72	1.4 (0.9–2.2)	61–120 g/day	30	1.7 (0.9–2.9)		
		>120 g/day	0	–	>120 g/day	36	0.9 (0.4–1.8)	>120 g/day	53	2.1 (1.1–3.9)		
						<i>p</i> =0.06				<i>p</i> =0.47		<i>p</i> =0.01
López-Carrillo <i>et al.</i> (1998), Mexico	220 newly diagnosed adenocarcinoma of the stomach; 757 population-based controls	Non-beer consumer	105	1.0	Non-wine consumer	133	1.0	Non-liquor consumer	114	1.0		
		<1 drink/day	60	1.06 (0.64–1.73)	<1 drink	54	2.08 (1.26–3.44)	<1 drink/day	17	0.78 (0.38–1.61)		
		≥1 drink/day	54	1.04 (0.55–1.94)	≥1 drink	32	2.93 (1.27–6.75)	≥1 drink/day	89	1.83 (1.07–3.10)		
						<i>p</i> =0.005			<i>p</i> =0.175			
				<i>p</i> =0.115								
Ye <i>et al.</i> (1999), Sweden, 1989–95	90 gastric cardia, 260 and 164 distal gastric cancer of intestinal and diffuse types; 1164 frequency-matched controls	Light beer	118	1.0	Non-drinker	65	1.0	Non-drinker	58	1.0		
		<400 mL/month	24	0.9 (0.5–1.4)	1–59 mL/month	43	1.6 (1.0–2.6)	1–79 mL/month	41	0.9 (0.5–1.5)		
		400–2399 mL/month	24	0.9 (0.5–1.4)	60–199 mL/month	15	0.6 (0.3–1.2)	80–319 mL/month	32	0.8 (0.5–1.5)		
		≥2400 mL/month	22	0.9 (0.5–1.5)	200–599 mL/month	25	1.3 (0.7–2.4)	≥320 mL/month	32	1.4 (0.7–2.8)		
					<i>p</i> =0.60	≥600 mL/month	15	1.1 (0.6–2.3)			<i>p</i> =0.42	
						<i>p</i> =0.90						

Table 2.41 (continued)

Reference, location, period	Cohort/cases and controls	Beer			Wine			Hard liquor		
		Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)	Exposure	Cases	Relative risk (95% CI)
Wu <i>et al.</i> (2001), Los Angeles; USA, 1992–97	277 cardia, 443 non-cardia; 1356 controls	None		1.0	None		1.0	None		1.0
		<7 drinks/week		0.90 (0.7–1.3)	<7 drinks/week		0.90 (0.7–1.2)	<7 drinks/week		0.63 (0.5–0.9)
		7–14 drinks/week		1.01 (0.7–1.6)	7–14 drinks/week		0.77 (0.5–1.3)	7–14 drinks/week		0.61 (0.4–1.0)
		≥15 drinks/week		1.67 (1.1–2.6)	≥15 drinks/week		0.44 (0.2–1.2)	≥15 drinks/week		0.70 (0.4–1.1)
				<i>p</i> =0.09			<i>p</i> =0.04			<i>p</i> =0.02

CI, confidence interval

Table 2.42 Cohort and case-control studies of stomach cancer and alcoholic beverage consumption in men and women

Study reference	Description	Drinking level	Men		Women	
			No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Cohort study						
Kato <i>et al.</i> (1992a), Japan	9753	None	8	1.00	18	1.00
	Japanese men and women; age: men, ≥ 40 years; women, ≥ 30 years; response rate, 85.9%; follow-up 1986–91	Occasional	9	2.31 (0.88–6.07)	3	1.12 (0.32–3.90)
		Daily <50mL	6	1.31 (0.45–3.81)	1	1.29 (0.17–9.69)
		Daily ≥50 mL	12	3.63 (1.44–9.11)		
Case-control studies						
Kabat <i>et al.</i> (1993), USA, 1981–90	152 (122 men, 31 women) cases; 4162 men, 2222 women controls; matched by age, sex, race, hospital	Non-drinker		1.0		1.0
		Occasional		1.0 (0.6–1.7)		0.6 (0.3–1.4)
		1–3.9 oz/day		0.5 (0.3–0.9)		0.6 (0.2–1.8)
		≥4 oz/day		0.7 (0.4–1.3)		0.9 (0.3–3.1)

Table 2.42 (continued)

Study reference	Description	Drinking level	Men		Women	
			No. of cases	Relative risk (95% CI)	No. of cases	Relative risk (95% CI)
Zaridze <i>et al.</i> (2000), Moscow, Russia, 1996–97	489 (248 men, 200 women), histologically confirmed; 610 (292 men, 318 women) hospital-based controls	<i>Vodka (L/year)</i>				
		Never	28	1.0	95	1.0
		Low <2.6	78	2.0 (1.1–3.7)	62	1.5 (1.0–2.4)
		Medium 2.6–10.4	81	2.3 (1.3–4.2)		
		High >10.4	61	1.7 (0.9–3.1) <i>p</i> =0.20	45	1.3 (0.8–2.2) <i>p</i> =0.17

CI, confidence interval

When stratified by gender, the results for men were statistically significant while those for women showed similar point estimates but insignificant trends. Kato *et al.* (1992a) examined the risk for men and women separately in a clinical epidemiological study and observed an increased risk for stomach cancer in daily consumers of alcoholic beverages compared with non-drinkers, but this association was not statistically significant. In a case–control study conducted in Japan, light drinkers showed the lowest risk among both men and women, and heavy drinkers showed the highest risk among men. In other words, the association was J-shaped among men and U-shaped among women (Kikuchi *et al.*, 2002).

2.8 Cancers of the colon and/or rectum

Most of the studies of alcoholic beverage consumption and colorectal cancer included in the previous Monograph (IARC, 1988) were based on information about heavy alcoholic beverage drinkers or alcoholics and persons employed in the brewery industry, or were case–control studies; only five cohort studies were reviewed. Since that time, several additional cohort studies, case–control studies, as well as meta-analyses and a pooling project, representing research from Asia, Australia, Europe, North and South America, have been published. In total, these provide important information on associations of alcoholic beverage consumption and the risk for colorectal cancer overall, risk for specific anatomical sites within the large bowel and relationships with specific alcoholic beverages. In addition, several studies carefully considered potential confounding factors such as sex, age, level of obesity and smoking status, and others also included diet and physical activity. Finally, this large body of evidence allows for international comparisons of the strength and consistency of associations between alcoholic beverage intake and risk for colorectal cancer.

2.8.1 Cohort studies

(a) Special populations (Table 2.43)

Nine studies examined the risk for colon cancer and eight studies examined the risk for rectal cancer among heavy alcoholic beverage drinkers, alcoholics or brewery workers (Sundby, 1967; Hakulinen *et al.*, 1974; Monson & Lyon, 1975; Adelstein & White, 1976; Dean *et al.*, 1979; Jensen, 1979; Robinette *et al.*, 1979; Schmidt & Popham, 1981; Carstensen *et al.*, 1990).

Among the nine studies on colon cancer, the number of observed deaths or incident cases ranged from three to 82. Six studies showed no evidence of an association. In two studies, there were non-statistically significant elevated risks (relative risk, 1.2–1.3) among brewery workers (Dean *et al.*, 1979, Carstensen *et al.*, 1990).

Among the eight studies of rectal cancer, the number of observed deaths or incident cases ranged from none to 85. While five reported no excess risk for rectal cancer, two

Table 2.43 Cohort studies of colon and rectal cancers and alcoholic beverage consumption in special populations

Reference, location	Study subjects	Organ site (ICD code)	No. of cases	No. of deaths expected	Relative risk (95% CI)	Adjustment factors	Comments
Sundby (1967), Norway	Alcoholics from Oslo psychiatric departments, 1722 men, 1925–62; aged 15–70 years	Colon Rectum	9 12	9.4 6.4			Local reference
Hakulinen <i>et al.</i> (1974), Helsinki, Finland	Approximately 205 000 male alcohol misusers and mean of 4370 male chronic alcoholics aged >30 years, registered as chronic alcoholics between 1967 and 1970, morbidity during same period determined from Finnish Cancer Registry	Colon	<i>Misusers</i> 82 <i>Alcoholics</i> 3	86.6 ($p>0.1$) 1.63 ($p>0.5$)		Age	Local reference
Monson & Lyon (1975), Massachusetts, USA	1139 men and 243 women admitted in 1930, 1935 or 1940 to a mental hospital with a diagnosis of chronic alcoholism; followed until January 1971; 66% had complete follow-up.	Colon (ICD 153) Rectum (ICD 154)	7 4	11.2 5.7	<i>PCMR</i> 0.6 (0.3–1.3) 0.7 (0.2–1.8)	Age	Compared with US population; proportion
Adelstein & White (1976), England and Wales	1595 male and 475 female alcoholics followed up to 21 years; two sources: Mental Health Enquiry admission form; patient records from patients diagnosed with alcoholism; 15–90 years old	Intestine (ICD 152, 153) Rectum (ICD 154)	6 men 3 women 4 men 0 woman	4.92 1.90 3.32 0.92	NC/NG NC/NG	Age	Reference death rates are the sex-specific rates of England and Wales for 1972.

Table 2.43 (continued)

Reference, location	Study subjects	Organ site (ICD code)	No. of cases	No. of deaths expected	Relative risk (95% CI)	Adjustment factors	Comments
Dean <i>et al.</i> , (1979), Dublin, Ireland	Deaths between 1954 and 1973 among male blue-collar brewery workers	Colon (ICD 153)	32	24.1	1.3 (0.9–1.9)	Age	Compared with Dublin skilled and unskilled manual workers
		Rectum (ICD 154)	32	19.7	1.6 (1.1–2.3)		
Jensen (1979), Denmark	14 313 Danish brewery workers employed at least 6 months in 1939–63; followed for cancer incidence and mortality in 1943–73; age not given; workers are allowed 2.1 L of free beer/day (77.7 g pure alcohol).	Colon	<i>Incidence</i>		1.0 (0.8–1.4) 1.0 (0.8–1.3)	Age, sex	Local male population
			50	48			
		Rectum	<i>Mortality</i>		1.1 (0.8–1.4) 1.1 (0.9–1.5)		
			63	58			
Robinette <i>et al.</i> (1979), USA	4401 chronic alcoholic male veterans, hospitalized in 1944–45 and followed in 1946–74 for mortality; 29 years follow-up, age not given	Large intestine (ICD 153)	7	NC/NG	0.8 (0.3–1.9)	Age	Compared with age-matched male veterans hospitalized for nasopharyngitis
		Rectum (ICD 154)	6	NC/NG	3.3 (0.7–22.4)		
Schmidt & Popham (1981), Ontario, Canada	9889 alcoholic men aged ≥15 years admitted to the clinical service of the Addiction Research Foundation of Ontario between 1951 and 1970; maximum 21 years of follow-up	Large intestine (ICD 153)	19	18.2	1.0 ^a	Age	Local reference population; CI not reported
		Rectum (ICD 154)	10	9.9	1.0 ^a		

Table 2.43 (continued)

Reference, location	Study subjects	Organ site (ICD code)	No. of cases	No. of deaths expected	Relative risk (95% CI)	Adjustment factors	Comments
Carstensen <i>et al.</i> (1990), Sweden	6230 men occupied in the Swedish brewery industry at the time of the 1960 census and followed between 1961 and 1979; 20–69 years of age	Colon (ICD 153)	48	41	1.2 (0.9–1.5)	Age	Local male population
		Rectum (ICD 154)	49	29	1.7 (1.3–2.2) <i>p</i> <0.001		

CI, confidence interval; ICD, International Classification of Diseases; NC/NG, not calculated/not given; PCMR, proportionate cancer mortality ratio

^a Confidence interval not given

found statistically significant 1.6–1.7-fold higher risks for men who had been employed in the brewery industry (Dean *et al.*, 1979; Carstensen *et al.*, 1990). Another study, based on six deaths, reported a non-significant 3.4-fold higher risk for rectal cancer mortality for chronic alcoholic male US veterans compared with US veterans hospitalized for nasopharyngitis (Robinette *et al.*, 1979).

(b) *General population (Table 2.44)*

Seven studies provided results for colon and rectum combined, and four of these observed no association of alcoholic beverage consumption with mortality from (Garland *et al.*, 1985; Kono *et al.*, 1986) or incidence of (Flood *et al.*, 2002; Sanjoaquin *et al.*, 2004) colorectal cancer. Based on data from the large US Cancer Prevention Study, Thun *et al.* (1997) reported a non-significant ($P=0.06$) inverse trend for the relationship between alcoholic beverage intake and the risk for mortality from colorectal cancer in women and no association in men. In a study of residents of a US retirement community, Wu *et al.* (1987) found a significant 2.4-fold higher risk for colorectal cancer among men, but not among women, who consumed 30 mL alcohol per day. Similarly, in a study of Seventh Day Adventists, the relative risk for colorectal cancer was 2.0 (95% CI, 1.0–4.2) for those who consumed alcoholic beverages at least once a week compared with those who drank alcoholic beverages less than once a week (Singh & Fraser, 1998).

At least 16 prospective cohort studies reported on the relationship between alcoholic beverage intake and the risk for colon cancer in China, Japan, northern Europe, the United Kingdom and the USA. Six studies reported no association (Gordon & Kannel, 1984; Goldbohm *et al.*, 1994; Harnack *et al.*, 2002; Pedersen *et al.*, 2003; Wei *et al.*, 2004; Chen *et al.*, 2005a). In the study of Klatsky *et al.* (1988), a significant association was observed in women but not in men. Of the nine studies that reported statistically significant positive associations between alcoholic beverage intake and risk for colon cancer, six were conducted in Japanese populations or in American men of Japanese descent (Hirayama, 1989; Chyou *et al.*, 1996; Murata *et al.*, 1996; Otani *et al.*, 2003; Shimizu *et al.*, 2003; Wakai *et al.*, 2005). In these studies, the magnitude of association ranged from 1.4 to 5.4 for the highest compared with the lowest (i.e. none) level of alcoholic beverage intake. In studies in the USA (Su & Arab, 2004; Wei *et al.*, 2004), the magnitude of risk was 1.6–1.7 for intake of approximately 1–2 drinks per day compared with non-drinkers. In the Finnish study of smokers, there was a 3.6-fold higher risk for colon cancer among those who consumed at least two drinks per day compared with those who consumed less than 0.5 drinks per day (Glynn *et al.*, 1996). None of the prospective cohort studies reported significantly lower risks for colon cancer associated with alcoholic beverage intake. Most studies adjusted for the potential confounding effects of age, body-mass index, smoking status and socioeconomic status or education; some also adjusted for physical activity and/or specific dietary factors (as described in detail below).

Table 2.44 Cohort studies of colon and rectal cancer and alcoholic beverage consumption

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Gordon & Kannel (1984), Framingham, MA, USA, Framingham Study	4747 men and women, aged 29–62 years at initial examination in 1948, and queried on alcoholic beverage intake biannually beginning in 1950–54; followed for 22 years for mortality	Interview by physician for average number of drinks per 30-day period	Colon	~10 oz ethanol/month	17 men 19 women	1.22 0.80	Adjusted for age, cigarettes/day, systolic blood pressure, relative weight, lipoproteins; no significant relationship between alcohol consumption and colon cancer
Garland <i>et al.</i> (1985), Chicago, IL, USA, Western Electric Cohort Study	1954 men, aged 40–55 years employed for at least 2 years at the Western Electric Company; no personal history of cancer; queried on total diet at baseline and at 1 year; followed for 19 years for mortality; cause of death from death certificates; vital status known for 99.9%	In-person 28-day diet history interviews by trained nutritionists	Colorectal	Ethanol (mL/day)	49		Compared alcoholic beverage intake reported at initial examination; no difference in mean alcoholic beverage intake between men who died of colorectal cancer and all others (alive and dead); no information regarding the exposure or relative risks given
Kono <i>et al.</i> (1986), Japan, Japanese Physicians Cohort Study	5135 male Japanese doctors surveyed on smoking and drinking habits in 1965; followed 19 years through to 1983 for mortality; cause of death determined from death certificate; vital status known for 99%; ages not given	Self-administered standardized questionnaire to assess current daily alcoholic beverage intake	Colorectal (ICD-8 153–154)	Non-drinker Former drinker Occasional drinker <2 go/day ≥2 go/day	8 4 12 8 7	1.0 1.2 (0.4–4.0) 1.3 (0.5–3.2) 1.1 (0.4–3.0) 1.4 (0.5–4.0)	Adjusted for age, smoking habits; 1 go of sake ≈ 27 mL alcohol

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments			
Wu <i>et al.</i> (1987), Los Angeles, CA, USA	11 644 (4163 men, 7456 women) residents of a retirement community with no personal history of colorectal cancer, surveyed in 1981–82; vital status or cancer incidence determined by biennial questionnaire, hospital pathology reports, health department; vital status known for 95%; age not given	Mailed, self-administered standardized questionnaire to assess average weekly alcohol intake	Colorectal	Non-daily	58 men	1.0	Adjusted for age; results similar for men after adjustment for physical activity, body mass index, smoking; for men, results similar for right and left colon, but with lower statistical significance for left colon; for women, an association was apparent (not significant) for the left colon.			
				1–30 mL ethanol/day		2.2 (1.1–4.4)				
				≥30 mL ethanol/day		2.4 (1.3–4.5)				
				Non-daily	68 women	1.0				
				1–30 mL ethanol/day		1.1 (0.6–2.1)				
				≥30 mL ethanol/day		1.4 (0.8–2.6)				
Klatsky <i>et al.</i> (1988), Oakland, CA, Kaiser-Permanente Multiphasic Health Examination Cohort	106 203 white and black men and women who underwent multiphasic examination in 1978–84; followed for cancer incidence until 1984; age not given; vital status not given	Standardized questionnaire to assess usual daily intake over the previous year	Colon (ICD-8153)	Never drinker	30	1.0	Adjusted for sex, age, race, body mass index, coffee use, total serum cholesterol, education, smoking; associations stronger after excluding cases diagnosed within 6 months after examination; associations for colon cancer showed a significant association in women but not men; no differences in associations by beverage type			
				Former drinker	6	0.8 (0.3–2.1)				
				<1 drink/day	98	1.2 (0.7–1.8)				
								1–2 drinks/day	49	1.6 (0.9–2.6)
								≥3 drinks/day	20	1.7 (0.9–3.2)
										<i>p</i> -trend=0.11
						Rectum (ICD-8154)		Never drinker	6	1.0
			Former drinker	4	2.2 (0.6–8.2)					
			<1 drink/day	29	1.4 (0.6–3.6)					
			1–2 drinks/day	17	2.3 (0.8–6.3)					
				≥3 drinks/day	10	3.2 (1.1–9.6)				
						<i>p</i> -trend=0.03				

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments	
Hirayama (1989), Japan, Six Prefecture Study	122 261 male and 142 857 female Japanese adults, aged 40 years and older surveyed in 1965; followed for 17 years; all residents from 6 prefectures	Interviewer-administered standardized questionnaire to assess usual alcoholic beverage intake	Sigmoid colon	Non-drinker	43 men	1.0	Adjusted for age; smoking, diet, sex; highest risk observed for daily beer drinkers, although sake and shochu also associated with a significantly increased risk for sigmoid colon cancer; information regarding women's consumption of alcohol was limited.	
				Infrequent (1–2 times/month)	48 women	2.03		
				Occasional (1–2 times/week)		3.83 ($p<0.05$)		
				Daily		5.42 ($p<0.01$)		
Goldbohm <i>et al.</i> (1994) ^a , Netherlands Cohort Study	58 279 men and 62 573 women, aged 55–69 years with no history of non-skin cancer, surveyed in 1986; follow-up for cancer incidence through the cancer registries through to 1989, or 3.3. years with 100% follow-up; estimated complete case ascertainment for 95% of cases; case-cohort design with 3346 total cohort members in analysis; 204 municipal population registries throughout the country used	Mailed self-administered standardized questionnaire to assess habitual intake	Colon	Non-drinker	63	1.0	Adjusted for sex, age, family history, smoking, body-mass index, education, history of gall bladder surgery, intake of energy, energy-adjusted fat, meat protein, fibre; cases that occurred in first year of follow-up were excluded; for colon cancer, no difference in risk between men and women; associations did not differ according to any specific beverage type.	
				Drinker	51	0.7 (0.5–1.0)		
				1–4.9 g ethanol/day	34	0.6 (0.4–0.9)		
				5–14.9 g ethanol/day	36	0.9 (0.5–1.6)		
				15–29.9 g ethanol/day	21	1.1 (0.3–3.6)		
			Rectum	≥30 g ethanol/day	21	1.1 (0.3–3.6)		p -trend=0.79
				Abstainers	19	1.0		
				1–4.9 g ethanol/day	26	1.2 (0.6–2.4)		
				5–14.9 g ethanol/day	17	0.8 (0.4–1.6)		
				15–29.9 ethanol/day	25	1.5 (0.7–3.2)		
≥30 g ethanol/day	19	2.0 (0.4–9.6)	p -trend=0.09					

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments				
Chyou <i>et al.</i> , (1996) ^a , Oahu, Hawaii, USA, Honolulu Heart Study	7945 American men of Japanese descent, born 1900–19, residents of Oahu, identified by the Selective Service draft file of 1942; no personal history of colorectal cancer; interviewed between 1965 and 1968 and followed through to 1995 for cancer incidence using Hawaii Tumor Registry; vital status, 98.2%	24-h diet recall including usual monthly intake of beer, spirits and wine (including sake)	Colon	0 oz/month	120	1.0	Adjusted for age, body-mass index, smoking, serum cholesterol, heart rate, monounsaturated fatty acids, calories from alcohol; in multivariate analysis, calories from alcohol significantly associated with colon cancer; amount of alcoholic beverages consumed associated with rectal cancer				
				<4 oz/month	44	0.7 (0.5–9.0)					
				4–<24 oz/month	76	1.1 (0.8–1.4)					
				≥24 oz/month	88	1.4 (1.0–1.8)					
		Rectum	0 oz/month	32	1.0						
			< oz/month	19	1.1 (0.6–2.0)						
			4–<24 oz/month	35	2.0 (1.2–3.2)						
			≥24	37	2.3 (1.4–3.7)						
						<i>p</i> -trend=0.005					
						<i>p</i> -trend=0.0001					
Glynn <i>et al.</i> (1996) ^a , Southwest Finland, α -Tocopherol β -Carotene Cancer Prevention Study	27 109 Finnish men, aged 50–69 years, who smoked five or more cigarettes per day; included those with a personal history of non-melanoma skin cancer and in-situ cancer; men randomized to a supplement that contained α -tocopherol, β -carotene, both, or placebo; complete diet and smoking data; followed up to 8 years for cancer incidence using the Finish Cancer Registry; 100% complete	Self-administered diet history standardized questionnaire to assess usual consumption over the previous 12 months	Colon (ICD-9153)	Q1 ≤5.3 g ethanol/day	5	1.0	Adjusted for age, physical activity during work, intake of total energy, starch, sweets, sugar, coffee, calcium; results for men in the no β -carotene arm; for colorectal cancer combined, associations strongest for beer and wine intake; in the β -carotene arms, no associations with total alcoholic beverage intake or any beverage				
				Q2 >5.3–≤13.4 g ethanol/day	7	1.5 (0.5–4.8)					
				Q3 >13.4–≤27.7 g ethanol/day	8	1.8 (0.6–5.6)					
				Q4 >27.7 g ethanol/day	15	3.6 (1.3–10.4)					
									<i>p</i> -trend=0.01		
			Rectum (ICD-9154)	Q1 ≤5.3 g ethanol/day	3	1.0					
				Q2 >5.3–≤13.4 g ethanol/day	3	1.0 (0.2–5.1)					
				Q3 >13.4–≤27.7 g ethanol/day	7	2.3 (0.6–9.0)					
Q4 >27.7 g ethanol/day	5	1.5 (0.3–6.7)									
						<i>p</i> -trend=0.37					

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Murata <i>et al.</i> (1996), Chiba, Japan	Nested case-control study; 17 200 men who underwent gastric screening in 1984; cancer cases identified through the Chiba Cancer Registry over the 9-year follow-up; 153 colon cancers and 154 rectal cancers identified and matched to two controls on birth year (± 2 years), first digit of address code	Self-administered standardized questionnaire at time of screening to assess current drinking	Colon (ICD-9153)	0 cup/day	13	1.0	Matched on birth year, address code; exposure is sake-equivalents (1 cup = 27 mL ethanol); associations not modified by cigarette smoking; associations strongest for proximal colon compared with sigmoid colon; CI not reported
				0.1–1.0 cup/day	31	3.5 ($p < 0.01$)	
				1.1–2.0 cups/day	10	1.9	
				≥ 2.1 cups/day	7	3.2 ($p < 0.05$) p -trend < 0.05	
			Rectum (ICD-9154)	0 cup/day	21	1.0	
				0.1–1.0 cup/day	11	0.8	
				1.1–2.0 cups/day	9	1.9	
				≥ 2.1 cups/day	2	1.4 p -trend > 0.05	
Thun <i>et al.</i> (1997), USA, Cancer Prevention Study II	251 420 women and 238 206 men, aged 30–104 years enrolled beginning in 1982; followed through to 1991 for cancer mortality; excludes people with cirrhosis or non-skin cancer at baseline; complete follow-up on nearly 98% of the cohort	Mailed, self-administered standardized questionnaire to assess current alcoholic beverage intake	Colon (ICD-9153)	None	211	<i>Men</i> 1.0	Adjusted for age, race, education, body-mass index, smoking, crude index of fat intake, vegetable consumption; other cancers not colorectal; in women use of hormone therapy; values based on men and women who reported no heart disease or hypertension; use of medication for reported conditions, stroke or diabetes at baseline.
				Rectum (ICD-9154)	Less than daily	216	
			1 drink/day		111	1.0 (0.8–1.3)	
			2–3 drinks/day		182	1.1 (0.9–1.4)	
				≥ 4 drinks/day	131	1.2 (1.0–1.5) p -trend=0.1	
				None	305	<i>Women</i> 1.0	
				Less than daily	131	0.8 (0.7–1.0)	
				1 drink/day	40	0.6 (0.4–0.8)	
				2–3 drinks/day	76	0.9 (0.7–1.2)	
				≥ 4 drinks/day	24	0.7 (0.5–1.1) p -trend=0.06	

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Singh & Fraser (1998) ^a , California, USA, Adventist Health Study	32 051 non-hispanic white women, aged ≥ 25 years, with no history of cancer completed a questionnaire in 1976; incidence of cancer over 6 years of follow-up determined from annual mailings and review of medical records (97% complete follow-up), or by linking to two California tumour registries	Mailed, self-administered standardized questionnaire	Colon (135 cases) (ICD-9153), Rectum (22 cases) (ICD-9154)	<1 time/week ≥ 1 time/week	138 8	1.0 2.0 (1.0–4.2)	Adjusted for sex, age, parental history of colon cancer; study population had a low prevalence of alcohol consumption; no data specific to rectal cancer given
Flood <i>et al.</i> (2002), USA, Breast Cancer Detection and Demonstration Project	45 264 women, aged 40–93 years participated in a breast cancer screening programme and completed a dietary questionnaire in 1987–89 and follow-up questionnaire in 1995–98 to report incident cancer; 1993–1995 follow-up; no personal history of colorectal cancer or implausible high or low levels of energy intake; 125 women reported consuming more than 6 drinks per day; 90% complete follow-up	Mailed, self-administered standardized questionnaire for usual intake	Colon or rectum (ICD-O 153.0–153.4, 153.6–153.9, 154.0–154.1)	0 serving/day 0.01–0.50 servings/day 0.51–1.00 servings/day 1.01–2.00 servings/day >2.00 servings/day	301 101 52 25 11	1.0 0.9 (0.7–1.2) 1.0 (0.7–1.3) 0.9 (0.6–1.4) 1.2 (0.6–2.1) <i>p</i> -trend=0.84	Adjusted for energy, dietary folate, methionine, smoking; no confounding by NSAID use, smoking, education, body mass index, height, physical activity, vitamin D calcium, red meat, grain, total fat or fibre intake; no interaction of alcoholic beverages with folate intake or NSAID use; interaction with smoking when association of alcoholic beverages with colorectal cancer observed only in nonsmokers

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Harnack <i>et al.</i> (2002) ^a , Iowa, USA, Iowa Women's Health Study	35 216 postmenopausal women aged 55–69 years, with no personal history of non-skin cancer completed a mailed questionnaire in 1986; followed through to 1998 for cancer incidence using Iowa Health Registry and national death index for vital status; 99% complete vital status	Mailed, self-administered standardized questionnaire assessed usual intake over the last year.	Colon (ICD-O18.0–18.9)	<20 g ethanol/day	572	1.0	Adjusted for age, pack-years cigarettes, body-mass index, estrogen use, intake of calcium, vitamin E, energy; for total colon, distal colon and rectal cancer, no interaction with folate intake; for proximal colon, lower risk for those with high folate and low alcoholic beverage intake; there also appeared to be an interaction of alcohol with haeme and zinc intake (Lee <i>et al.</i> , 2004)
			Rectum (ICD-O20.0)	≥20 g ethanol/day	26	1.1 (0.7–1.6)	
				<20 g ethanol/day	116	1.0	
				≥20 g ethanol/day	7	0.9 (0.4–2.1)	
Otani <i>et al.</i> (2003), multicentre, Japan, Japan Public Health Center Study	42 540 male and 47 464 female Japanese, aged 40–69 years; no personal history of cancer; followed from 1990 or 1993 through to 1999; cancer incidence determined from population-based tumour registries, hospital records or death certificates; 99.6% complete follow-up.	Self-administered standardized questionnaire to assess current and past alcoholic beverage intake; former and never-drinkers combined	Colon (ICD-O 180–189)	Non-drinker	62	1.0	Adjusted for age, family history of colorectal cancer, body-mass index, smoking status, physical activity, centre location; in men, no interaction of smoking with alcoholic beverage consumption for colon, rectal or colorectal cancer; no associations for colorectal cancer in women
				Occasional	16	0.8 (0.4–1.3)	
				1–149 g ethanol/week	51	1.0 (0.7–1.4)	
				150–229 g ethanol/week	71	1.3 (0.9–1.8)	
				≥300 g ethanol/week	99	1.9 (1.4–2.7) <i>p</i> -trend=0.001	
			Rectum (ICD-O 199–209)	Non-drinker	25	1.0	
				Occasional	8	1.0 (0.5–2.3)	
				1–149 g ethanol/week	32	1.6 (0.9–2.6)	
				150–229 g ethanol/week	36	1.7 (1.0–1.4)	
				≥300 g ethanol/week	47	2.4 (1.5–4.0) <i>p</i> -trend=0.005	

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments	
Pedersen <i>et al.</i> (2003), Copenhagen, Denmark, Copenhagen Centre for Prospective Population Studies	15 491 men and 13 641 women, aged 23–95 years; no history of non-skin cancer; participated in one of three prospective studies initiated in 1964, 1970 or 1976; followed for a mean of 14.7 years through to 1998; follow-up 99.3% complete; a nationwide cancer register used	Self-administered standardized questionnaire to assess average daily intake of alcoholic beverages on weekend days and on weekdays	Colon (ICD-7 153 or ICD-10 18.0–18.9)	<1 drink/week	96	1.0	Adjusted for sex, age, smoking, body-mass index, study of origin No differences in association between men and women; no interactions with smoking; no significant associations with any specific type of beverage although positive trends of rectal cancer with beer and liquor intake	
				1–6 drinks/week	129	1.0 (0.8–1.3)		
				7–13 drinks/week	77	0.9 (0.7–1.2)		
				14–27 drinks/week	68	0.9 (0.6–1.2)		
				28–40 drinks/week	27	1.1 (0.7–1.7)		
			≥41 drinks/week	14	0.8 (0.5–1.5)			
			Rectum (ICD-7 154 or ICD-10 20.0)	<1 drink/week	28	1.0		<i>p</i> -trend=0.58
				1–6 drinks/week	60	1.5 (0.9–2.3)		
				7–13 drinks/week	43	1.5 (0.9–2.5)		
				14–27 drinks/week	43	1.7 (1.0–2.8)		
28–40 drinks/week	17	2.1 (1.1–4.0)						
≥41 drinks/week	11	2.2 (1.0–4.6)						
Shimizu <i>et al.</i> (2003), Takayama, Japan	13 392 men and 15 659 women, aged ≥35 years; no personal history of non-melanoma skin cancer, surveyed in 1992; cancer incidence determined from hospital records; followed through to 2000	Self-administered standardized questionnaire to assess usual alcoholic beverage intake	Colon	No alcohol	5	1.0	Adjusted for age, height, body-mass index, smoking, years of education; significant dose–response relationship between alcohol consumption and colon cancer in both sexes	
				≤36.7 g ethanol/day	45	1.8 (0.7–4.5)		
				>36.7 g ethanol/day	58	2.7 (1.1–6.8)		
						<i>p</i> -trend=0.01		
						<i>Women</i>		
			Rectum	No alcohol	34	1.0		
				≤3.75 g ethanol/day	28	1.1 (0.6–2.0)		
				>3.75 g ethanol/day	32	1.8 (1.0–3.2)		
						<i>p</i> -trend=0.03		
						<i>Men</i>		
	No alcohol	8	1.0					
	≤36.7 g ethanol/day	20	0.6 (0.2–1.4)					
	>36.7 g ethanol/day	31	1.2 (0.5–2.7)					
			<i>p</i> -trend=0.06					
			<i>Women</i>					
	No alcohol	7	1.0					
	≤3.75 g ethanol/day	15	1.2 (0.4–3.3)					
	>3.75 g ethanol/day	19	1.8 (0.7–4.6)					
		<i>p</i> -trend=0.17						

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Sanjoaquin <i>et al.</i> (2004), United Kingdom, Oxford Vegetarian Study	10 998 vegetarians and non-vegetarians (4162 men, 6836 women), aged 16–89 years; no personal history of cancer; surveyed in 1980–84, followed for an average of 17 years; cancer incidence determined from the National Health Service cancer registry	Self-administered standardized questionnaire	Colorectal	<1 unit/week	30	1.0	Adjusted for sex, age, smoking status; association with alcohol partially confounded by smoking
				1–7 units/week	39	1.5 (0.9–2.5)	
				>7 units/week	26	1.5 (0.9–2.7) <i>p</i> -trend=0.12	
Su & Arab (2004), USA, NHANES I Epidemiologic Follow-up Study	3887 men and 6531 women, aged 25–74 years; no personal history of non-skin cancer; screened in 1982–84; cancer incidence from self-report and cancer mortality from proxy and national death index; followed through to July 1993; follow-up 92.2% complete	Interviewer-administered standardized questionnaire to assess usual consumption over the previous year, as well as intake at younger ages	Colon (ICD-O 153)	Non-drinker	63	1.0	Adjusted for sex, age, race, body-mass index, education, intake of poultry, non-poultry meat, seafood, multivitamin use, history of colonic polyps, smoking status; no difference in associations by sex; no association with beer or wine; stronger positive associations with liquor intake, greater number of years drinking, younger age at start drinking; consistent drinking positively associated with risk for colon cancer but no association for quitters
				<1 drink/day	22	1.1 (0.6–1.8)	
				≥1 drink/day	26	1.7 (1.0–2.8) <i>p</i> -trend=0.04	
				<i>Years drinking</i>			
				0	52	1.0	
				0–17	3	0.7 (0.2–2.3)	
17–34	17	1.3 (0.7–2.4)					
>34	39	1.7 (1.1–2.8) <i>p</i> -trend=0.02					

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Wei <i>et al.</i> (2004), USA (two cohorts), Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS)	87 733 women, aged 30–55 years from the Nurses' Health Study and 46 632 men, aged 40–75 years from the Health Professionals Follow-up Study; no personal history of non-skin cancer; follow-up for cancer incidence through biennial questionnaire with confirmation from medical records, and for vital status through proxy report or national death index; women followed up from 1980 through to May 2001; men followed up from 1986 through to January 2000	Self-administered standardized questionnaire to assess average intake over the previous year	Colon	0 g ethanol/day	37	Men - HPFS 1.0	Adjusted for age, family history of cancer, body-mass index, physical activity, intake of beef, pork, lamb, processed meat, calcium, folate, height, pack-years smoking before age 30, history of endoscopy; associations of alcohol with colon and rectal cancer were not statistically significantly different. In the combined analysis of NHS and HPFS, there were statistically significant positive associations with colon cancer (p -trend=0.001) but not rectal cancer (p -trend=0.11). In an earlier analysis of the HPFS, there was a statistically significant interaction of alcohol with folate intake (Giovannucci <i>et al.</i> , 1995)
				<10 g ethanol/day	149	1.1 (0.8–1.5)	
				10–19 g ethanol/day	98	1.3 (0.9–1.9)	
				≥20 g ethanol/day	111	1.5 (1.0–2.3)	
				Past	72	1.3 (0.9–2.0)	
						p -trend=0.003	
			Rectum	0 g ethanol/day	200	Women - NHS 1.0	
				<10 g ethanol/day	281	1.0 (0.8–1.2)	
				10–19 g ethanol/day	106	1.0 (0.8–1.3)	
				≥20 g ethanol/day	69	1.1 (0.9–1.5)	
				Past	16	0.6 (0.4–1.1)	
						p -trend=0.27	
HPFS: 46 632 men, aged 40–75 years; followed 1986–2000	Rectum	0 g ethanol/day	11	1.0			
		<10 g ethanol/day	43	0.9 (0.5–1.8)			
		10–19 g ethanol/day	35	1.3 (0.7–2.6)			
		≥20 g ethanol/day	28	1.1 (0.5–2.3)			
		Past	18	1.1 (0.5–2.3)			
				p -trend=0.6			
NHS: 87 733 women, aged 30–55 years; followed 1980–2000	Rectum	0 g ethanol/day	56	1.0			
		<10 g ethanol/day	91	1.1 (0.8–1.6)			
		10–19 g ethanol/day	28	1.0 (0.6–1.5)			
		≥20 g ethanol/day	24	1.5 (0.9–2.4)			
		Past	5	0.7 (0.3–1.8)			
				p -trend=0.23			

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments					
Chen <i>et al.</i> (2005a), Zhejiang, China	30 952 men and 33 148 women screened for colorectal cancer in 1989–90, aged ≥ 30 years; no history of cancer; followed for 10.6 years through to 2001; follow-up 99.9% complete	Interviewer-administered standardized questionnaire to assess drinking status and usual intake over the previous year	Colon (ICD-O 153.0–153.7)	Non-drinker	61	1.0	Adjusted for sex, age, smoking status, occupation, education, marital status; no differences in risk for men and women; only one case among former drinkers					
				Former drinker	1	0.4 (0.1–2.8)						
				Occasional	22	1.1 (0.6–1.8)						
			Rectum (ICD-O 154–154.1)	Daily	23	1.0 (0.5–1.8)						
				Non-drinker	73	1.0						
				Former drinker	0	NS						
Wakai <i>et al.</i> (2005), Japan, Japan Collaborative Cohort Study	23 708 men and 34 028 women, aged 40–79 years; no history of colorectal cancer; underwent municipal health check-up in 1988–90 through to 1997; followed for cancer incidence and vital status with linkage to cancer registry and review of death certificates; follow-up 96.7% complete	Standardized questionnaire to assess drinking status and usual intake	Colon	Non-drinker	24	<i>Men</i> 1.0	Adjusted for age, area, education, family history of colorectal cancer, body-mass index, smoking habits, walking time, sedentary work, intake of green leafy vegetables, beef; 1 go \approx 22 g ethanol; association between drinking habits and risk of colon cancer in men; 'J' shaped association was found between alcohol intake and risk of rectal cancer; lowest not among light drinkers.					
				Former drinker	19	2.0 (1.1–3.7)						
				0–0.9 go/day	43	2.0 (1.2–3.3)						
				1.0–1.9 go/day	63	2.2 (1.4–3.6)						
				2.0–2.9 go/day	36	1.8 (1.0–3.0)						
				≥ 3.0 go/day	20	2.4 (1.3–4.4)						
										<i>Women</i>		
										Non-drinker	149	1.0
										Former drinker	6	1.6 (0.7–3.6)
										0–0.9 go/day	22	1.1 (0.7–1.7)
										≥ 1 go/day	5	1.2 (0.5–3.0)
												<i>p</i> -trend=0.96

Table 2.44 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Wakai <i>et al.</i> (2005) (contd)			Rectum	<i>Men</i>			
				Non-drinker	30	1.0	
				Former drinker	14	1.3 (0.7–2.4)	
				0–0.9 go/day	16	0.6 (0.3–1.1)	
				1.0–1.9 go/day	35	1.0 (0.6–1.7)	
				2.0–2.9 go/day	29	1.2 (0.7–2.0)	
				≥3.0 go/day	12	1.3 (0.7–2.6)	<i>p</i> -trend=0.027
				<i>Women</i>			
				Non-drinker	50	1.0	
				Former drinker	1	0.8 (0.1–5.8)	
				0–0.9 go/day	5	0.7 (0.3–1.7)	
				≥1 go/day	2	1.5 (0.4–6.5)	<i>p</i> -trend=0.36

CI, confidence interval; ICD, International Classification of Diseases; NS, not significant; NSAID, non-steroidal anti-inflammatory drugs

^aStudies included in the meta-analysis of Moskal *et al.* (2007)

Fourteen prospective cohort studies assessed associations of alcoholic beverage intake with the risk for rectal cancer. Eight of these found no association (Goldbohm *et al.*, 1994; Glynn *et al.*, 1996; Murata *et al.*, 1996; Harnack *et al.*, 2002; Wei *et al.*, 2004; Chen *et al.*, 2005a; Wakai *et al.*, 2005). Similarly to colon cancer, most of the six studies that showed a positive association between alcoholic beverage consumption and rectal cancer were conducted in Japanese populations or men of Japanese descent (Hirayama, 1989; Chyou *et al.*, 1996; Otani *et al.*, 2003; Shimizu *et al.*, 2003), although one study from the USA (Klatsky *et al.*, 1988) and one from Denmark (Pedersen *et al.*, 2003) also found significantly positive associations. In general, the magnitude of association for rectal cancer was similar to, although slightly lower than, that for colon cancer in most studies.

(c) *Meta-analyses (Table 2.45)*

Despite the large number of cohort studies that assessed associations of alcoholic beverage consumption with risk for colon and/or rectal cancer and the large sample sizes included in many of them, the available evidence from these studies is limited for several reasons. First, most studies had very few cases (<50) in the highest category of alcoholic beverage intake, which limits the power to obtain precise estimates of modest risks. Second, it is not clear whether associations might differ according to anatomical site within the colon (i.e. proximal versus distal colon) or by type of alcoholic beverage. Third, associations in some studies might be confounded or modified by gender, level of obesity, diet or other lifestyle factors. To address these issues, Cho *et al.* (2004) conducted a detailed analysis of the relationship between alcoholic beverage consumption and the risk for colorectal cancer using pooled data from eight large cohort studies conducted in Europe or North America. The criteria for study inclusion in the pooling project were: (a) prospective cohort; (b) inclusion of at least 50 cases of colorectal cancer; (c) assessment of long-term dietary intake; (d) a validation study of dietary assessment; and (e) measurement of alcoholic beverage intake. As described in Table 2.45, this analysis included more than 4600 cases among approximately 490 000 men and women, aged 15–107 years at baseline, and reported follow-up rates were between 94 and 100%. In multivariate analyses that adjusted for age, tobacco smoking, body-mass index, education, height, physical activity, family history of colorectal cancer, use of non-steroidal anti-inflammatory drugs, use of multivitamins, energy intake and intake of other dietary factors, the relative risks for colorectal cancer across the five increasing levels of intake were 0.94, 0.97, 1.01, 1.16 and 1.41 (p for trend=0.001) compared with non-drinkers. The strength of the associations did not differ between men and women (relative risks for the highest versus the lowest categories of intake were 1.41 for both). While the risk for colorectal cancer was slightly stronger for wine intake (relative risk, 1.82 for ≥ 30 g alcohol per day compared with 0 g of alcohol per day) than for beer (relative risk, 1.37) or liquor (relative risk, 1.21), the differences among types of alcoholic beverage were not statistically significant. In addition, associations were not

Table 2.45 Meta-analyses of colon, rectal and colorectal cancer and alcoholic beverage consumption

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Longnecker <i>et al.</i> (1990), meta-analysis of 5 prospective cohort studies and 22 case-control studies	Eligibility for inclusion: (a) alcoholic beverage intake had to be determined quantitatively by personal history; (b) study results had to be able to be translated into a numerical measure of association.		Colon or rectum	All relative risks for an intake of 24 g ethanol/day	<i>Subgroups (no. of studies)</i> All (27) Men (13) Women (13) <i>Colon</i> (14) <i>Rectum</i> (14) Cohort (5) Case-control (22)	1.10 (1.05–1.14) 1.1 (1.0–1.2) 1.1 (1.0–1.2) 1.1 (1.0–1.2) 1.1 (1.0–1.2) 1.3 (1.2–1.5) 1.1 (1.0–1.1)	Weak association between alcohol consumption and risk for colorectal cancer

Table 2.45 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Cho <i>et al.</i> (2004), pooling project of 8 cohort studies: ATBC Cancer Prevention Study; Canadian National Breast Screening Study; Health Professionals Follow-up Study; Iowa Women's Health Study; Netherlands Cohort Study; New York State Cohort; Nurses' Health Study; Sweden Mammography Study	489 979 men and women, aged 15–107 years at baseline; follow-up of 6–16 years; follow-up conducted through cancer and death registries, or self-report and medical record review; estimated follow-up rates ranged from 94 to 100% (one study had no information on follow-up rate); total of 4687 cases identified	Most questionnaires assessed usual consumption	Colorectal	<i>Total alcohol</i>			Adjusted for age, smoking, body-mass index, education, height, physical activity, family history of colorectal cancer, NSAID use, multivitamin use, energy intake, red meat intake, total milk intake, folate intake from food, alcohol intake from other beverages; for women also adjusted for use of oral contraceptives and postmenopausal hormone therapy
				0 g ethanol/day	1466	1.0	
				>0–<5g ethanol/day	1475	0.94 (0.86–1.03)	
				5–<15 g ethanol/day	849	0.97 (0.88–1.06)	
				15–<30 g ethanol/day	485	1.01 (0.86–1.18)	
				30–<45 g ethanol/day	244	1.16 (0.99–1.36)	
				≥45 g ethanol/day	168	1.41 (1.16–1.72)	
						<i>p</i> -trend<0.001	
				<i>Beer</i>			
				0 g ethanol/day	2612	1.0	
				>0–<30 g ethanol/day	1219	1.01 (0.89–1.13)	
				≥30 g ethanol/day	67	1.37 (1.00–1.87)	
						<i>p</i> -trend=0.2	
<i>Wine</i>							
0 g ethanol/day	2078	1.0					
>0–<30 g ethanol/day	1768	0.97 (0.89–1.05)					
≥30 g ethanol/day	52	1.82 (1.28–2.59)					
		<i>p</i> -trend=0.001					
<i>Liquor</i>							
0 g ethanol/day	2392	1.0					
>0–<30 g ethanol/day	1347	0.98 (0.88–1.09)					
≥30 g ethanol/day	159	1.21 (0.99–1.47)					
		<i>p</i> -trend=0.1					

Table 2.45 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments	
Cho <i>et al.</i> (2004) (contd)			Colon	<i>Total alcohol</i>	Not reported	1.0		
				0 g ethanol/day				
				>0–<5 g ethanol/day				0.92 (0.84–1.01)
				5–<15 g ethanol/day				0.94 (0.84–1.05)
				15–<30 g ethanol/day				1.01 (0.82–1.24)
				30–<45 g ethanol/day				1.08 (0.89–1.31)
				≥45 g ethanol/day				1.45 (1.14–1.83) <i>p</i> -trend<0.001
			Rectum	<i>Total alcohol</i>	Not reported	1.0		
				0 g ethanol/day				
				> 0–<5 g ethanol/day				1.01 (0.83–1.22)
				5–<15 g ethanol/day				0.99 (0.82–1.19)
				15–<30 g ethanol/day				1.05 (0.83–1.32)
				30–<45 g ethanol/day				1.42 (1.07–1.88)
				≥45 g ethanol/day				1.49 (1.49–2.12) <i>p</i> -trend=0.006

Table 2.45 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors/comments
Moskal <i>et al.</i> (2007), meta-analysis of 16 prospective cohort studies from Asia, Europe and USA (cohorts included are noted in Table 2.44)	Criteria for inclusion were: (a) prospective cohort that evaluated the association of alcoholic beverage intake with risk for colorectal cancer; (b) published in English between 1990 and June 2005; (c) references in MEDLINE; (d) colorectal cancer incidence as the end-point; (e) provide relative risks and 95% CIs; (f) for dose-response analysis, had to report at least three categories of exposure, number of cases and comparison subjects for each category; five cohort studies for colorectal, 14 studies for colon and 12 studies for rectal cancer included 6300 cases.	All studies collected self-reported alcoholic beverage intake	Colorectal, colon or rectum	All relative risks for an increase of 100 g ethanol/week	<i>Subgroup (no. of studies)</i> All (7) Men (3) Women (3) Asia (4) Europe (2) USA (1) <i>Colon</i> All (14) Men (7) Women (3) Asia (7) Europe (3) USA (4) <i>Rectum</i> All (12) Men (6) Women (3) Asia (7) Europe (3) USA (2)	<i>Colorectal</i> 1.19 (1.14–1.27) 1.21 (1.02–1.43) 1.05 (0.92–1.20) 1.21 (1.14–1.27) 1.44 (1.10–1.87) 1.02 (0.87–1.20) <i>Colon</i> 1.15 (1.07–1.23) 1.18 (1.13–1.24) 1.14 (1.00–1.30) 1.15 (1.10–1.21) 1.14 (0.85–1.52) 1.23 (1.12–1.35) <i>Rectum</i> 1.15 (1.10–1.21) 1.19 (1.12–1.26) 1.16 (0.94–1.44) 1.16 (1.09–1.23) 1.10 (1.02–1.20) 1.43 (1.18–1.72)	Adjustment factors not reported; results also showed dose-response relationships for colon and for rectum ($p < 0.05$); relative risks for colon: 25 g/week, 1.02; 50 g/week, 1.07; 100 g/week, 1.15; relative risks for rectum: 25 g/week, 1.04; 50 g/week, 1.07; 100 g/week, 1.15

ATBC, α -Tocopherol β -Carotene; CI, confidence interval; ICD, international Classification of Diseases; NSAID, non-steroidal anti-inflammatory drugs

significantly different among anatomical sites (i.e. total colon versus rectum, proximal versus distal colon), and associations of specific beverage types also did not differ by anatomical site. Finally, as described in detail below, only body-mass index appeared to modify significantly the relationship between alcoholic beverage consumption and risk for colorectal cancer in the cohort-pooling project. The interactions of alcoholic beverages with multivitamin use, total folate intake, methionine intake, tobacco smoking and, in postmenopausal women, use of hormone therapy were not statistically significant ($P>0.2$).

Moskal *et al.* (2007) conducted a large meta-analysis that included 16 prospective cohort studies published between 1990 and 2005. Inclusion criteria for that analysis are shown in Table 2.45. In the meta-analysis, the average relative risk associated with an increase in consumption of 100 g ethanol per week was 1.19 for colorectal cancer, 1.15 for colon cancer and 1.15 for rectal cancer. In general, associations were only slightly stronger for men than for women. There was no consistent pattern of differences in magnitude of associations among Asian, European, or US studies; however, there was evidence of geographical heterogeneity for colon cancer ($P=0.003$).

2.8.2 Case-control studies (Table 2.46)

Thirty-eight case-control studies have investigated alcoholic beverage consumption and the risk for colon, rectal or colorectal cancer. The total number of cases included ranged from as few as 25 to as many as 1225.

Nine of the 38 studies provided results for colon and rectum combined. Among these, there was no evidence of a statistically significant association in four studies (Higginson, 1966; Wynder *et al.*, 1969; Manousos *et al.*, 1983; Boutron *et al.*, 1995) and a non-significant positive association in three others (Stocks, 1957; Pernu, 1960; Yamada *et al.*, 1997). A strong positive association was found in the study of Muñoz *et al.* (1998) in Argentina where there was a threefold higher risk for colorectal cancer associated with intake of ≥ 24 g alcohol per day compared with < 24 g alcohol per day. Conversely, Olsen and Kronborg (1993) reported a lower risk for colorectal cancer associated with four or more Kcal of total energy from alcoholic beverage intake compared with 0 Kcal per day (relative risk, 0.4; 95% CI, 0.3–1.0).

Twenty-six case-control studies examined the relationship between alcoholic beverage consumption and the risk for colon cancer specifically. There was no evidence of a significant association in 15 of these (Wynder & Shigematsu, 1967; Graham *et al.*, 1978; Tuyns *et al.*, 1982; Miller *et al.*, 1983; Tajima & Tominaga, 1985; Kune *et al.*, 1987; Ferraroni *et al.*, 1989; Peters *et al.*, 1989; Slattery *et al.*, 1990; Choi & Kahyo, 1991b; Riboli *et al.*, 1991; Gerhardsson de Verdier *et al.*, 1993; Newcomb *et al.*, 1993; Tavani *et al.*, 1998; Ji *et al.*, 2002). One study reported a significant inverse relationship between alcoholic beverage consumption and the risk for colon cancer (Hoshiyama *et al.*, 1993). In one study, a twofold higher risk for colon cancer was observed for > 12.9 g alcohol per day in women (95% CI, 0.9–4.5) and no association in men (Potter

Table 2.46 Case–control studies of colon and rectal cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Stocks (1957), United Kingdom, 1929–32	166 colorectal; from hospital with a special interviewer appointed	1750 hospital-based; aged 45–74 years	Interview	<i>Beer drinking</i> <Daily ≥Daily	74 92 24 141	Obs/Exp <i>Men</i> 1.0 1.4 (0.9–2.1) <i>Women</i> No association	Adjusted for age and sex; heavy cigarette smoking occurred with frequent beer drinking in women.
Pernu (1960), Helsinki, Finland, 1944–58	666 intestines (317 men, 349 women); all ages; prevalent cases treated at several Finnish Hospitals between 1944 and 1958; 53% histologically confirmed; response rate, 30%	1773 population; aged ≥ 30 years; selected by a group of Parish Sisters; response rate, 39.7%	Mailed self-administered standardized questionnaires	Abstainer Moderate drinker Heavy drinker Abstainer Moderate drinker Heavy drinker		<i>Men</i> 1.0 1.1 2.1 <i>Women</i> 1.0 1.1 –	No adjustment factors; cases were over-represented on early stage disease [calculated relative risks based on the data presented]; CI not reported.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Higginson (1966), Kansas, USA, 1959	340 colorectal (196 men, 144 women); selected from seven Kansas hospitals and interviewed before surgery; 100% histologically confirmed; response rate not given	1020 (588 men, 432 women) hospital-based; matched (3:1) for sex, age (± 10 years), race; response rate not given	Interviewer-administered standardized questionnaire	Non-drinker Light drinker Moderate drinker Heavy drinker		1.0 0.9 0.8 1.0	No adjustment factors; assessed exposure 2 years before diagnosis; no differences in associations according to alcoholic beverage type [calculated relative risks presented]; CI not reported; number of cases not reported.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Wynder & Shigematsu (1967), New York, USA, 1959–61, 1963–64	288 colon (174 men, 114 women) and 204 rectal (140 men, 64 women) identified from hospital; histological confirmation not given; response rate not given	273 (206 men, 67 women); matched on age, hospital; response rate not given	Interview	<i>Colon</i>	<i>Men</i>		No adjustment for social or other behavioural factors; no association in men or women; for men, there was a higher proportion of heavy drinkers among cases versus controls; no association for women; rectal cancer associated with heavy drinking; more male beer drinkers than controls.
				Never	28		
				1 per month to < 1 per day	70		
				1–2 per day	31		
				3–4 per day	28		
				≥7 per day	14		
				Sporadic heavy	3		
				<i>Rectal</i>			
				Never	24		
				1 per month to < 1 per day	34		
1–2 per day	38						
3–4 per day	21						
≥7 per day	22						
Sporadic heavy	3						

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Wynder & Shigematsu (1967) (contd)				<i>Colon</i>			
				Never	60		
				1 per month to < 1 per day	34		
				1-2 per day	17		
				3-4 per day	2		
				≥7 per day	0		
				Sporadic heavy	0		
				<i>Rectal</i>			
				Never	40		
				1 per month to < 1 per day	17		
				1-2 per day	4		
				3-4 per day	1		
				≥7 per day	1		
				Sporadic heavy	0		

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Wynder <i>et al.</i> (1969), Japan	69 colon (38 men, 31 women) and 88 rectal (42 men, 46 women) from the Japan Cancer Hospital and the National Cancer Institute Hospital; histological confirmation not given; response rate not given	307 (160 men, 147 women) representing two different groups: (1) with cancer other than gastrointestinal; (2) patients with non-malignant disease; matched on age, hospital; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i> Men Women <i>Rectal</i> Men Women	38 31 42 46		Authors state there were no meaningful differences in alcoholic beverage consumption between cases and controls; relative risks not reported.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Williams & Horm (1977), USA, 1969–71 (Third National Cancer Survey)	Colon (294 men, 359 women) age ≥ 35 years; participants in Third National Cancer Survey Rectal (165 males, 138 females) age ≥ 35 years; participants in Third National Cancer Survey	1494 men, 2829 women with other cancers. 1623 male, 3050 female with other cancer	Interviewer-administered standardized questionnaire	<i>Colon</i>		<i>Men</i>	Adjusted for age, race, smoking; controls excluded cancers of the lung, larynx, mouth, oesophagus, and bladder; for men, statistically significant associations were observed for high levels of wine, beer and spirit intake with risk for colon cancer.
				None	NG	1.0	
				<50 oz/year	52	1.4	
				≥ 50 oz/year	96	1.5 ($p < 0.05$)	
				<i>Women</i>			
				None	NG	1.0	
				<50 oz/year	47	1.2	
				≥ 50 oz/year	29	1.4	
				<i>Rectal</i>			
				None	NG	1.0	
<50 oz/year	27	0.8					
≥ 50 oz/year	42	0.7					
				<i>Women</i>			
				None	NG	1.0	
				<50 oz/year	11	0.8	
				≥ 50 oz/year	14	2.0 ($p < 0.05$)	
Graham <i>et al.</i> (1978), New York, USA, 1959–65	256 colon and 330 rectal; white men admitted to Roswell Park Institute; 100% histologically confirmed; response rate not given	783 (colon) and 628 (rectal) hospital-based white men; frequency matched on age; response rate not given	Interviews			No association with colon or rectum for total alcohol, beer, wine or whiskey	No adjustments; the authors noted that data were also collected for women but did not present those results; they stated that results were similar.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Tuyns <i>et al.</i> (1982), France, 1975–80	142 colon (80 men, 82 women) and 198 rectal (104 men, 94 women) identified in Calvados	Population-based; random sample from the same area; response rate, 75%	Interviewer-administered standardized questionnaire	<i>Colon</i>			Adjusted for sex, age
				Non-consumer	21	1.0	
				Consumer	121	1.4 (0.3–5.7)	
				<i>Rectal</i>			
				Non-consumer	26	1.0	
				Consumer	172	1.6 (0.5–5.5)	
Manousos <i>et al.</i> (1983), Athens, Greece, 1979–80	100 colon or rectal (of which 35 were rectal) admitted to one of two large teaching hospitals in Athens; 100% histologically confirmed; response rate, 100%	100 hospital-based admitted to the orthopaedic department; matched for sex, age (± 5 years), hospital; response rate, 100%	Interview	<i>Colorectal</i>			Matched on sex and age; further adjustment for meat and vegetable consumption attenuated the association; no associations for wine, ouzo, brandy or other hard liquor; relative risk and CI not reported
				0 glasses of beer/week	68		
				1–10 glasses of beer/week	24	<i>p</i> -trend >0.25	
				≥ 11 glasses of beer/week	8		
				<i>Rectal</i>			
				0 glasses of beer/week	27		
1–10 glasses of beer/week	5	<i>p</i> -trend >0.5					
≥ 11 glasses of beer/week	3						

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Miller <i>et al.</i> (1983), Canada, 1976–78	348 colon (171 men, 177 women) and 194 rectal (114 men, 80 women) newly diagnosed in Ontario or Calgary; histological confirmation not given; response rate not given	Two series: (1) 542 neighbourhood; individually matched on age (± 5 years), sex, area of residence; (2) 535 hospital-based who underwent abdominal surgery in same hospital as the case; frequency-matched on sex, age; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>		<i>Men</i>	Adjusted for age, saturated fat food group; the two control groups were combined for all analyses; for the association of beer intake with rectal cancer, a marginally significant trend for women ($p=0.09$) but not for men ($p=0.22$); wine and spirit intake not examined
				0 g ethanol/day	1.0		
				0.1–47.6 g ethanol/day	1.2		
				>47.6 g ethanol/day	1.4	p -trend=0.1	
						<i>Women</i>	
				0 g ethanol/day	1.0		
				0.1–17.7 g ethanol/day	1.0		
				>17.7 g ethanol/day	1.0	p -trend=0.41	
				<i>Rectal</i>		<i>Men</i>	
				0 g ethanol/day	1.0		
0.1–47.6 g ethanol/day	0.5 ($p<0.05$)						
>47.6 g ethanol/day	1.3	p -trend=0.43					
		<i>Women</i>					
0 g ethanol/day	1.0						
0.1–17.7 g ethanol/day	1.3						
>17.7 g ethanol/day	0.8	p -trend=0.34					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Pickle <i>et al.</i> (1984), Nebraska, USA, 1970–77	58 colon (ICD 153; 11 living and 15 deceased men, 13 living and 19 deceased women) and 28 rectal (ICD 154; 5 living and 9 deceased men, 5 living, 9 deceased women) identified through search of medical records in two counties in Nebraska; 100% histologically confirmed; response rate not given	176 hospital-based (44 living and 45 deceased men, 43 living and 44 deceased women) selected from admission lists; matched to the case (2:1) by hospital, sex, race, age (± 5 years); response rate not given	Interviewer-administered standardized questionnaire	Commercial beer <i>Colon</i> Non-drinker >0 drink/week <i>Rectal</i> Non-drinker >0 drink/week		1.0 2.7 (1.3–5.5) 1.0 1.4 (0.5–3.7)	Adjusted for sex, ever smoked cigarettes, ever smoked pipe; additional analyses for commercial beer consumption and colon cancer examined dose (p -trend=0.05); analyses were also conducted for home-made beer and for commercial and home-made wine consumption; no significant associations for either colon or rectal cancer.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments	
Tajima & Tominaga (1985), Japan, 1981–84	Colon (27 men, 15 women) and rectal (25 men, 26 women), aged 40–70 years; seen at the Aichi Cancer Center; 100% histologically confirmed; response rate not given	182 hospital-based men; matched on age (± 5 years), time of interview (± 6 months); response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>		<i>Men</i>	Adjusted for age; data also collected for women but only the results for men were presented; some evidence of an inverse association with sake intake	
				Non-drinker		1.0		
				Drinker		0.68		
				<i>Rectal</i>		<i>Men</i>		
				Non-drinker		1.0		
				Drinker		0.60		
						($p > 0.5$)		
Kabat <i>et al.</i> (1986), New York, USA, 1976–81	218 rectal (130 men, 88 women), aged 20–80 years; diagnosed at Memorial Sloane Cancer Center in New York; 100% histologically confirmed; response rate not given	585 (336 men, 249 women) hospital-based with diseases not associated with smoking; matched to cases (1–3:1) on sex, age (± 8 years), calendar year of hospital interview (± 2 years); response rate not given	Interviewer-administered standardized questionnaire				<i>Men</i>	Matched on sex, age, calendar year of hospital interview, religion, education; in men, heavy beer consumption associated with an increased risk for rectal cancer
				Never	30	1.0		
				<1 oz/day	31	1.6 (0.9–2.8)		
				1–7.9 oz/day	26	1.3 (0.7–2.4)		
				8–31.9 oz/day	21	1.8 (0.9–3.5)		
				≥ 32 oz/day	22	3.5 (1.8–7.0)		
						<i>Women</i>		
				Never	67	1.0		
				<1 oz/day	12	0.5 (0.3–1.0)		
				1–7.9 oz/day	7	0.5 (0.2–1.2)		
8–31.9 oz/day	2	0.7 (0.1–3.2)						
≥ 32 oz/day	0	–						

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Potter & McMichael (1986), Adelaide, Australia, 1979–80 (colon), 1979–81 (rectal)	220 colon (121 men, 99 women) and 199 rectal (124 men, 75 women), aged 30–74 years; identified from the South Australian Cancer Registry; histological confirmation not given; response rate, 82.8%	438 colon (241 men, 197 women) and 396 rectal (248 men, 148 women) selected from the electoral rolls of Adelaide; matched 2:1 to cases on sex, age; response rate, 69%	Self-administered dietary questionnaire	<i>Colon</i>		<i>Men</i>	Matched on sex, age; in analysis for specific beverage types, colon cancer significantly associated with spirit intake but not beer or wine in men and women; in multivariate analysis adjusted for occupation, protein and fibre intake, spirit intake remained significantly associated with colon cancer in men.
				≤0.1 g ethanol/day		1.0	
				0.1–4.0 g ethanol/day		0.6 (0.3–1.3)	
				4.1–12.8 g ethanol/day		0.4 (0.2–1.0)	
				12.9–31.8 g ethanol/day		0.8 (0.4–1.7)	
				>31.8 g ethanol/day		1.0 (0.5–2.1)	
						<i>Women</i>	
≤0.1 g ethanol/day		1.0					
0.1–0.95 g ethanol/day		1.4 (0.7–2.7)					
0.96–3.9 g ethanol/day		1.2 (0.5–2.6)					
4.0–12.9 g ethanol/day		2.0 (0.9–4.4)					
>12.9 g ethanol/day		2.0 (0.9–4.5)					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Potter & McMichael (1986) (contd)				<i>Rectal</i>		<i>Men</i>	For women, the association was attenuated after adjustment for oral contraceptive use, parity and fibre and protein intake; rectal cancer significantly associated with spirit intake in men and wine intake in women; <i>p</i> -trend not reported
				≤0.1 g ethanol/day		1.0	
				0.1–4.0 g ethanol/day		0.7 (0.3–1.3)	
				4.1–12.8 g ethanol/day		0.8 (0.4–1.5)	
				12.9–31.8 g ethanol/day		0.6 (0.3–1.2)	
				>31.8 g ethanol/day		0.7 (0.4–1.5)	
						<i>Women</i>	
				≤0.1 g ethanol/day		1.0	
				0.1–0.95 g ethanol/day		0.6 (0.2–1.3)	
				0.96–3.9 g ethanol/day		1.7 (0.7–3.9)	
			4.0–12.9 g ethanol/day		1.1 (0.5–2.5)		
			>12.9 g ethanol/day		1.5 (0.6–3.7)		

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Kune <i>et al.</i> (1987), Melbourne, Australia	715 colorectal (383 men, 325 women), aged 35–75 years; histological confirmation not given; response rate not given	727 (396 men, 328 women) population-based; matched on sex, age; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>		<i>Men</i>	Adjusted for sex, age, beef, fat, milk, fibre, vegetable, vitamin C, pork, fish, vitamin supplement intake; for colon cancer, no associations with any beverage type; for men and women, beer consumption associated with a higher risk for rectal cancer; spirit intake associated with a lower risk for rectal cancer in men; <i>p</i> -values and CI not reported
				0 g ethanol/day	1.0		
				1–112 g ethanol/day	1.4		
				113–280 g ethanol/day	1.0		
				≥281 g ethanol/day	1.0		
					<i>Women</i>		
				0 g ethanol/day	1.0		
				1–112 g ethanol/day	1.1		
				113–280 g ethanol/day	1.2		
				≥281 g ethanol/day	1.4		
					<i>Men</i>		
				<i>Rectal</i>		<i>Men</i>	
0 g ethanol/day	1.0						
1–112 g ethanol/day	1.5						
113–280 g ethanol/day	1.1						
≥281 g ethanol/day	1.5						
	<i>Women</i>						
0 g ethanol/day	1.0						
1–112 g ethanol/day	1.3						
113–280 g ethanol/day	1.5						
≥281 g ethanol/day	0.9						

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Ferraroni <i>et al.</i> (1989), Milan, Italy, 1983–88	455 colon (221 men, 234 women) and 295 rectal (170 men, 125 women); aged 75 years; identified from the four largest teaching and general hospitals in Milan; 100% histologically confirmed; response rate not given	1944 (1334 men, 610 women) hospital-based; admitted to one of several Milan area hospitals; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>	290	1.0	Adjusted for sex, age, social class, education, marital status, smoking, coffee; no associations with any specific beverage type; in a subsequent analysis of 828 colon and 498 rectal cancer cases and 2024 controls, there was an inverse trend for risk for colon cancer associated with beer intake and no association with rectal cancer (La Vecchia <i>et al.</i> , 1993); CI not reported.
				<3 drinks/day	107	1.1	
				3–6 drinks/day	58	1.2	
				>6 drinks/day		<i>p</i> =0.67	
				<i>Rectal</i>	187	1.0	
				<3 drinks/day	62	0.8	
3–6 drinks/day	46	0.9					
				>6 drinks/day		<i>p</i> =0.46	

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Peters <i>et al.</i> (1989), Los Angeles, USA, 1974–82	106 colon and 41 rectal white men, aged 24–44 years; residents of California identified through the Los Angeles County Cancer Surveillance Program; 100% histologically confirmed; response rate, 65%	147 population-based; identified by an algorithm that used the house of the index case as a reference point; matched (1:1) on race, sex, date of birth (± 5 years), neighbourhood; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>			Adjusted for age and education; no associations with any specific beverage type
				0–9 g ethanol/day	61	1.0	
				10–39 g ethanol/day	39	1.0 (0.5–1.9)	
				40–69 g ethanol/day	25	0.8 (0.4–1.5)	
				≥ 70 g ethanol/day	20	1.6 (0.6–3.7)	
				<i>Rectal</i>			
0–9 g ethanol/day	61	1.0					
10–39 g ethanol/day	39	1.2 (0.5–2.7)					
40–69 g ethanol/day	25	0.6 (0.2–1.8)					
≥ 70 g ethanol/day	20	1.4 (0.4–4.5)					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments			
Freudenheim <i>et al.</i> (1990), New York, USA, 1978–86	422 rectal (277 men, 145 women), aged ≥ 40 years; identified from hospital pathology and surgical records; 100% histologically confirmed; response rate not given	277 men and 145 women; population-based; matched (1:1) on sex, age, neighbourhood; response rate, 57%	Interviewer-administered standardized questionnaire	<i>Drink-years (drinks/year \times years drinking)</i> Quartile 1 Quartile 2 Quartile 3 Quartile 4		<i>Men</i> 1.0 1.1 (0.7–1.8) 1.0 (0.6–1.7) 1.8 (1.1–2.9) <i>p</i> -trend=0.06	Matched on sex, age, neighbourhood; associations for lifetime alcohol intake; in men, significant associations of rectal cancer with total alcohol and beer which persisted after adjustment for total calories, fat, dietary fibre, vitamin C or carotene. In a subsequent analysis, some evidence of an interaction of folate with alcoholic beverage intake on risk for rectal cancer in men (Freudenheim <i>et al.</i> , 1991).			
								Tertile 1 Tertile 2 Tertile 3		<i>Women</i> 1.0 0.9 (0.5–1.7) 1.9 (1.0–3.6) <i>p</i> -trend >0.05

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Longnecker (1990), USA multi-site, 1986–88	251 right colon and 383 rectal (men only), aged 31 years; only identified from records departments at 49 New England hospitals and through the Massachusetts Cancer Registry in an additional 19 hospitals; histological confirmation not given; response rate, 66%	992, aged ≥ 31 years; selected from in-law relatives, friends of cases and population lists or Health Care Financing Administration for those aged ≥ 65 years and older; matched on age (± 5 years), state; response rate, 65%	Telephone interviewer-administered questionnaire followed by a mailed self-administered standardized questionnaire	<i>Right colon</i>	71	1.0	Adjusted for age, income, tobacco smoking; results for consumption 5 years prior to diagnosis; similar for associations of alcohol intake 20 years prior to diagnosis for both right colon and rectal cancer; associations for colon and rectal strongest for beer intake with no significant associations for wine or liquor; significant association of alcoholic beverage consumption with right colon and with rectal cancer for those with low calcium or low vitamin D intake, but not for those with high calcium or high vitamin D intake
				0 drink/day	59	0.9 (0.6–1.3)	
				0.5 drink/day	31	1.0 (0.6–1.5)	
				1 drink/day	27	1.0 (0.6–1.7)	
				2 drinks/day	40	1.7 (1.1–2.7)	
				3–4 drinks/day	21	1.8 (1.0–3.2)	
				≥ 5.0 drinks/day		<i>p</i> -trend=0.007	
				<i>Rectal</i>	97	1.0	
				0 drink/day	107	1.1 (0.8–1.5)	
				0.5 drink/day	46	0.9 (0.6–1.4)	
1 drink/day	48	1.2 (0.8–1.9)					
2 drinks/day	64	1.7 (1.1–2.5)					
3–4 drinks/day	30	1.5 (0.9–2.5)					
≥ 5.0 drinks/day		<i>p</i> -trend=0.007					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Slattery <i>et al.</i> (1990), Utah, USA, 1979–83	231 colon (ICD-0 153.0–154.0; 112 men, 119 women), aged 40–79 years; identified through the Utah Cancer Registry; 100% histologically confirmed; response rate, 71%	391 (185 men, 206 women) population-based; selected using random-digit dialling; response rate, 74%	Interviewer-administered standardized questionnaire	Never	60	1.0	Men: adjusted for age, religion, body-mass index, calories, crude fibre intake, pipe use, caffeine intake for multiple logistic models; women: unadjusted; associations did not differ by colon subsite (ascending versus descending).
				1–15 g ethanol/week	26	1.4 (0.7–3.0)	
				>15 g ethanol/week	26	1.1 (0.5–2.4)	
				Never	100	1.0	
				1–15 g ethanol/week	15	1.1 (0.5–2.1)	
				>15 g ethanol/week	4	0.6 (0.2–1.9)	
Choi & Kahyo (1991b), Seoul, Republic of Korea, 1986–90	114 colon (ICD-9 153; 63 men, 51 women) and 133 rectal (ICD-9 154; 67 men, 66 women) identified from the Korea Cancer Hospital of Seoul; 100% histologically confirmed; response rate not given	189 male colon, 153 female colon, 201 male rectal, 198 female rectal selected from patients without cancer at the same hospital; matched 3:1 on sex, birth year (± 5 years), admission date; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>			Adjusted for age, marital status, education, cigarette smoking, diet; too few female drinkers so results limited to men
				Non-drinker	19	1.0	
				Light	14	0.6 (0.3–1.4)	
				Moderate	18	1.1 (0.5–2.5)	
				Medium–heavy	10	1.0 (0.4–2.3)	
				Heavy	2	0.7 (0.1–3.6)	
				<i>Rectal</i>			
				Non-drinker	11	1.0	
				Light	22	2.2 (1.0–7.5)	
				Moderate	16	2.0 (0.8–4.9)	
				Medium–heavy	14	2.5 (1.1–5.6)	
				Heavy	4	4.7 (1.3–2.8)	

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Hu <i>et al.</i> (1991), Harbin, China, 1985–88	111 colon and 225 rectal, aged 30–75 years; from local hospitals; 100% histologically confirmed; response rate not given	335 hospital-based, aged 30–74 years; selected from the same hospitals as cases; matched on sex, age (± 5 years), residential area; response rate not given.	Interviewer-administered standardized questionnaire	<i>Colon</i> <1.0 kg/year ≥ 1.0 kg/year <i>Rectal</i> <1.0 kg/year ≥ 1.0 kg/year		<i>Men and women</i> 1.0 6.42 ($p < 0.01$) <i>Men</i> 1.0 2.1 ($p < 0.05$)	Adjusted for green vegetable, chives and celery intake Adjusted for grain, chives and celery intake Results for current consumption; in multivariate analysis, no association with alcoholic beverage in women; CI not reported

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Riboli <i>et al.</i> (1991), Marseilles, France, 1979–85	196 colon (92 men, 104 women) and 193 rectal (95 men, 98 women) identified from 11 major hospitals; 100% histologically confirmed; response rate, 100%; age not given	389 selected from specialized medical centres for treatment of injury or trauma; matched 1:1 on sex, age (± 2 years); response rate, 90%	Interviewer-administered standardized questionnaire	<i>Colon</i>		<i>Men</i>	Adjusted for age, calories, fibre from fruit and vegetables; for colon cancer, no significant associations with any specific beverage type; rectal cancer includes those with multiple locations (i.e. colon and rectum); for rectal cancer, only significant association was with beer intake and no association with wine or distilled beverages.
				0 mL ethanol/day	5	1.0	
				1–30.1 mL ethanol/day	22	0.9	
				30.2–53.9 mL ethanol/day	22	0.9	
				54–90.7 mL ethanol/day	19	0.8	
				>90.7 mL ethanol/day	24	1.0	
						<i>Women</i>	
				0 mL ethanol/day	29	1.0	
				1–9.9 mL ethanol/day	22	1.4	
				10–15.5 mL ethanol/day	14	0.9	
15.6–25.8 mL ethanol/day	19	1.3					
>90.7 mL ethanol/day	20	1.4					
		<i>p</i> -trend=0.43					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Riboli <i>et al.</i> (1991) (contd)				<i>Rectal</i>			<i>Men</i>
				0 mL ethanol/day	3	1.0	
				1–30.1 mL ethanol/day	20	1.1	
				30.2–53.9 mL ethanol/day	20	1.0	
				54–90.7 mL ethanol/day	28	1.5	
				>90.7 mL ethanol/day	24	1.3	<i>p</i> -trend=0.42
							<i>Women</i>
				0 mL ethanol/day	21	1.0	
				1–9.9 mL ethanol/day	23	2.0	
				10–15.5 mL ethanol/day	15	1.2	
				15.6–25.8 mL ethanol/day	21	1.7	
				>90.7 mL ethanol/day	18	1.5	<i>p</i> -trend=0.33

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Gerhardsson de Verdier <i>et al.</i> (1993), Stockholm, Sweden, 1986–88	352 colon (163 men, 189 women) and 217 rectal (107 men, 110 women), aged 40–80 years; identified through local hospital and the regional cancer registry; 100% histologically confirmed; response rate, 79%	512 (236 men, 276 women) population-based; selected from complete register of the population; frequency-matched on sex, year of birth (10-year categories); response rate, 82%	Self-administered standardized questionnaire	<i>Colon</i>			Adjusted for sex, year of birth, total energy, protein, dietary fibre, body mass, physical activity, smoking; no differences in associations between men and women; no associations with any specific beverage type
				0–9.9 g ethanol/day	282	1.0	
				10.0–19.9 g ethanol/day	37	0.7 (0.5–1.2)	
				20.0–29.9 g ethanol/day	18	1.2 (0.6–2.3)	
				≥30 g ethanol/day	15	0.9 (0.4–1.8)	
				<i>Rectal</i>			
				0–9.9 g ethanol/day	166	1.0	
10.0–19.9 g ethanol/day	30	1.0 (0.6–1.6)					
20.0–29.9 g ethanol/day	11	1.2 (0.6–2.7)					
≥30 g ethanol/day	10	1.1 (0.5–2.4)					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Hoshiyama <i>et al.</i> (1993), Saitama, Japan, 1984–90	79 colon (37 men, 42 women) and 102 rectal (61 men, 41 women), aged 40–69 years; admitted to a single cancer centre hospital; 100% histologically confirmed; response rate not given	653 (343 men, 310 women) population-based; identified from electoral rolls; frequency-matched on sex, age, class; response rate, 27.5%	Interviewer-administered standardized questionnaires	<i>Colon</i>			Adjusted for sex and age; heavier drinking not associated with increased risk for colon or rectal cancer
				Never	42	1.0	
				Past	2	0.4 (0.0–2.0)	
				Occasional	18	0.6 (0.3–1.1)	
				<50 mL ethanol/day	9	0.3 (0.1–0.8)	
				≥50 mL ethanol/day	9	0.3 (0.1–0.9)	
				<i>Rectal</i>			
				Never	41	1.0	
				Past	2	0.3 (0.0–1.7)	
				Occasional	19	0.5 (0.2–1.0)	
<50 mL ethanol/day	19	0.5 (0.2–1.1)					
≥50 mL ethanol/day	21	0.6 (0.3–1.3)					
Meyer & White (1993), Washington, USA, 1985–89	424 colon, men and women aged 30–62 years; identified through the Seattle-Puget Sound SEER Registry; histological confirmation not given; response rate, 74.7%	414 population-based; identified by random-digit dialling; frequency-matched on sex, age, residence; response rate, 79.1%	Mailed self-administered questionnaire				Adjusted for age, interviewer; no CI provided; the test for trend is that for analysis associated with one-category increment; wine and liquor, but not beer, were associated with colon cancer in men, but no clear associations with beverage type in women.
				<i>Men</i>			
				0 g ethanol/day		1.0	
				0.1–9.9 g ethanol/day		1.9	
				10–29 g ethanol/day		1.7	
				≥30 g ethanol/day		2.6	
				Total consumption		(1.04–1.54)	
						<i>p</i> -trend <0.05	
				<i>Women</i>			
				0 g ethanol/day		1.0	
0.1–9.9 g ethanol/day		1.3					
10–29 g ethanol/day		1.8					
≥30 g ethanol/day		2.5					
Total consumption		(1.03–1.72)					
		<i>p</i> -trend <0.05					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments			
Newcomb <i>et al.</i> (1993), Wisconsin, USA, 1990–91	779 women (536 colon and 243 rectal), aged < 75 years; identified by Wisconsin Cancer Reporting System; histological confirmation not given; response rate, 70%	2315 women; population-based; those aged <65 years selected from the driver's licence lists; those aged 65–74 years identified from the Health Care Financing Administration; response rate, 90%	Telephone interviewer-administered standardized questionnaire	<i>Colon</i>	None	122	1.0	Adjusted for age, body-mass index, screening sigmoidoscopy history, family history of colorectal cancer; colon cancer positively associated with liquor intake, inversely associated with wine intake and not associated with beer intake; rectal cancer positively associated with beer intake and not associated with wine or liquor intake		
				1–2 drinks/week	239	1.0 (0.8–1.3)				
				3–5 drinks/week	77	0.9 (0.6–1.3)				
				6–10 drinks/week	46	0.9 (0.6–1.4)				
				≥11 drinks/week	33	1.3 (0.8–2.2)				
						<i>Rectum</i>				<i>p</i> -trend=0.61
				None	47	1.0				
				1–2 drinks/week	93	0.9 (0.6–1.4)				
				3–5 drinks/week	48	1.5 (0.9–2.3)				
				6–10 drinks/week	26	1.3 (0.8–2.2)				
≥11 drinks/week	19	1.9 (1.0–3.5)	<i>p</i> -trend=0.01							

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Olsen & Kronborg (1993), Funen, Denmark, 1986–90	49 colorectal (21 men, 28 women), aged 45–74 years; selected in two steps from a screening clinical trial, first those with a positive Haemocult II-test, and then those with a cancer on colonoscopy; histologically confirmed; response rate not given	362 (157 men, 205 women); identified as those with a negative Haemocult II-test; matched on date of test, sex, age from first step of selection; response rate not given	Interviewer-administered standardized questionnaire	0% of kcal 1–3% of kcal ≥4% of kcal	17 10 18	1.0 1.4 (0.8–2.3) 0.6 (0.3–1.0)	Adjusted for sex, age, dietary fibre; cases and controls selected from screenees of a Haemocult clinical trial; no statistically significant associations were found between alcohol consumption and cancer.

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Boutron <i>et al.</i> (1995), Côte d'Or, France, 1985–90	171 colorectal (109 men, 62 women), aged 30–79 years; identified from all gastroenterology practices of the region; 100% histologically confirmed; response rate, 79.9%	309 (159 men, 150 women) population-based; selected from the census lists; frequency-matched on age, sex; response rate, 53.5%	Interviewer-administered standardized questionnaire	<10 g ethanol/day	16	<i>Men</i> 1.0	Adjusted for age; for men, a 2.5-fold higher risk associated with cider intake but not with beer or liquors; for women, a 3.4-fold higher risk for colorectal cancer associated with beer intake and no association with cider or liquor intake
				10–19 g ethanol/day	12	1.5 (0.6–4.4)	
				20–39 g ethanol/day	26	1.2 (0.6–2.6)	
				40–59 g ethanol/day	24	1.9 (0.9–4.5)	
				≥60 g ethanol/day	31	1.3 (0.6–2.9) <i>p</i> > 0.1	
						<i>Women</i> 1.0	
		<5 g ethanol/day	41	1.0			
		5–9 g ethanol/day	4	0.6 (0.2–1.8)			
		≥10 g ethanol/day	17	0.9 (0.5–1.9) <i>p</i> > 0.1			
Le Marchand <i>et al.</i> (1997), Hawaii, USA, 1987–91	825 colon (467 men, 358 women) and 350 rectal (221 men, 129 women); identified through the Hawaii Tumor Registry; 100% histologically confirmed; response rate, 66%; age <84 years	1175 (825 men, 350 women); identified from list of Oahu residents who had participated in a Department of Health survey; matched 1:1 on sex, age (±2.4 years); response rate, 71%	Interviewer-administered standardized questionnaire	<i>Right colon</i>		<i>Men</i> 1.0	Adjusted for age, family history of colorectal cancer, pack-years, lifetime physical activity, body-mass index 5 years ago, intake of egg, dietary fibre, calcium, total calories; caloric intake, physical activity and obesity were independently associated with colorectal cancer.
				Never		2.6 (1.4–5.2)	
				Past		2.0 (1.0–3.4)	
				Current		<i>Women</i> 1.0	
				Never		3.1 (1.0–9.4)	
				Past		2.5 (0.9–7.0)	
		Current					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Le Marchand <i>et al.</i> (1997) (contd)				<i>Left colon</i>		<i>Men</i>	
				Never		1.0	
				Past		1.7 (0.8–3.3)	
				Current		1.1 (0.7–2.0)	
						<i>Women</i>	
				Never		1.0	
				Past		1.3 (0.5–3.4)	
				Current		1.0 (0.5–2.3)	
				<i>Rectal</i>		<i>Men</i>	
				Never		1.0	
				Past		1.4 (0.8–2.4)	
				Current		1.1 (0.6–2.0)	
						<i>Women</i>	
				Never		1.0	
Past		1.5 (0.6–4.1)					
Current		1.0 (0.3–3.0)					
Yamada <i>et al.</i> (1997), Tokyo, Japan, 1991–93	66 colorectal (55 men, 11 women) (excluded <i>in situ</i>), aged 34–80 years; examinees of a multiphasic health check-up; 100% histologically confirmed; response rate not given	132 (110 men, 22 women); identified from the same multi-phasic examination; matched 2:1 on sex, age, number of prior health check-ups; response rate not given	Self-administered standardized questionnaire	0 g ethanol/day 1–20 g ethanol/day 21–40 g ethanol/day ≥41 g ethanol/day	23 24 55 30	1.0 1.1 (0.4–3.1) 0.7 (0.3–1.9) 2.0 (0.7–5.4) <i>p</i> -trend=0.09	Adjusted for sex, age, body-mass index, cigarettes smoked per day

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Muñoz <i>et al.</i> (1998), Córdoba, Argentina, 1993–97	146 colon and 44 rectal (89 men, 101 women), aged 23–79 years; admitted to several hospitals in area; 100% histologically confirmed; response rate not given	393 (201 men, 192 women) hospital-based, aged 23–79 years; response rate not given	Interviewer-administered standardized questionnaire	Non-drinker <24 g ethanol/day ≥24 g ethanol/day	40 59 91	1.0 2.2 (1.4–3.7) 3.1 (1.8–5.2) <i>p</i> -trend=0.001	Adjusted for sex, age, social class, body-mass index; no differences in associations between men and women

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Tavani <i>et al.</i> (1998), Italy multi-site, 1991–96	1225 colon (ICD-10 C18.0–18.7; 688 men, 537 women) and 728 rectal (ICD-10 C19 and C20; 437 men, 291 women), aged 24–74 years; identified from area major teaching hospitals; 100% histologically confirmed; response rate, ~96%	4154 (2073 men, 2081 women) hospital-based, aged 20–74 years; admitted to the same network of hospitals; response rate, ~96%	Interviewer-administered standardized questionnaire	<i>Colon</i> Never drinker Ex-drinker 1–11.8 g ethanol/day 11.8–22.7 g ethanol/day 22.7–34.4 g ethanol/day 34.4–51.8 g ethanol/day ≥51.8 g ethanol/day	248 89 169 190 188 172 169	1.0 1.2 (0.9–1.6) 1.2 (0.9–1.5) 1.3 (1.0–1.6) 1.2 (0.9–1.5) 1.1 (0.8–1.4) 1.0 (0.8–1.3) <i>p</i> -trend=0.001	Adjusted for sex, age, education, physical activity, smoking status, family history, intake of β-carotene, vitamin C, total energy; no evidence of interaction with sex or cigarette smoking; strongest associations with spirit, grappa or amari consumption but no association with wine or beer; no differences in associations according to site within the colon

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Tavani <i>et al.</i> (1998) (contd)				<i>Rectum</i>			
				Never drinker	147	1.0	
				Ex-drinker	51	1.1 (0.7–1.5)	
				1–11.8 g ethanol/day	87	1.1 (0.8–1.5)	
				11.8–22.7 g ethanol/day	132	1.5 (1.1–1.9)	
				22.7–34.4 g ethanol/day	114	1.2 (0.9–1.6)	
				34.4–51.8 g ethanol/day	97	0.9 (0.7–1.3)	
				≥51.8 g ethanol/day	100	0.9 (0.7–1.2)	<i>p</i> -trend=0.657

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments	
Ji <i>et al.</i> (2002), Shanghai, China, 1990–92	931 colon (ICD-9 153.0–153.9; 462 men, 469 women) and 874 rectal (ICD-9 154.0–154.9; 463 men, 411 women), aged 30–74 years; identified through the Shanghai Cancer Registry; 95% colon, 98% rectal histologically confirmed; response rate, 92% colon, 91% rectal	1552 (851 men, 701 women) population-based; randomly selected from among Shanghai residents based on personal identification cards; frequency-matched on sex, age (± 5 years); response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>				Adjusted for age, income, cigarette smoking; body-mass index, years of education, diet, history of colorectal polyps and proxy interview status did not confound associations; no differences in risk between proximal and distal colon; for men, associations appeared to be restricted to hard liquor; interaction of alcoholic beverage consumption and cigarette smoking not statistically significant.
				Non-drinker	248	<i>Men</i>	1.0	
				Former drinker	41		2.3 (1.4–3.7)	
				Current drinker	173		1.0 (0.8–1.3)	
						<i>Women</i>		
				Non-drinker	448		1.0	
				Former drinker	6		1.4 (0.4–4.3)	
				Current drinker	15		0.7 (0.4–1.3)	
						<i>Rectum</i>		
				Non-drinker	255	<i>Men</i>	1.0	
				Former drinker	34		1.1 (0.9–1.4)	
				Current drinker	174		0.6 (0.4–1.0)	
		<i>Women</i>						
Non-drinker	390		1.0					
Former drinker	4		1.2 (0.7–2.3)					
Current drinker	17		1.1 (0.3–4.1)					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments				
Sharpe <i>et al.</i> (2002), Montréal, Canada, multisite, 1979–85	355 colon and 230 rectal (ICD-9 153–154; all men), aged 35–70 years; diagnosed at all large hospitals in the region; 100% histologically confirmed; response rate, 85.6%	500 population-based; identified from random-digit dialling or from electoral lists; frequency-matched on age, area of residence; response rate, 72%	Interviewer-administered standardized questionnaire	<i>Proximal colon</i>	Never drank weekly	41	1.0	Adjusted for age, respondent status, ethnicity, family income, years of education, marital status, cigarette smoking; no meaningful associations with wine or spirit intake; heavy beer intake associated with proximal colon, distal colon and rectal cancer			
				Drank weekly	55	1.1 (0.6–1.7)					
				Drank daily	80	1.0 (0.6–1.7)					
							<i>Distal colon</i>		Never drank weekly	28	1.0
							Drank weekly		51	1.4 (0.9–2.5)	
							Drank daily		100	2.3 (1.4–3.7)	
										<i>Rectum</i>	
							Never drank weekly		37	1.0	
							Drank weekly		74	1.5 (0.9–2.4)	
							Drank daily		119	1.6 (1.0–2.6)	
										<i>p</i> -trend=0.06	

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Ho <i>et al.</i> (2004), Hong Kong, 1998–2000	452 colon (251 men, 201 women) and 357 rectal (213 men, 144 women), aged 20–85 years; identified from three public hospitals; 100% histologically confirmed; response rate, 82.2%	926 (530 men, 396 women) hospital-based; inpatients identified from the same departments as the cases admitted for acute, non-malignant surgical conditions; matched on sex, age (± 5 years); response rate, 95.5%	Interviewer-administered standardized questionnaire	<i>Colon</i>			Adjusted for sex, age, geographical distribution, marital status, education, physical activity, analgesia intake, family history of colorectal cancer, smoking habit, diet; showed an inverse relationship with time since stopping drinking.
				Never	219	1.0	
				Former drinker	97	1.0 (0.7–1.3)	
				Current drinker	133	1.5 (1.1–2.0) <i>p</i> -trend=0.02	
				<i>Rectal</i>			
				Never	164	1.0	
Former drinker	84	1.1 (0.7–1.5)					
Current drinker	111	1.3 (1.0–1.9) <i>p</i> -trend=0.1					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Kim <i>et al.</i> (2004), Seoul, Republic of Korea 1998–2000	111 colon and 132 rectal (127 men, 107 women), aged 30–79 years; selected from two university hospitals; 100% histologically confirmed; response rate not given	225 (108 men, 117 women) hospital-based; aged 30–79 years; response rate not given	Interviewer-administered standardized questionnaire	<i>Colon</i>			Adjusted for sex, age, total energy intake, family history of colorectal cancer, body mass index, smoking, vigorous physical activity, red meat intake, <i>MTHFR</i> genotype; no evidence of an interaction of alcoholic beverages with <i>MTHFR</i> genotype on risk for colon, rectal or colorectal cancer
				<5 g ethanol/day	58	1.0	
				5–29 g ethanol/day	23	1.2 (0.6–2.7)	
				≥30 g ethanol/day	30	2.7 (1.2–6.1)	
				<i>Rectal</i>			
				<5 g ethanol/day	81	1.0	
5–29 g ethanol/day	24	0.7 (0.4–1.5)					
≥30 g ethanol/day	27	1.4 (0.7–3.0)					

Table 2.46 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors/ comments
Murtaugh <i>et al.</i> (2004), northern California and Utah, USA, 1997–2001	952 incident rectal, aged 30–79 years, English speaking; in California, cases were members of the Kaiser Permanente Medical Care Program and identified by the Kaiser and Northern California Tumor Registry, in Utah cases were identified by the Utah SEER registry; response rate, 65%	1205; frequency-matched on sex, age (± 5 years); in California, controls selected from the membership lists of Kaiser; in Utah, controls ≥ 65 years randomly selected from social security lists and those aged < 65 years selected from driver's licence lists; response rate, 65.2%	Interviewer-administered diet history	None	251	<i>Men</i>	Adjusted for age, energy, fibre, calcium intake, physical activity; results for alcohol intake in the last 20 years; similar results observed for intake in the previous 10 years; cases with a previous colorectal tumour, familial adenomatous polyposis, ulcerative colitis and Crohn disease were ineligible; not clear if similar exclusion was made for controls; no associations with specific beverage type; results from 10-year use reported when 20-year use data were missing
				Low	183	1.0	
				High	172	0.9 (0.7–1.2)	
				None	227	1.3 (0.9–1.7)	
				Low	116	1.0	
				High	72	1.1 (0.8–1.4)	
						<i>Women</i>	
						1.2 (0.8–1.7)	

CI, confidence interval; MTHFR, methylenetetrahydrofolate reductase; SEER, Surveillance, Epidemiology and End Result

& McMichael, 1986). In the nine studies that showed a significant positive association, the relative risks ranged from approximately 1.5 to 6.4 for the highest versus the lowest level of alcoholic beverage intake (Williams & Horm, 1977; Pickle *et al.*, 1984; Longnecker, 1990; Hu *et al.*, 1991; Meyer & White, 1993; Le Marchand *et al.*, 1997; Sharpe *et al.*, 2002; Ho *et al.*, 2004; Kim *et al.*, 2004). Overall, there were no consistent differences in associations between the proximal and distal colon among the case-control studies.

At least 28 case-control studies have investigated rectal cancer, 18 of which showed no statistically significant association with alcoholic beverage consumption (Wynder & Shigematsu, 1967; Graham *et al.*, 1978; Tuyns *et al.*, 1982; Manousos *et al.*, 1983; Miller *et al.*, 1983; Pickle *et al.*, 1984; Tajima & Tominaga, 1985; Potter & McMichael, 1986; Kune *et al.*, 1987; Ferraroni *et al.*, 1989; Peters *et al.*, 1989; Riboli *et al.*, 1991; Gerhardsson de Verdier *et al.*, 1993; Hoshiyama *et al.*, 1993; Le Marchand *et al.*, 1997; Tavani *et al.*, 1998; Ji *et al.*, 2002; Kim *et al.*, 2004). In two other studies, the relative risk for heavy versus light drinkers was 1.3 (95% CI, 0.9–1.7) (Murtaugh *et al.*, 2004) and that for current versus never drinkers was 1.5 (95% CI, 0.9–1.9) (Ho *et al.*, 2004). Eight studies showed a positive association (Williams & Horm, 1977; Kabat *et al.*, 1986; Freudenheim *et al.*, 1990; Longnecker, 1990; Choi & Kahyo, 1991b; Hu *et al.*, 1991; Newcomb *et al.*, 1993; Sharpe *et al.*, 2002).

The meta-analysis of Longnecker *et al.* (1990) included data from 22 case-control studies (Table 2.45). In that analysis, the relative risk for colorectal cancer associated with an intake of 24 g alcohol per day was 1.07 (95% CI, 1.02–1.12). It should be noted that the results for the five cohort studies were stronger (relative risk, 1.3) than those for case-control studies.

2.8.3 *Potential confounding*

Several studies assessed whether an association between alcoholic beverage consumption and risk for colorectal cancer might be confounded by obesity and/or other lifestyle factors. For heavy alcoholic beverage drinkers and alcoholics, it is reasonable to assume that poor diet in particular could contribute to an apparent association. However, based on studies of alcoholics or men who worked in the brewery industry, there is only limited evidence of an elevated risk for colon or rectal cancer. As noted in the Tables, nearly all of the cohort studies adjusted for sex, age and smoking status, and some included covariates for body-mass index, dietary factors and physical activity. In addition, as described previously, one of the criteria for inclusion of data into the cohort pooling project was available information on diet. This allowed for a detailed assessment of potential confounding by specific dietary factors including total energy, fat, meat, fibre and specific micronutrients. Even after adjustment for all of the dietary factors considered, the association of alcoholic beverage intake with colorectal cancer persisted.

2.8.4 *Effect modification*

Whether the association between alcoholic beverage consumption and the risk for colorectal cancer is modified by gender or lifestyle factors has been examined in some studies (see Tables 2.44–2.46 for details). Some data suggest that associations are stronger for men than for women; levels of alcoholic beverage intake are on average higher among men but, in some studies, the number of cases among women with a high alcoholic beverage intake was insufficient to conduct a detailed analysis. Overall, there is little evidence of a meaningful difference in the association of alcoholic beverage intake with risk for colorectal cancer between men and women.

A few studies examined effect modification by cigarette smoking. In one cohort study, the association of alcoholic beverage consumption with the risk for colorectal cancer was observed only among nonsmokers (Flood *et al.*, 2002). However, at least three other cohort studies (Murata *et al.*, 1996; Otani *et al.*, 2003; Pedersen *et al.*, 2003) and two case–control studies (Tavani *et al.*, 1998; Ji *et al.*, 2002) failed to demonstrate any significant effect modification by smoking.

There is growing interest in the potential effect modification of folate intake. Freudenheim *et al.* (1991) found a nearly fivefold higher risk for rectal cancer among men with a high alcoholic beverage/low folate intake compared with men with a low alcoholic beverage/high folate intake. Subsequently, these findings were supported by those of Giovannucci *et al.* (1995) who found no elevated risk for colon cancer associated with high alcoholic beverage intake among men with high folate intake. However, data from at least two other cohort studies (Flood *et al.*, 2002; Harnack *et al.*, 2002) failed to support a significant interaction between alcoholic beverage and folate intake. In many studies, the power to detect significant interactions might have been limited. Therefore, the modifying effects of folate on alcoholic beverages were also examined in the large cohort pooling project. While not statistically significant ($P>0.2$), the results indicated a slightly stronger association of alcoholic beverage consumption with colorectal cancer for those with low folate intake and essentially no association for those with high folate intake.

Whether the degree of obesity modifies the relationship between alcoholic beverage consumption and risk for colorectal cancer remains unclear since few studies to date have had adequate power to consider this interaction carefully. In the cohort pooling project, the positive association with alcohol consumption was slightly stronger in leaner individuals than in heavier individuals; the relative risk associated with ≥ 30 g ethanol per day compared with 0 g ethanol per day was 1.84 for persons whose body-mass index was < 22 kg/m² but 1.08 for persons with a body-mass index of ≥ 25 kg/m² (p for interaction=0.03).

2.8.5 *Conclusion*

In summary, there is little evidence of a higher than expected risk for colon or rectal cancer among heavy alcoholic beverage drinkers, alcoholics or brewery workers. However, a large body of evidence from prospective cohort studies reported a statistically significant positive association between alcoholic beverage intake and the risk for colon, rectal or colorectal cancer, and no study reported a significant inverse association. These findings are supported by those of a large cohort pooling project and a recent meta-analysis of cohort studies. Although the evidence from individual case-control studies is less consistent, a meta-analysis of 22 case-control studies also supported a positive association. In contrast, two individual case-control studies found an inverse association. The positive association of alcoholic beverage consumption with risk for colorectal cancer does not appear to be confounded by other lifestyle or socio-demographic factors, since most large cohort and case-control studies adjusted for the potential confounding effects of gender, race/ethnicity, age, body-mass index, smoking status and socioeconomic status or education; some of these also adjusted for physical activity and/or specific dietary factors.

Based on data from the pooling project and the most recent meta-analysis of prospective cohort studies, the strength of association appears to be modest with a relative risk of 1.4 for an intake of ≥ 45 g alcohol per day compared with 0 g per day. However, there is uncertainty regarding the dose-response relationship.

The association between alcoholic beverage consumption and the risk for colorectal cancer does not appear to vary according to anatomical site within the large bowel or type of alcoholic beverage. Similarly, based on the available information, there is no consistent evidence of effect modification by gender or smoking status. Whether degree of obesity or dietary factors such as folate intake modify the relationship is unclear, since only a few studies have examined these interactions.

2.9 **Cancer of the pancreas**

2.9.1 *Cohort studies*

(a) Special populations (Table 2.47)

Ten cohort studies of men and women with a high alcoholic beverage intake (i.e. among alcoholics or brewery workers) have reported on the risk for pancreatic cancer. Four studies (Carstensen *et al.*, 1990; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Karlson *et al.*, 1997) found a significant excess risk among heavy alcoholic beverage drinkers compared with the national population, although all of these studies were based on small numbers of cases (i.e. < 50). One study of men employed in a brewery in Sweden (and who were allowed a ration of 1 L of beer per day) and who were followed-up for nearly 20 years reported a significant excess rate of pancreatic cancer. The authors noted that a large reduction in the number of breweries occurred during the

Table 2.47 Cohort studies of pancreatic cancer in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hakulinen <i>et al.</i> (1974), Finland, Alcohol Misuse Records and Alcoholics	205 000 male 'alcohol misusers' registered for convictions for drunkenness, 1944–59; 4370 alcoholic men on Social Welfare Register, aged ≥ 30 years, 1967–70; follow-up until 1970	Incidence rates compared with national population rates	Population rate (Exp) Alcoholics (Obs)	2.2 4	NS		Results not stated for cohort of alcoholics on Social Register; no individual exposure data; no information on potential confounders
Monson & Lyon (1975), Massachusetts, USA	1382 men and women hospitalized with alcoholism in 1930, 1935, 1940; mortality follow-up until 1971	Mortality rates compared with US whites	Population rate (Exp) Alcoholics (Obs)	5.1 3	1.0 0.6	Age, sex, calendar time	Half lost to follow-up; no individual exposure data; no information on potential confounders
Dean <i>et al.</i> (1979), Ireland, Dublin Brewers	1628 deaths recorded 1954–73 in male brewery workers (average intake, 58 g/day)	Mortality rates compared with local population rates	Population rate (Exp) Brewers (Obs)	14 17	1.0 1.09 (NS)		Predominantly beer intake; no individual exposure data; no information on potential confounders

Table 2.47 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Jensen (1979), Denmark, Danish Brewery Workers Union	14 313 brewers (free 2-L daily ration of beer) and 1063 mineral water factory workers, recruited from 1943; follow-up until 1973; 44 cases identified through registry/death certificates	Incidence and mortality rates compared with national rates	Population rate (Exp)	40	<i>Incidence</i> 1.0	Age, sex, area, time	No individual exposure data; no information on potential confounders
			Brewers (Obs)	44	1.09 (0.80–1.47)		
			Population rate (Exp)	41	1.0		
			Brewers (Obs)	44	1.08 (0.78–1.44)		
Robinette <i>et al.</i> (1979), US Army Veterans	4401 men hospitalized with alcoholism and 4401 with nasopharyngitis recruited 1944–45; matched by age; follow-up of mortality until 1975	None	Nasopharyngitis Alcoholism	5 4	1.0 0.87 (0.22–3.25) ^a	Age	Mortality only; ~50% aged <30 years at entry; no individual exposure data; no information on potential confounders
Schmidt & Popham (1981), Ontario, Canada	9889 men hospitalized for alcoholism, 1951–70; follow-up until 1971	Mortality rates compared with regional rates	Population rate (Exp) Alcoholics (Obs)	9.24 11	1.0 1.19 (NS)		No individual exposure data; no information on potential confounders

Table 2.47 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI) <i>p</i> -value	Adjustment factors	Comments
Carstensen <i>et al.</i> (1990), Sweden, Cancer Environment Register	6230 male brewers listed in 1960 census, aged 20–69 years (ration of 1 L/day); follow-up until 1979; 38 cases identified through registry	Incidence rates compared with national rates	Population rate (Exp)	23	1.0	Age, follow-up period, region	Reduction in breweries in 1960–80 so potential misclassification of jobs probable, no individual exposure data; no information on potential confounders
			Brewers (Obs)	38	1.66 (1.18–2.28) <i>p</i> -value <0.01		
Tønnesen <i>et al.</i> (1994), Denmark, Copenhagen Alcoholics	18 307 male and female alcoholics, recruited 1954–87 from outpatient clinics (~200 g ethanol/day); follow-up until 1987	Incidence rates compared with national rates	Population rate (Exp)	31	1.0	Age, sex, calendar time	Most drank beer; not adjusted for smoking; no individual exposure data; no information on potential confounders
			Alcoholics (Obs)	41	1.3 (1.0–1.8) <i>p</i> -value ≤0.05		
Sigvardsson <i>et al.</i> (1996), Sweden	15 508 alcoholic women (Temperance Board records/convictions) in 1947–77 and comparison group of 15 508 women, matched by age and region (population register); follow-up not stated; 48 cases identified by registry	Incidence rates in alcoholics compared with rates in matched comparison group	Comparison group	18	1.0	Matching factors	Excluded ~6000 older women with no identity number; large changes in alcoholic beverage availability and attitudes during follow-up; no individual exposure data; no information on potential confounders
			Alcoholics	48	2.7 (1.6–4.6)		

Table 2.47 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Karlson <i>et al.</i> (1997); Ye <i>et al.</i> (2002), Sweden, Inpatient Hospital Register (retrospective cohort)	Karlson <i>et al.</i> (1997): Analytical cohort of 4043 patients discharged with pancreatitis associated with alcoholism, 1965–83; mean age, 46 years; follow-up until 1989; 15 cases (13 men, 2 women) (excluding 1 year of follow-up) Ye <i>et al.</i> (2002): 178 688 male and female patients with hospital discharge of alcoholism, 1964–95; 305 cases identified through cancer registry (excluding 1 year of follow-up)	Incidence rates compared with national rates	Population (Exp) Alcoholics (Obs) Population (Exp) Alcoholics (Obs)	Not stated 15 222 305	1.0 2.9 (1.6–4.8) 1.0 1.4 (1.2–1.5)	Age, sex, calendar year	No individual exposure data; no information on potential confounders Increased risk in men and women separately, but not adjusted for smoking; increased risk among younger patients

CI, confidence interval; Exp, expected; NS, not significant; Obs, observed; SIR, standardized incidence ratio; SMR, standardized mortality ratio

^a 90% confidence interval

follow-up period (1960–80), and that potential misclassification of exposure is probable (Carstensen *et al.*, 1990). Three cohort studies of alcoholics in Sweden and Denmark also reported significant excess rates of pancreatic cancer compared with national incidence rates (Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Ye *et al.*, 2002), matched by age, sex and calendar time.

None of these studies provided individual exposure data and thus dose–response relationships could not be examined and potential confounding factors such as cigarette smoking could not be taken into account. Finally, it must be noted that high alcoholic beverage consumption may induce chronic pancreatitis, a known risk factor for pancreatic cancer. One study based on hospital discharge records in Sweden found that the rate of pancreatic cancer among patients with pancreatitis associated with alcoholism was higher than that among the national population, but similar to the rates found among patients with chronic or recurrent pancreatitis as a whole (Karlson *et al.*, 1997).

(b) *General population (Table 2.48)*

Twelve cohort studies examined alcoholic beverage consumption and the subsequent risk for pancreatic cancer in the general population. Three studies reported a significant excess risk with increased alcoholic beverage intake (Klatsky *et al.*, 1981; Heuch *et al.*, 1983; Zheng *et al.*, 1993). An early report from the Kaiser-Permanente study found a significantly increased risk for men and women who drank ≥ 6 drinks per day compared with non-drinkers (Klatsky *et al.*, 1981), although this was not confirmed in a subsequent follow-up (Hiatt *et al.*, 1988; Friedman & van den Eeden, 1993). Another study reported an excess risk among those with a frequent intake (i.e. ≥ 14 times per month) compared with none or very limited use (Heuch *et al.*, 1983). [Data on smoking history were only available for a sub-sample of the cohort (~5000 men) and this relative risk estimate was therefore based on small numbers. Further, the excess risk appeared to be weaker among cases without histological confirmation, which suggests that some selection bias may have occurred.] A cohort study conducted among the Lutheran Brotherhood in the USA also reported a significant threefold excess risk for death from pancreatic cancer among men who drank 10 or more times per month compared with never drinkers after adjustment for age and smoking, based on 57 deaths (Zheng *et al.*, 1993).

The majority of the studies, most of which were conducted in the USA and Japan among populations with low to moderate alcoholic beverage intake, have not found a significant association between alcoholic beverage intake and pancreatic cancer. One cohort study in Japan reported a significant excess risk among former drinkers compared with never drinkers (Inoue *et al.*, 2003), which was seen in both men and women. [Former drinkers may have ceased drinking because they are ill, causing a spuriously high relative risk in this category.]

All of these cohort studies adjusted for cigarette smoking, and some incorporated adjustments for other potential confounders such as diet, diabetes and family history.

Table 2.48 Cohort/nested case–control studies of pancreatic cancer and alcoholic beverage consumption in the general population

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Klatsky <i>et al.</i> (1981); Hiatt <i>et al.</i> (1988); Friedman & van den Eeden (1993), USA, Kaiser-Permanente Medical Care Program	Klatsky <i>et al.</i> (1981): Nested case–control study of 8060 men and women in health plan; recruited 1964–68; high-intake group (2084) matched to 3 controls with varying intake (age, date, race, sex, smoking, location); follow-up till 1976; 16 deaths identified from death certificates	Self-administered questionnaire	<i>Usual drinks/day</i> 0 ≤2 3–5 ≥6	16 deaths 2 5 3 6	Not stated ≥6 versus ≤2, $p=<0.01$	Matching factors	

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
(contd)	Hiatt <i>et al.</i> (1988)/ Analytical cohort of 122 984 men and women receiving health check-ups; baseline at 1978; follow-up until 1984; 48 cases identified through hospital discharge data and cancer registry. histologically confirmed, 76%		<i>Drinks/day</i> None Past <1 >1	48	1.0 2.6 (0.8–8.6) 1.3 (0.5–3.1) 0.9 (0.3–2.7)	Age, sex, race, blood glucose level, smoking, coffee	

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
(contd)	Friedman & van den Eeden (1993): Nested case-control study from original recruitment date of 1964; aged 15–94 years; follow-up until 1988; 450 cancers identified through hospital discharge data and cancer registry verified through medical records; 2687 controls matched on age, sex, site, date of recruitment		<i>Use in last year (drinks/day)</i> None <3 ≥3	450	1.0 1.12 (0.85–1.48) 1.35 (0.90–2.03)	Age, race, smoking	35% of cases diagnosed within 1 year of entry; no association with getting drunk on workdays, drinking in the morning, heavy alcohol user (yes versus no) or spouse having a drinking problem

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Kono <i>et al.</i> (1986), Japan, Japanese Physicians	Analytical cohort of 5135 men recruited in 1965; follow-up until 1983; 14 deaths identified from death certificates; response rate, 51%	Self-administered questionnaire	<i>Intake in last 20 years</i>			Age, smoking	No association for daily versus none; low response rate
			None	3	1.0		
			Former	2	1.9 (0.3–11.7)		
			Occasional	5	1.4 (0.3–5.9)		
			<2 go (sake)/day	1	0.4 (0.0–4.0)		
			≥2 go (sake)/day	3	1.5 (0.3–7.9)		
Zheng <i>et al.</i> (1993), USA, Lutheran Brotherhood Insurance Society	Analytical cohort of 17 633 men, aged ≥35 years, recruited 1966; follow-up until 1986; 57 deaths identified from death certificates	Self-administered questionnaire	<i>Total intake (times/month)</i>			Age, smoking	Low alcohol intake (26% ≤2.5 drinks/week); significant increased risk for beer and spirits
			Never	7	1.0		
			<3	13	2.0 (0.5–5.2)		
			3–9	13	3.6 (1.4–9.3)		
			≥10	18	3.1 (1.2–8.0)		
Shibata <i>et al.</i> (1994), USA, Laguna Hills Residents, Los Angeles	Analytical cohort of 13 976 men and women recruited 1982; 80% aged 65–80 years; follow-up until 1990; 65 cases identified from pathology reports from participating hospitals	Self-administered questionnaire	<i>Drinks/day</i>			Age, sex, smoking	
			<1	24	1.0		
			1–2	27	1.01 (0.58–1.77)		
			>2	12	0.91 (0.44–1.88)		

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Harnack <i>et al.</i> (1997), USA, Iowa Women's Health Study	Analytical cohort of 33 976 women, aged 55–69 years, recruited 1986; follow-up for incidence and mortality through registry until 1994; 66 cases (verification not stated)	Self-administered questionnaire	<i>Drinks/week</i>				Age, smoking	Increased risk for spirits (>1 unit/ week, 2.1) and also seen in never smokers, but small numbers
			None	29	1.0			
			0.5–2	18	1.46 (0.81–2.63)			
			>2	19	1.65 (0.90–3.03)			
			<i>p</i> for trend		0.11			
Coughlin <i>et al.</i> (2000), USA, Columbia, Puerto Rico, American Cancer Society, Cancer Prevention Study-II	Analytical cohort of 1.2 million men and women, recruited 1982, aged ≥30 years; mortality follow-up until 1996; 3751 deaths (1967 men, 1784 women) identified from death certificates	Self-administered questionnaire	<i>Drinks/day</i>				Age, race, education, family history, gallstones, diabetes, body-mass index, smoking, red meat, citrus fruit and juices, vegetable intake	Cases not verified; no interaction with smoking
			<i>Men</i>					
			None	329	1.0			
			Some	198	0.9 (0.8–1.1)			
			1	226	0.9 (0.8–1.1)			
			>1	564	0.9 (0.8–1.1)			
			<i>Women</i>					
			None	390	1.0			
Some	194	0.9 (0.8–1.1)						
1	151	0.8 (0.7–1.0)						
>1	244	0.9 (0.8–1.1)						

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Michaud <i>et al.</i> (2001), USA, HPFS and NHS	Analytical cohort of 136 593 men and women, using data from 1980 and 1986; follow-up until 1996 (women, aged >30 years); and 1998 (men, aged 40–75 years); self-reported cases verified by pathology and medical records	Self-administered questionnaire	<i>Intake (g/day)</i> 0 0.1–1.4 1.5–4.9 5–29.9 ≥30 <i>p</i> for trend	288	1.0 0.78 (0.47–1.30) 1.15 (0.78–1.69) 1.0 (0.69–1.44) 1.0 (0.57–1.76) 0.94	Age, smoking, body-mass index, diabetes, cholecystectomy, energy intake, time period	No association for type of beverage or with past heavy drinking; no association by body mass index, age or smoking
Stolzenberg-Solomon <i>et al.</i> (2001), Finland, ATBC Cancer Prevention Study	Analytical cohort of 27 101 male smokers, aged 50–69 years, recruited 1985; follow-up until 1997; 157 cases identified through cancer registry; histologically confirmed, 79%	Self-administered questionnaire	<i>Intake (g/day)</i> None <5.4 5.4–13.4 13.5–27.7 ≥27.8 <i>p</i> for trend	14 39 38 32 34	1.0 1.39 (0.75–2.56) 1.39 (0.75–2.56) 1.24 (0.66–2.32) 1.40 (0.75–2.62) 0.71	Age, intervention arm, adjustment for other factors made little difference	

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Isaksson <i>et al.</i> (2002), Sweden, Swedish Twin Registry	Analytical cohort of 21 884 men and women recruited in 1961, aged 36–75 years; followed-up between 1969 and 1997; 176 cases identified through cancer registry; histologically confirmed, 90%	Self-administered questionnaire; alcohol consumption derived from 1967 questionnaire	<i>Alcohol intake (g/month)</i>			Age, sex, smoking		
			None	52	1.0			
			1–209	86	0.89 (0.61–1.30)			
			≥210	11	0.78 (0.39–1.55)			
Lin <i>et al.</i> (2002), Japan, Japan Collaborative Cohort	99 527 men and women, recruited 1988–90, undergoing health check, aged 40–79 years; follow-up until 1997 for mortality; 191 deaths (94 men, 97 women) with information on alcoholic beverages	Self-administered questionnaire	<i>Intake (g/day)</i>			Age, smoking	No association in women; no association by duration or lifetime intake	
			None	Men	Men			
			Former	26	1.0			
			0–29	6	0.74 (0.30–1.82)			
			30–69	35	1.16 (0.66–2.04)			
			≥60	20	1.07 (0.56–2.06)			
	7	0.98 (0.39–2.46)						
		<i>p</i> for trend			0.76			

Table 2.48 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Inoue <i>et al.</i> (2003), Japan, HERPACC	Nested case–control study of hospital patients, aged 32–85 years, recruited 1988–99; follow-up until 2000; 200 cases (122 men, 78 women), 2000 controls (non-malignant), matched by age, sex	Self-administered questionnaire	<i>Alcohol drinking</i> Never Former Current	111 37 52	1.0 3.70 (2.28–6.00) 0.50 (0.34–0.73)	Age, sex, family history, diabetes, physical activity, bowel habits, raw vegetable intake	Increased risk in men and women, separately; the increased risk in former drinkers may be due to ill-health.

ATBC, α -Tocopherol β -Carotene; CI, confidence interval; HERPACC, Hospital-based Epidemiologic Research Program at Aichi Cancer Center; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study

However, where crude and multivariate data were presented together, adjustment for these factors appeared to make little difference to the estimates for alcoholic beverage intake.

There are very limited data on the effect of duration of alcoholic beverage drinking or cessation of drinking on the risk for pancreatic cancer; those studies that have reported risks for former drinkers compared with never drinkers have shown highly inconsistent results.

2.9.2 Case-control studies (Table 2.49)

Twenty-nine case-control studies have published quantitative data on the association of alcoholic beverage intake and the risk for pancreatic cancer. Most studies found no association (see Table 2.49). Several studies suggested that heavy alcoholic beverage consumption (≥ 15 drinks/week) may be associated with an increased risk for pancreatic cancer (Falk *et al.*, 1988; Cuzick & Babiker, 1989; Ferraroni *et al.*, 1989; Olsen *et al.*, 1989; Silverman, 2001). Other studies have reported significant reductions in risk with increasing alcoholic beverage intake (Gold *et al.*, 1985; Baghurst *et al.*, 1991; Talamini *et al.*, 1999).

There is no consistent evidence that intake of any specific type of beverage is associated with risk for pancreatic cancer.

The difference in findings may be partly due to differences in study design. In many of these case-control studies, a large proportion of cases were deceased, which resulted in interviews being conducted among the next of kin. Although some studies suggest that spouse proxies give reasonable estimates of alcoholic beverage intake, many interviews were conducted with a child, friend or other relative, which may result in substantial exposure misclassification and/or recall bias. Further, studies that only included cases that were histologically verified may not be representative of all cases and may lead to bias if high alcoholic beverage intake is associated with reduced access to medical care. In addition, selection bias due to low response rates, possible confounding by tobacco smoking, failure to exclude controls who had tobacco- and alcohol-related diseases and chance findings as a result of small sample size may also contribute to these discrepant results.

2.10 Cancer of the lung

A possible link between alcoholic beverage consumption and the risk for lung cancer has long been speculated; however, epidemiological evidence has been considered to be inconclusive. The data available to the previous IARC Working Group (IARC, 1988) did not allow the conclusion that the association between consumption of alcoholic beverages and lung cancer was causal.

Lung cancer is the most common and fatal cancer in the world. The major cause of lung cancer is tobacco smoking, to which 80–90% of cases are attributable. A high

Table 2.49 Case-control studies of pancreatic cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Williams & Horm (1977), USA, Third National Cancer Survey, 1969-71	7518 (all sites, men and women), aged ≥ 35 years; histological confirmation not stated; 57% randomly selected	Randomly selected patients with cancer of other non-related sites	Interviewer-administered questionnaire	<i>Glasses/</i>		Age, race, smoking	
				<i>year</i>	<i>Men</i>		
				None	1.0		
				51	0.72		
				≥ 52	1.34		
					<i>Women</i>		
	None	1.0					
	51	0.58					
	≥ 52	0.59					
MacMahon <i>et al.</i> (1981), Boston, Rhode Island, USA, 1974-79	369 (218 men, 151 women), aged ≤ 79 years; 100% histologically confirmed; response rate, ~68%	644 hospital-based, matched by physician, excluding pancreas/liver disease and tobacco-/alcohol-related diseases; 42% other cancers; response rate, ~61%	Interviewer-administered questionnaire	<i>Alcohol drinking</i>		Physician, time of hospitalization, age	No proxies used; no association in men or women separately, or by type of beverage
				Non-drinker	1.0		
				Ever	0.9 (0.6-1.3)		
				Regular	0.8 (0.5-1.3)		
Manousos <i>et al.</i> (1981), Greece, 1976-77	50 (32 men, 18 women), all ages; 100% histologically confirmed; response rate not stated	206 hospital-based (non-malignant, excluding liver/pancreas disease); response rate not stated	Not stated; standard record form obtained from patient	<i>Alcohol drinking (g/day)</i>		Age, sex	
				≤ 10	1.0		
				> 10	0.7 (0.3-1.3)		

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Durbec <i>et al.</i> (1983), France, 1979–80	69 (37 men, 32 women), aged 30–90 years; 100% histologically confirmed; response rate not stated	199 population-based (door-to-door); matched by age, sex, type of residence (no digestive diseases); response rate not stated	Interviewer-administered questionnaire	<i>Alcohol intake (g/day)</i> Per 10 g/day Duration (per year)	1.24 (1.05–1.44) 0.72 (0.53–0.98)	Matching factors plus carbohydrate, fats; adjustment for smoking made no difference	
Wynder <i>et al.</i> (1983), USA, American Health Foundation, 1977–81	275 (153 men, 122 women), aged 20–80 years; 100% histologically confirmed; response rate, 45%	7994 hospital-based (non-tobacco-related diseases); matched by age, sex, race, ward; response rate, 35%	Interviewer-administered questionnaire	<i>Alcohol use (oz/day)</i> 0 <1 1–3 3–5 ≥5	<i>Men only</i> 1.0 1.2 (0.70–1.96) 1.1 (0.64–1.96) 1.0 (0.51–2.01) 1.6 (0.92–2.63)	Age, smoking	No association for women
Gold <i>et al.</i> (1985), Baltimore, USA, 1978–80	201 men and women; age range not stated; 62% histologically confirmed; response rate, 70%	201 hospital- and population-based; hospital (non-malignant) matched on age, sex, race, hospital, date of admission; population (random-digit dialling) matched on age, sex, telephone exchange area; response rate not stated	Interviewer-administered questionnaire	<i>Wine intake 1 year ago (glasses/week)</i> Never Ever	1.0 0.52 (0.32–0.84) <i>p</i> -value=0.007 (population controls)	Matching factors plus religion, occupation, smoking	Relative risk, 0.86 (NS) for hospital controls; 75% of case interviews with proxies

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mack <i>et al.</i> (1986) Los Angeles, USA, 1976	490, aged <65 years; ~80% histologically confirmed; response rate, 67%	Population-based (neighbourhood algorithm); matched by age, sex, race, area; response rate not stated	Interviewer-administered questionnaire	<i>Alcohol (g/day)</i> Reference <40 40–79 ≥80	1.0 0.7 (0.5–1.1) 0.8 (0.5–1.3) 1.2 (0.7–2.2)	Matching factors	~75% cases had proxy information; no association by smoking status
Norell <i>et al.</i> (1986), Sweden, 1982–84	99 (55 men, 44 women), aged 40–79 years; final diagnosis based on resection or autopsy (61%), radiology and biopsy (33%), or clinical and radiological evidence alone (6%); response rate, ~80%	138 population-based (birth records); matched by age, sex; 163 hospital (hernia); matched by age, sex; response rate, 85 and 90%	Self-administered questionnaire, followed by telephone interview if necessary	<i>Past intake (g/day)</i> 0–1 2–9 ≥10 0–1 2–9 ≥10	<i>Population controls</i> 1.0 0.7 (0.5–1.2) 0.6 (0.3–1.1) <i>Hospital controls</i> 1.0 0.5 (0.3–0.9) 0.5 (0.3–1.0)	Matching factors	16% of cases had proxy information
Voirol <i>et al.</i> (1987), Switzerland, 1976–80	88 (43 men, 45 women) confirmed by clinicians; age range not stated; 67% histologically confirmed	336 population-based; matched by age; response rate, 64%	Interviewer-administered questionnaire	<i>Beer (per dL intake)</i> None 1.3 <i>Wine (per dL intake)</i> None 1.8	1.0 2.85 (significant) 1.0 0.86 (NS)		

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Falk <i>et al.</i> (1988), Louisiana, USA, 1979–83	363; 82% histologically confirmed; response rate, 86%	1234 hospital-based (non-malignant); matched on age, sex, race; response rate, 87%	Interviewer-administered questionnaire	<i>Highest intake (drinks/week)</i> None <6 6–11 12–26 ≥27	<i>Men only</i> 1.0 2.04 1.38 1.07 1.50	Age, respondent type, smoking, residence, income, diabetes, fruit intake	53% cases and 13% controls with proxy information; no association in women; no association by type of beverage
Cuzick & Babiker (1989), United Kingdom, 1983–86	216, all ages; 30% histologically confirmed; response rate not stated	212 hospital-based (non-malignant); 67 general practitioners; response rate not stated	Interviewer-administered questionnaire	<i>Intake 1 year ago (units/week)</i> None <4 4–14 ≥15 Former	1.0 0.95 0.97 1.73 2.71 (significant) <i>p</i> for trend <0.1	Age, sex, social class, urbanization, smoking	Increased risk for intake 10 years ago (≥15 units/week: relative risk, 2.3); strongest association with beer
Ferraroni <i>et al.</i> (1989), Italy, 1983–88	214, aged <75 years; 100% histologically confirmed; response rate, >98%	1944 hospital-based (non-malignant, non-digestive tract disorders, not related to tobacco, alcohol or coffee intake, and not requiring long-term modification to diet); response rate, >98%	Interviewer-administered questionnaire	<i>Alcohol intake (drinks/day)</i> <3 3–6 >6 <i>p</i> for trend	1.0 1.14 1.46 NS	Age, sex, social class, education, marital status, smoking, coffee intake	Most (>90%) drank wine only

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Olsen <i>et al.</i> (1989), Minneapolis, USA, 1980–83	212 men (death as stated on death certificate), aged 40–84 years; 66% histologically confirmed; response rate, 85%	220 population-based (random-digit dialling); matched by age, race; response rate, >70%	Interviewer-administered questionnaire	<i>Intake 2 years before death (drinks/day)</i> 0 1 2–3 ≥4	1.0 0.77 (0.47–1.30) 1.42 (0.67–3.03) 2.69 (1.00–7.27)	Age, education, diabetes, smoking, meat, vegetable intake	100% proxy information from cases and controls; increased risk for high intake of beer (≥4 drinks/ day)

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments	
Bouchardy <i>et al.</i> (1990), pooled analysis of studies in France, Italy, Switzerland, 1976-85	494 Italy: 245, aged <75 years; 100% histologically confirmed; recruited 1983–88; response rate, >97% France: 171; age range not stated (mean age, 63 years); 64% histologically confirmed; recruited 1982–85; response rate, >80% Switzerland: 91; age range not stated; 67% histologically confirmed; recruited 1976–81; response rate, 16%	1704 Italy: 1082 hospital-based (non-malignant, non-digestive tract disorders, unrelated to tobacco or alcohol); response rate, >97% France: 268 hospital-based (first group cancer unrelated to tobacco, second group non-malignant unrelated to tobacco); matched by age, sex, interviewer; response rate not stated Switzerland: 383 population-based (through population register); matched by age, sex; response rate, 64%	Interviewer-administered questionnaire	<i>Alcohol intake (glasses/day)</i>			Age, sex, social class, smoking	No association for wine, beer or spirits; significant negative association with increasing alcohol intake in the French study, due to wine consumption; significant positive association with beer intake in the Swiss study; no difference by smoking status
				None	1.0			
				<2	0.9 (0.6–1.2)			
				<3	0.9 (0.6–1.2)			
				<4	1.1 (0.7–1.7)			
				4–5	0.7 (0.5–1.1)			
				6–7	1.0 (0.6–1.6)			
				≥8	0.8 (0.5–1.3)			
<i>p</i> for trend	NS							

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Baghurst <i>et al.</i> (1991), Australia, 1984–87	104 (52 men, 52 women), all ages; verified through medical records; response rate, 62%	253 population-based (electoral roll); matched by age, sex; response rate, ~50%	Self-administered questionnaire checked by interviewer	<i>Intake 1 year before interview (g/day)</i>	1.0	Age, sex, smoking	Proxy interview required for ~10% cases
				None	0.64 (0.34–1.23)		
				0–4.4	0.41 (0.20–0.82)		
				4.5–17.8	0.41 (0.19–0.87)		
				≥17.9	0.41 (0.19–0.87)		
					<i>p</i> for trend=0.004		
Farrow & Davis (1990), Washington, USA, 1982–86	148 men, aged 20–74 years; 46% histologically confirmed; response rate, 68%	188 population-based (random-digit dialling); matched by age; response rate, 68%	Telephone-interview questionnaire	<i>Usual intake 3 years before diagnosis (drinks/week)</i>	1.0	Age, smoking, race, education	No association for type of beverage
				<4	0.7 (0.4–1.2)		
				4–14	0.8 (0.5–1.4)		
				≥15	0.8 (0.5–1.4)		
Ghadirian <i>et al.</i> (1991), Canada, 1984–88	179 (97 men, 82 women), aged 35–79 years; all clinical or histological diagnoses; response rate, 60%	239 population-based (random digit-dialling and telephone directory listings); matched by age, sex, area; response rate not stated	Interviewer-administered questionnaire	<i>Total intake (g)</i>	1.0	Age, sex, education, response status	75% of case interviews with proxies (17% controls); no association for type of beverage
				Never	0.59 (0.26–1.34)		
				2840	1.0 (0.44–2.29)		
				11 171	0.71 (0.31–1.61)		
				34 554	0.65 (0.30–1.44)		
709 560	0.65 (0.30–1.44)						

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Jain <i>et al.</i> (1991), Canada, 1983–86	249 men and women admitted to hospital, aged 35–79 years; 69% histologically confirmed; response rate, 46%	505 population-based (residence lists); matched by age, sex, borough, proxy; response rate, 39%	Interviewer-administered questionnaire	<i>Lifetime intake</i> (g) None 0–32 600 32 600–162 150 ≥162 150 per 250 000 g	1.0 0.91 (0.55–1.52) 0.78 (0.47–1.31) 0.86 (0.50–1.47) 0.94 (0.79–1.12)	Matching factors plus smoking, energy intake, fibre intake	78% cases had proxy interview, matched with proxy control; no association with type of beverage
Bueno de Mesquita <i>et al.</i> (1992), Netherlands, 1984–88	176 men and women, aged 35–79 years; 68% histologically confirmed; response rate, >90%	487 population-based (local registries); matched by age, sex; response rate, >65%	Interviewer-administered questionnaire	<i>Lifetime intake</i> (g) Never <22 471 22 472–128 971 ≥128 972	1.0 0.97 (0.53–1.77) 0.93 (0.49–1.76) 1.25 (0.65–2.43) <i>p</i> for trend=0.55	Age, sex, response status, lifetime smoking, energy intake, vegetables	Significant negative association for white wine; 42% of case interviews with proxy (29% controls)
Lyon <i>et al.</i> (1992), Utah, USA, 1984–87	149 reviewed by medical records, aged 40–79 years; response rate, 88%	363 population-based (random-digit dialling, HCFA); matched by age, sex, county; response rate, 77%	Interviewer-administered questionnaire (by telephone)	<i>Alcohol use</i> Never Ever	1.0 1.6 (1.08–2.38)	None	100% information from proxies

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mizuno <i>et al.</i> (1992), Japan, 1989–90	124 (68 men, 56 women); histological confirmation not stated; response rate not stated	124 hospital-based (non-malignant); matched by age, sex, hospital; response rate not stated	Questionnaire (not stated if self- or interviewer-administered)	<i>Frequency of intake (times/week)</i> None 1–2 1–2 3–5 Every day	1.0 1.20 (0.51–2.85) 1.07 (0.35–3.26) 0.74 (0.28–1.95) 1.24 (0.56–2.71)	Matching factors	No association with age when drinking started duration, or quantity of sake or beer; controls included patients with digestive diseases
Kalapothaki <i>et al.</i> (1993), Greece, 1991–92	181 undergoing surgery (115 men, 66 women); 100% histologically confirmed; response rate, 90%	181 hospital-based (excluding disease related to diet, non-malignant, no gastrointestinal disease) and 181 visitors (residents of area and visitors to hospital); matched by age, sex, hospital; response rate, 93%	Interviewer-administered questionnaire	<i>Glasses/day</i> 0 <1 1–2 3–4 ≥4 per 1 glass/day	<i>Visitor controls</i> 1.0 0.94 (0.52–1.72) 1.09 (0.52–2.26) 0.62 (0.20–1.91) 0.81 (0.39–1.68) 0.96 (0.83–1.11)	Matching factors (for continuous variable, past residence, education, diabetes)	No association with hospital controls

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zatonski <i>et al.</i> (1993), Poland, 1985–88	110 (68 men, 42 women), confirmed by clinical and pathological records; 44% histologically confirmed; response rate, 77%	195 population-based (method not stated); matched on age, sex, residence; response rate, 87%	Interviewer-administered questionnaire	<i>Lifetime intake</i> Never Ever	1.0 1.29 (0.67–2.48)	Age, sex, education, tea, coffee, smoking	71% of cases (0% of controls) used proxy; increased risk for spirits (Q4, 2.5; $p=0.07$), the most common drink consumed
Gullo <i>et al.</i> (1995), Italy, 1987–89	570 (319 men, 251 women), aged 22–79 years; 70% histologically confirmed	570 hospital-based (non-malignant); matched by age, sex, social class, region	Interviewer-administered questionnaire	<i>Alcohol (g/day)</i> 0 <50 50–100	1.0 0.76 (0.56–1.04) 1.06 (0.63–1.77)	Age, sex	No association for men or women; most drank wine
Ji <i>et al.</i> (1995), China, 1990–93	451 (264 men, 127 women) identified through registry, aged 30–74 years; 57% histologically/surgically confirmed; response rate, 78%	1552 population-based (resident registry); matched by age, sex; response rate not specified	Interviewer-administered questionnaire	<i>Alcohol intake (g/week)</i> None <161 161–332.4 332.5–564 ≥565	<i>Men</i> 1.0 0.7 (0.4–1.3) 1.1 (0.7–1.8) 0.9 (0.5–1.4) 0.9 (0.5–1.4)	Age, income (women only: green tea, education)	Next of kin attended interviews for 38% of cases, 10% of controls; no association with duration, lifetime alcohol intake or type of beverage

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Silverman <i>et al.</i> (1995); Silverman (2001), USA, 1986–89	486 surviving men and women (307 white, 179 black), aged 30–79 years; confirmed through medical records; response rate, 46% (white) and 44% (black)	2109 (1164 white, 945 black) population-based: 1. aged 30–64 years (random-digit dialing); matched by age, sex, ethnicity; response rate, 78% for both white and black; 2. aged 65–79 years (HCFA), stratified random sample; response rate, 73% (white) and 78% (black)	Interviewer-administered questionnaire	<i>Alcohol consumption (drinks/week)</i> Never 1–<8 8–<21 21–<57 ≥57 Never 1–<8 8–<21 21–<57 ≥57 <i>p</i> for trend Never 1–7 8–20 21–56 Never 1–7 8–20 21–56 <i>p</i> for trend	<i>White men</i> 1.0 0.8 (0.5–1.44) 0.8 (0.4–1.3) 1.0 (0.6–1.9) 1.4 (0.6–3.2) <i>Black men</i> 1.0 0.6 (0.2–1.6) 1.2 (0.5–2.6) 0.6 (0.2–1.6) 2.2 (0.9–5.6) 0.04 <i>White women</i> 1.0 0.7 (0.4–1.1) 0.4 (0.2–0.9) 0.9 (0.3–3.0) <i>Black women</i> 1.0 1.1 (0.5–2.2) 1.8 (0.9–4.0) 2.5 (1.02–5.9) 0.03	Age, area, cigarette smoking, gallbladder disease, diabetes	Never/ever drinking not significant except for white women (0.6; 95% CI, 0.4–0.97); no significant differences by beverage type; similar association found in nonsmokers

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Partanen <i>et al.</i> (1997), Finland, 1984–87	662 deceased men and women, aged 40–74 years; identified through cancer registry; response rate, 47%	1770 hospital-based (malignancies of the stomach, colon or rectum)	Self-administered questionnaire	<i>Distilled beverage intake in 1960s</i>	1.00	Age, sex, tobacco smoking	
				None/occasional	1.17 (0.92–1.48)		
				Moderate	1.22 (0.82–1.80)		
				Heavy			
				<i>Wine/beer</i>	1.00		
				None/occasional	1.16 (0.91–1.48)		
Tavani <i>et al.</i> (1997), Italy, 1983–92	361 men and women, aged 17–79 years; 100% histologically confirmed; response rate, ~97%	997 hospital-based (non-malignant, non-smoking-/alcohol-related); response rate, ~97%	Interviewer-administered questionnaire	<i>Usual intake (drinks/day)</i>	1.0	Age, sex, education, smoking, diabetes, pancreatitis, cholelithiasis	No proxy information; no association for type of beverage (90% of population drank wine) or duration
				None	0.9 (0.7–1.3)		
				<4	1.1 (0.7–1.7)		
				>4–7	1.4 (0.7–2.7)		
				>7–8	1.1 (0.5–2.2)		
				>8	0.57		
<i>p</i> for trend							

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Soler <i>et al.</i> (1998), Italy, 1983–92	362 men and women, aged <75 years; 100% histologically confirmed; response rate, ~97%	1552 hospital-based (non-malignant); response rate, ~97%	Interviewer-administered questionnaire; total alcohol intake (frequency, duration, quantity provided)	<i>Total alcohol intake</i> Low Intermediate High	1.0 0.83 (0.61–1.13) 1.20 (0.89–1.67)	Age, sex, area, education, smoking	No proxy interviews
Talamini <i>et al.</i> (1999), Italy, 1990–95	69 men (no pancreatitis); 100% histologically confirmed; response rate not specified	700 population-based (electoral roll) who had medical check-up, recruited 1985–87; response rate not specified	Interviewer-administered questionnaire	<i>Alcohol (g/day)</i> 0–40 41–80 > 80	1.0 0.5 (0.2–1.0) 0.4 (0.2–1.0)	Smoking	

Table 2.49 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Villeneuve <i>et al.</i> (2000), multisite, Canada, 1994–97	583 (322 men, 261 women), aged 30–76 years; 100% histologically confirmed; response rate, 55%	4813 population-based (health insurance records, Ministry of Finance records, random-digit dialling); matched by age, sex; response rate, 65–71%	Self-mailed questionnaire with telephone follow-up	<i>Alcohol (drinks/week)</i>		Age, area, parity, coffee, smoking, energy intake, fat intake	Proxies used for 24% of cases
				<i>Men</i>	1.0		
				0	0.83 (0.56–1.25)		
				<3	0.86 (0.57–1.28)		
				3–<7	1.20 (0.79–1.80)		
				7–<14	1.36 (0.93–2.00)		
				≥14			
				<i>Women</i>	1.0		
				0	0.90 (0.65–1.25)		
				<3	0.59 (0.34–1.02)		
3–<7	0.95 (0.57–1.56)						
≥7							
Lu <i>et al.</i> (2006), China, 2002–04	119 identified through hospital records and verified by pathology, surgical and clinical records; age range not stated; histological confirmation not stated; response rate not stated	238 population-based (procedure not stated); matched by age, sex, region, marital status; response rate not stated	Interviewer-administered questionnaire	<i>Alcohol duration (drink-years)</i>		Age, sex, smoking	Limited methodological details provided
				None	1.0		
				≤20	1.003 (CI not stated)		
				>20	3.68 (1.60–8.44)		
<i>p</i> for trend	Significant [not reported]						

CI, confidence interval; HCFA, Health Care Financial Administration; NS, not significant

correlation has been identified between use of tobacco and consumption of alcohol in many populations. As such, careful adjustment for smoking is one of the most important requirements for a valid interpretation of the effects of alcohol.

Factors important for causal inference, such as strength of the association, dose–response relationship, histological types, types of alcoholic beverage, and potential confounding by and interactions with tobacco smoking are considered here. The risks for lung cancer in relation to total alcoholic beverage consumption are summarized in Tables 2.50–2.52; the effects of alcoholic beverage consumption and the risk for lung cancer by histological types are presented in Tables 2.53 and 2.54; the effects of types of alcoholic beverage are presented in Tables 2.55–2.60; the combined or joint effects or effect modification of alcoholic beverage consumption and tobacco smoking are shown in Tables 2.61 and 2.62; the relationships between alcoholic beverage consumption and the risk for lung cancer among nonsmokers are shown in Tables 2.63 and 2.64.

2.10.1 *Total alcoholic beverage consumption*

(a) *Cohort studies of special populations (Table 2.50)*

All six studies based on cohorts of alcoholics—populations that have excessive alcoholic beverage intake—reported elevated mortality from lung cancer (Schmidt & Popham, 1981; Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Sørensen *et al.*, 1998; Boffetta *et al.*, 2001). However, due to the lack of control for tobacco smoking in all studies, the possibility that the observed association might be largely explained by the confounding effect of tobacco smoking can not be ruled out.

(b) *Cohort studies of the general population (Table 2.51)*

Among 20 cohort studies of the general population that provided tobacco smoking-adjusted risk estimates for total alcoholic beverage use, 10 reported an elevated risk for lung cancer associated with alcoholic beverage consumption, although it was seldom significant. Of the studies that examined high levels of alcoholic beverage intake (≥ 3 or ≥ 5 drinks/day), some reported elevated risks that became statistically significant at the highest category of alcoholic beverage consumption, all in men (Prescott *et al.*, 1999; Lu *et al.*, 2000a; Balder *et al.*, 2005). Studies that used low drinking levels (e.g. 1–2 drinks/day) as the highest category did not find a significant association between these relatively low exposures and risk for lung cancer (Kono *et al.*, 1986; Stemmermann *et al.*, 1990; Breslow *et al.*, 2000; Freudenheim *et al.*, 2005).

Most cohort studies that reported a positive association also demonstrated a significant dose–response relationship. Other studies observed no association between alcoholic beverages and the risk for lung cancer at the highest level of consumption for both genders (Korte *et al.*, 2002 [Cancer Prevention Study, II]; Nishino *et al.*, 2006; Rohrmann *et al.*, 2006) and in women (Prescott *et al.*, 1999).

Table 2.50 Cohort studies of total alcoholic beverage consumption and lung cancer in special populations

Reference, location, name of study	Cohort description	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schmidt & Popham (1981), Ontario, Canada, Cohort of Alcoholics	9889 men admitted for alcoholic treatment in 1951–70 in Ontario, Canada; mortality follow-up, 1951–71; mortality and cause-specific mortality ascertainment, death records and death certificates; 96% follow-up	Alcoholic	89 Local reference US veteran reference	SMR 1.7 ($p<0.01$) 2.7 ($p<0.01$) 4.4 ($p<0.01$) 2.2 ($p<0.01$) 0.98	Age Total 1–9 cigs/day 10–20 cigs/day 21–39 cigs/day	347 patients whose vital status could not be determined were assumed to be alive at the study cut-off date.
Adami <i>et al.</i> (1992a), Central Sweden, Cohort of alcoholics	9353 (8340 men, 1013 women) subjects with a hospital discharge of alcoholism; follow-up, 1965–84; case ascertainment, Nationwide Registry of Cause of Death	Alcoholic <i>Men</i> <i>Women</i> Age <50 years Age 50–64 years Age ≥65 years	76 3	SIR 2.1 (1.7–2.6) 2.7 (0.6–8.0) 6.7 (2.2–15.7) 3.5 (2.4–4.9) 1.5 (1.0–2.0)	Age, calendar year	Estimates not adjusted for smoking; updated analysis in Boffetta <i>et al.</i> (2001); cancers occurring during the first year of follow-up were excluded
Tønnesen <i>et al.</i> (1994), Copenhagen, Denmark, Cohort of Alcoholics	18 307 alcoholics (15 214 men, 3093 women) treated at a public outpatient clinic in Copenhagen in 1954–87; cancer case ascertainment, Danish Cancer Registry, 95%; mortality follow-up through population registry	<i>Alcoholic</i> Men Women Total	456 29 485	SIR 2.5 (2.3–2.7) 3.7 (2.5–5.4) 2.6 (2.3–2.8)	Age, sex, calendar period	Estimates not adjusted for smoking; reference, national cancer incidence

Table 2.50 (continued)

Reference, location, name of study	Cohort description	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Temperance Boards Study	Nested case-control study; 15 508 alcoholic women identified from the Temperance Board records; comparison group of 15 508 women individually matched on day of birth, region; follow-up, [1947–77]; case ascertainment, Swedish Cancer Registry	Alcoholic	139 (bronchus, lung) 4 (lung, unspecified)	5.0 (3.3–7.4) 4.0 (0.5–36.0)	Age, region	Estimate not adjusted for smoking
Sørensen <i>et al.</i> (1998), Denmark, Cohort of 1-year Survivors of Cirrhosis	11 605 1-year survivors of cirrhosis identified from Danish National Registry of Patients that covered all hospital admissions in Denmark; follow-up, 1977–93; 7165 alcoholic cirrhosis (5079 men, 2086 women); case ascertainment, Danish Cancer Registry (100%)	Alcoholic	135	SIR 2.1 (1.8–2.5)	Age, sex, calendar period	Estimate not adjusted for smoking; reference, national incidence rates

Table 2.50 (continued)

Reference, location, name of study	Cohort description	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Boffetta <i>et al.</i> (2001), Sweden, Cohort of Alcoholics	173 665 (138 195 men, 35 470 women) patients with a hospital discharge of alcoholism, aged ≥ 20 years; mortality follow-up, 1965–95; case ascertainment 98% (National Cancer Registry)	<i>Alcoholic</i> Men Women Total	1613 267 1880	SIR 2.2 (2.1–2.4) 4.2 (3.7–4.7) 2.4 (2.3–2.5)	Age, gender, calendar year	Estimates not adjusted for smoking; SIRs by histological type reported; reference, national incidence rates

CI, confidence interval; SIR, standardized incidence ratio; SMR standardized mortality ratio

Table 2.51 Cohort studies of total alcoholic beverage consumption and lung cancer in the general population

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Klatsky <i>et al.</i> (1981), California, USA, Kaiser-Permanente Study	8060 Kaiser-Permanente members who completed the self-administrated questionnaire; four groups of 2015 by level of alcoholic beverage drinking; follow-up, 1964–68 to 1976; cause-specific mortality ascertainment, California death index (82–92% death catchments)	Self-administered questionnaire	<i>Drinks/day</i> 0 ≤ 3 3–5 ≥ 6 ≥ 6 versus ≤ 2	15 7 16 24	SMR [1.0] [0.6] [1.1] [1.7] $p < 0.01$	Matched on sex, race, presence or absence of established cigarette smoking habit, examination date, age	Matching on smoking based on intensity; subjects were not removed if smoking habit could not be matched.

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kvåle <i>et al.</i> (1983), Norway, Three cohorts	16 713 subjects from three different cohorts who responded to a mailed questionnaire: 1. 7966 men from general population sample; 2. 3409 men from sibling roster of migrants to the USA; and 3. family members of patients in a case-control study (2410 men, 2928 women); follow-up, 1967–69 to 1978; cancer case ascertainment, Cancer Registry of Norway; 67% histologically confirmed as primary tumour: response rate, ~80%	Mailed questionnaire	<i>Men</i> Low Medium High	24 33 10	1.0 Not provided 1.3 ($p=0.37$)	Age, cigarette smoking (never, former and current smokers of 1–9, 10–19 and ≥ 20 cigs/day), region, urban/rural place of residence, socioeconomic group	Analysis for 10 602 men with information on smoking; interaction between alcoholic beverage and vitamin A intake statistically significant ($p<0.05$); definitions for low, medium and high alcohol intake not provided

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Pollack <i>et al.</i> (1984), Hawaii, Japan-Hawaii Cancer Study	8006 Japanese men born between 1900 and 1919 (also subjects for the Honolulu Heart Study); follow-up, 1965–68 to 1980; 100% case catchments; cancer case ascertainment, hospital records, death certificates and the Hawaii Tumor Registry; 100% histologically confirmed	Baseline interview questionnaire	Type of beverage <i>Beer</i> <i>Wine</i> <i>Liquor</i>	Not provided	See Table 2.55 See Table 2.57 See Table 2.59	Age, cigarette-smoking status (never, former and current smokers), alcohol content of the other two types of beverage (if significant)	Association between total alcoholic beverage consumption and risk for lung cancer not available; no significant interaction between cigarette smoking and alcoholic beverage consumption found; updated analysis in Stemmermann <i>et al.</i> (1990);

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kono <i>et al.</i> (1986), western Japan, Cohort of Male Japanese Physicians	5135 male physicians in western Japan; follow-up, 1965–83; vital status, 99%; cancer death ascertainment, death certificate; response rate, 51%	Baseline mailed questionnaire	Non-drinker	24	1.0	Age, smoking (non-, former and current smoker consuming <10, 10–19 or >20 cigs/day)	
			Former drinker	5	0.6 (0.2–1.5)		
			Occasional drinker	12	0.4 (0.2–0.8)		
			<i>Daily drinker</i>				
			<27 mL alcohol/day	17	0.8 (0.4–1.4)		
			≥ 27 mL alcohol/day	16	0.9 (0.5–1.7)		
			per 27 mL/day		[0.9] [0.7–1.1]		

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Stemmermann <i>et al.</i> (1990), Hawaii, Japan-Hawaii Cancer Study	7572 Japanese men born between 1900 and 1919 (also subjects for the Honolulu Heart Study); follow-up, 1965–68 to 1989; 100% case catchments; cancer case ascertainment, hospital records, death certificates, and the Hawaii Tumor Registry; cancer diagnoses not histologically confirmed excluded	Baseline interview questionnaire	<i>Alcohol (oz/month)</i> 0 <5 5–14 15–39 ≥40	209	1.0 0.8 (0.5–1.2) 0.9 (0.6–1.5) 1.4 (1.0–2.1) 1.1 (0.7–1.6) <i>p</i> for trend=0.09	Age, current smoking status (never, former, current smokers), age started smoking (current smokers), number of cigarettes smoked per day (current smokers), maximum number of cigarette smoked per day (former smokers), years of smoking with maximum number per day (former smokers)	Risk for lung cancer found not to be influenced by the type of alcoholic beverage consumed 1 oz = 0.0296 L

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chow <i>et al.</i> (1992), USA, Lutheran Brotherhood Insurance Society	17 818 white men, aged ≥35 years, life insurance policy holders of the Lutheran Brotherhood Insurance Society; follow-up, 1966–86; vital status, 77%; case ascertainment, death certificate; response rate, 69%	Mailed questionnaire at baseline	Times/month <i>Beer</i> <i>Liquor</i>		See Table 2.55 See Table 2.59	Age, industry/occupation, smoking status (never tobacco, other tobacco only, occasional/past daily cigarette use of 1–19, 20–29, ≥30, current daily cigarette use of 1–19, 20–29, ≥30)	Relative risk for total alcoholic beverage consumption and risk for lung cancer not available
Potter <i>et al.</i> (1992), Iowa, USA, Iowa Women's Health Study	41 837 women, aged 55–69 years, drawn from the 1985 driver's licence list and responded to a mail survey in 1986; follow-up, 1986–88; cancer case ascertainment, Health Registry of Iowa, 100%; nested case–control study; controls randomly selected from the non-patient population; response rate, 43%	Mailed questionnaire	Glasses/day <i>Beer</i> <i>Liquor</i>		See Table 2.55 See Table 2.59	Smoking (pack–years)	Nested case–control study; odds ratio for total alcoholic beverage consumption not available

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Doll <i>et al.</i> (1994), United Kingdom, British Male Doctors Study	12 321 male physicians born between 1900 and 1930 and returned the 1978 questionnaire; follow-up, 1978–91; cause-specific mortality ascertainment, death certificates	Mailed questionnaire	<i>Units/week</i> None 1–7 8–14 15–21 22–28 29–42 ≥ 43 <i>χ² test value of alcohol effect</i> None versus 1–14 Trend*	163	Mortality ratio [1.0] [1.6] [1.4] [0.9] [0.9] [1.3] [2.1] 0.9 (<i>p</i> >0.05) 0 (<i>p</i> >0.05)	Mortality standardized for age, smoking (never smokers, current smokers of 1–14, 15–24, 25 or more cigs/day, other current smokers, former smokers), year of death, history of previous disease	Relative risk for alcohol use on lung cancer mortality not given; mortality ratio calculated from the standardized mortality given in paper * Trend of 1–14 versus 15–28 versus ≥29 units/week
Murata <i>et al.</i> (1996), Japan, Chiba Gastric Screening Cohort	17 200 men who participated in Chiba gastric screening in 1984; follow-up, 1984–93; cancer case ascertainment, Chiba Cancer Registry; histological confirmation not given; nested case–control study	Self-administered questionnaire at baseline (prior to screening)	<i>Cups/day (27 mL ethanol/day)</i> 0 0.1–1.0 1.1–2.0 ≥ 2.1	38 28 31 10	1.0 1.0 [0.6–1.8] 2.4 [1.3–4.4] 1.8 [0.7–4.5]	Age, sex, city/county of address	Nested case–control study; controls individually matched 2:1 to cases by age, sex, city/county of address; odds ratio for alcoholic beverage drinking by smoking status reported

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Omenn <i>et al.</i> (1996), USA, β -Carotene and Retinol Efficacy Trial	Randomized, double-blinded, placebo controlled trial; 14 254 smokers (7982 men, 6272 women) and 4060 men occupationally exposed to asbestos; recruiting period, 1988–1994; end of study, 1995; case ascertainment, participant report and clinical record review; 81% histologically confirmed	Self-reported, collected routinely	Placebo group			Crude incidence rate ratio	Adjusted relative risk not provided; median alcohol intake for men, 3.0 g/day; 75th percentile, 18.7 g/day; median alcohol intake for women, 1.2 g/day; 75th percentile, 11.1 g/day
			<i>Non-drinkers</i>	63	[1.0]		
			<i>Drinkers</i>				
			Below median alcoholic beverage intake	16	[0.6]		
			3rd quartile of intake	39	[0.9]		
4th quartile of intake	29	[0.7]					
>30 g/day alcohol	20	[0.8]					
>50 g/day alcohol	9	[0.8]					

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Omenn <i>et al.</i> (1996) (contd)			Intervention group				
			Non-drinkers	68	[1.0]		
			<i>Drinkers</i>				
			Below median alcoholic beverage intake	29	[1.0]		
			3rd quartile of intake	35	[0.7]		
			4th quartile of intake	64	[1.3]		
			>30 g/day alcohol	43	[1.4]		
			>50 g/day alcohol	21	[1.4]		
Bandera <i>et al.</i> (1997), New York, USA, New York State Cohort	48 000 (27 544 men and 20 456 women) long-term residents of New York State; follow-up, 1980–87; case ascertainment, New York State Cancer Registry	Mailed questionnaire at baseline	Drinks/month			Age, education, cigarettes/day, years of smoking, total energy intake	Tertile range not reported
			<i>Men</i>				
			1st tertile	124	1.0		
			2nd tertile	95	0.8 (0.6–1.0)		
			3rd tertile	176	1.1 (0.9–1.4)		
					<i>p</i> for trend=0.001		
			<i>Women</i>				
			1st tertile	34	1.0		
			2nd tertile	43	1.2 (0.7–1.8)		
			3rd tertile	53	1.0 (0.6–1.6)		
					<i>p</i> for trend=0.80		

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Yong <i>et al.</i> (1997), USA, First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	10 068 subjects; follow-up, 1971–75 to 1992; follow-up, 96%; cancer case ascertainment, hospital records and death certificate	Baseline interview	Non-drinkers >5 g/day	Not given	1.0 1.2 (0.9–1.6)	Age, smoking status and pack–years smoked (8 categories), race, education, physical activity, body-mass index, total calorie intake	Alcoholic beverage consumption not the main focus of this study
Zhang <i>et al.</i> (1997), Zoucheng, Shandong, China	7809 men and 7994 women from probabilistic sample of general population in three counties, aged >20 years; mortality follow-up, 1982–94; cause-specific mortality ascertainment, county disease prevention and control centre	Baseline questionnaire, interviewer-administered	<i>Drinking/smoking</i> No/No Yes/No No/Yes Yes/Yes	1.0 3.1 4.2 2.5		Crude relative risk	No dose–response found for frequency, amount or duration of drinking; lung-cancer mortality found in crude analyses

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Prescott <i>et al.</i> (1999), Copenhagen, Denmark Three longitudinal population studies	Conducted in 1964–94: the Copenhagen City Heart Study, the Centre of Preventive Medicine, and the Copenhagen Male Study; 28 160 (15 107 men, 13 053 women) included; cancer follow-up, 99% (Danish Cancer Registry); response rate, 77%	Self-administered questionnaire	Drinks/week				Age, study cohort, education, smoking (current smoking: pack–years, duration of smoking)	No interaction between smoking and total consumption or type of alcoholic beverage found
			<i>Men</i>					
			<1	52	1.0			
			1–6	85	0.9 (0.6–1.2)			
			7–13	106	1.0 (0.7–1.4)			
			14–20	65	0.9 (0.6–1.3)			
			21–41	114	1.2 (0.9–1.7)			
			>41	58	1.6 (1.1–2.3)	<i>p</i> for trend=0.002		
			<i>Women</i>					
			<1	63	1.0			
			1–6	82	0.9 (0.6–1.3)			
			7–13	30	1.0 (0.6–1.6)			
14–20	11	1.0 (0.5–1.9)						
21–41	7	1.0 (0.5–2.2)						
>41	1	0.8 (0.1–5.8)	<i>p</i> for trend=0.94					

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Woodson <i>et al.</i> (1999), southwestern Finland, α -Tocopherol β -Carotene Cancer Prevention Study	27 111 white male smokers, aged 50–69 years in southwestern Finland; cancer incidence follow-up, 1985–94; cancer case ascertainment, Finland Cancer Registry and the Register of Causes of Death; 100% case ascertainment; 93% histologically confirmed; response rate, 93%	Self-administered food-use questionnaire at baseline	<i>Ethanol (g/day)</i> Non-drinkers Q1 0.04–5.2 Q2 5.3–13.3 Q3 13.4–27.6 Q4 27.7–278.5	1059 154 233 234 208 230	1.2 (0.9–1.4) 1.0 1.0 (0.8–1.2) 0.9 (0.8–1.1) 1.0 (0.8–1.2) <i>p</i> for trend=0.89	Age, body-mass index, years smoked, cigarettes per day, intervention group	Relative risk for alcoholic beverage drinking, reported also by type of alcoholic beverage and by smoking categories
Breslow <i>et al.</i> (2000), USA, National Health Interview Survey	Sub-cohort of 20 004 adults, 18 years or older, who completed the Cancer Epidemiology Supplement (8363 men, 11 641 women); follow-up, 1987–95; case ascertainment, National Death Index and Death certificate; response rate, 86%	Cancer Epidemiology Supplement questionnaire (in-home interview)	<i>Servings/week</i> Q1 0 Q2 0.02–0.5 Q3 0.5–4.4 Q4 >4.4	52 23 32 50	1.0 0.7 (0.4–1.3) 1.0 (0.6–1.6) 1.3 (0.8–2.0) <i>p</i> for trend <0.101	Age, gender, smoking duration (years), packs per day smoked	Deaths arising within the first year of follow-up excluded

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lu <i>et al.</i> (2000a), Yunnan, China, Cohort of Yunnan Tin Corporation Miners	7965 miners followed between 1992 and 1997, aged ≥ 40 years; 10 years of high-risk professional activity; completed the baseline questionnaire; did not have lung cancer; cases identified by expert panel	Interviewer-administered questionnaire	<i>Alcohol (g/day)</i> Non-drinkers <50 50–99 ≥ 100	137 29 62 71	1.0 1.0 (0.7–2.0) 1.4 (1.0–1.9) 1.5 (1.1–2.0)	Age, employment history, smoking	[From abstract and tables]

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Djoussé <i>et al.</i> (2002), Massachusetts, USA, Framingham Cohort Study (1948) and Framingham Offspring Study (1971)	In 1948, 5209 subjects aged 28–62 years at first examination; in 1971, 5124 children of the original cohort participated; study included 4265 subjects from the original cohort and 4973 from the offspring cohort; mean follow-up: original cohort, 32.8 years; offspring cohort, 16.2 years; cancer case ascertainment, self-report, hospitalization surveillance and National Death Index; 100% histologically confirmed	Follow-up examination	<i>Average intake (g/day)</i> 0 0.1–12 12.1–24 >24	269 44 100 39 86	1.0 1.2 (0.7–2.1) 1.1 (0.6–2.1) 1.3 (0.7–2.4)	Age, sex, smoking status, pack–years of cigarette smoking, year of birth	Nested case–control study; controls selected using the risk–set sampling method and matched by age, pack–year of cigarette smoking, sex, year of birth, smoking status; for former smoker cases, controls also matched by year since quitting smoking

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Korte <i>et al.</i> (2002), USA, Cancer Prevention Study (CPS) I and II	Pooled analysis including unpublished results from the CPS I and II; CPS I, 379 575 men, 489 741 women; CPS II, 226 871 men, 230 552 women		Ethanol (g/month)	Not provided		Smoking		
			<i>CPS I</i>					
			Men					
			Non-drinker					
			1–499					1.0
			500–999					0.9 (0.8–1.0)
			1000–1999					1.0 (0.9–1.1)
			≥2000					1.2 (1.1–1.3)
			Women					
			Non-drinker					
			1–499					1.0
			500–999					1.0 (0.8–1.2)
			1000–1999					1.2 (0.9–1.6)
			≥2000					1.8 (1.3–2.3)
			<i>CPS II</i>					
			Men					
Non-drinker								
1–499	1.0							
500–999	0.9 (0.8–1.0)							
1000–1999	1.0 (0.9–1.2)							
≥2000	1.0 (0.9–1.1)							
Women								
Non-drinker								
1–499	1.2 (1.0–1.4)							
500–999	1.0							
1000–1999	0.9 (0.8–1.1)							
≥2000	1.1 (0.9–1.3)							
	1.3 (1.0–1.5)							
	1.1 (0.8–1.5)							

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Korte <i>et al.</i> (2002) (contd)	Meta-analysis of cohort studies including 8 published studies and unpublished data from CPSI and CPSII		<i>Ethanol (g/month)</i> Non-drinker 1–499 500–999 1000–1999 ≥2000		1.0 1.0 (0.9–1.0) 1.0 (0.9–1.1) 1.2 (1.0–1.3) 1.4 (1.2–1.6)	Smoking	
Balder <i>et al.</i> (2005), Netherlands Cohort Study on Diet and Cancer	58 279 men in 204 municipalities in Netherlands, aged 55–69 years; cancer follow-up, 1986–95; case ascertainment, Netherlands Cancer Registry and Netherlands Pathology Registry; case-cohort design (2335 men randomly sampled from the large cohort)	Mailed questionnaire	<i>Median intake (g/day)</i> Q1 0 Q2 2.2 Q3 9.3 Q4 23 Q5 42	183 241 337 333 311	1.0 1.1 (0.8–1.5) 1.2 (0.9–1.7) 1.1 (0.8–1.5) 1.6 (1.1–2.2) <i>p</i> for trend=0.03	Age, total energy intake (kJ), current cigarette smoker (yes/no), number of cigarettes smoked per day, years of smoking cigarettes, higher vocational or university education, family history of lung cancer, physical activity, body-mass index	

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Freudenheim <i>et al.</i> (2005), pooled analysis of 7 prospective studies	α -Tocopherol β -Carotene Cancer Prevention Study (men), Canadian National Breast Screening Study (women), Health Professional Study (men), Iowa Women's Health Study (women), Netherlands Cohort Study (women and men), New York State Cohort (women and men), Nurses' Health Study (women); total, 399 767 participants (137 335 men, 262 432 women)	Diet assessment by questionnaire	Intake (g/day)		Pooled relative risk	Education, body-mass index, energy intake, smoking status (never, past, current), smoking duration for past and current smokers, cigarettes smoked daily for current smokers; for specific alcoholic beverage, other two alcoholic beverage types were also adjusted in the model	Pooled relative risk for histological type reported; relative risk for alcohol drinking by smoking status reported; study-specific relative risk reported	
			<i>Men</i>	None	254			1.0
			>0-<5	373	0.9 (0.7-1.0)			
			5-<15	432	1.0 (0.8-1.2)			
			15-<30	324	0.8 (0.6-1.1)			
			≥ 30	379	1.2 (0.9-1.6)			
					<i>p</i> for trend=0.03			
			<i>Women</i>	None	467			1.0
			>0-<5	344	0.8 (0.7-0.9)			
			5-<15	252	0.8 (0.7-1.0)			
15-<30	130	0.9 (0.7-1.1)						
≥ 30	182	1.2 (0.9-1.4)						
		<i>p</i> for trend=0.03						

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Nishino <i>et al.</i> (2006), Japan, Japan Collaborative Cohort	110 792 inhabitants, aged 40–79 years, of 45 study areas throughout Japan; follow-up, 1988–99; 28 536 men included in the analysis	Self-administered questionnaire at baseline	Never drinkers	91	1.0	Age, smoking (current smoking: 6 categories of number of pack-years; former smoking: 5 categories for number of years since quitting), family history of lung cancer, intake of green vegetables, oranges and fruit other than oranges	Analysis for men only; relative risks by smoking status reported
			Ever drinkers	286	1.0 (0.7–1.3)		
			<i>Current drinkers</i> (ethanol g/day)				
			24.9	113	0.8 (0.6–1.1)		
			25.0–49.9	85	0.9 (0.6–1.3)		
50.0	38	1.0 (0.6–1.5)	<i>p</i> for trend = 0.32				
Former drinkers	50	1.7 (1.2–2.5)					

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Rohrmann <i>et al.</i> (2006), 10 European countries, European Prospective Investigation into Cancer and Nutrition	521 457 from 10 European countries; most study centres recruited from the general population; other sources of recruitment included members of insurance plans, blood donors, mammographic screening, employees of enterprises, civil servants; 478 590 subjects included in the analysis (142 798 men, 335 792 women); baseline, 1992–2000; end of follow-up, 1999–2003; cases ascertainment, cancer registry and active follow-up; 97% histologically confirmed	Dietary instruments developed specifically for each country	Ethanol (g/day)				Results stratified by age, sex, study centre; hazard ratios adjusted for smoking status, smoking duration, height, weight, fruit consumption, red meat consumption, processed meat consumption, education, physical activity at work, total non-ethanol energy intake	Relative risks reported by histological type and by smoking status; interaction <i>p</i> -value reported
			<i>Both genders</i>					
			Intake at recruitment					
			Non-drinker	146	1.22 (1.0–1.5)			
			0.1–4.9	310	1.0			
			5–14.9	232	0.8 (0.6–0.9)			
			15–29.9	169	0.8 (0.7–1.0)			
			30–59.9	184	1.0 (0.8–1.2)			
			≥60	78	0.9 (0.7–1.1)			
					<i>p</i> for trend=0.31			
			Mean lifelong intake					
			Non-drinker	30	1.0 (6.7–1.5)			
0.1–4.9	228	1.0						
5–14.9	229	0.8 (0.7–1.0)						
15–29.9	201	1.0 (0.8–1.2)						
30–59.9	117	0.9 (0.7–1.1)						
≥60	82	1.3 (0.9–1.7)						
		<i>p</i> for trend=0.12						

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Rohrmann <i>et al.</i> (2006) (contd)			<i>Men</i>				
			Intake at recruitment				
			Non-drinker	61	1.1 (0.8–1.6)		
			0.1–4.9	121	1.0		
			5–14.9	118	0.7 (0.5–0.9)		
			15–29.9	108	0.8 (0.6–1.0)		
			30–59.9	128	0.9 (0.7–1.1)		
			≥60	70	0.8 (0.6–1.1)		
			Mean lifelong intake				
			Non-drinker	9	1.4 (0.7–2.9)		
			0.1–4.9	57	1.0		
			5–14.9	106	0.8 (0.5–1.1)		
			15–29.9	135	0.9 (0.7–1.3)		
			30–59.9	104	0.8 (0.6–1.2)		
			≥60	80	1.2 (0.8–1.8)		
			<i>Women</i>				
			Intake at recruitment				
		Non-drinker	85	1.3 (1.0–1.7)			
		0.1–4.9	189	1.0			
		5–14.9	114	0.8 (0.6–1.0)			
		15–29.9	61	0.9 (0.7–1.2)			
		30–59.9	56	1.1 (0.8–1.5)			
		≥60	8	0.9 (0.4–1.8)			

Table 2.51 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Rohrmann <i>et al.</i> (2006) (contd)			Mean lifelong intake				
			Nondrinker	21	0.9 (0.5–1.4)		
			0.1–4.9	171	1.0		
			5–14.9	123	0.8 (0.7–1.1)		
			15–29.9	66	1.1 (0.8–1.5)		
			30–59.9	13	0.9 (0.5–1.6)		
≥60	2	1.3 (0.3–5.5)					

CI, confidence interval; oz, ounce (1 oz = 29.6 mL); SIR, standardized incidence ratio; SMR, standardized mortality ratio

A meta-analysis (Korte *et al.*, 2002) found a significantly increased risk for lung cancer with an ethanol intake of at least 2000 g per month (≥ 5 drinks/day): the weighted odds ratio from case-control studies was 1.5 (95% CI, 1.0–2.3) and the weighted relative risk from cohort studies was 1.4 (95% CI, 1.2–1.6). [The weighted odds ratio for case-control studies was based on only one study and the relative risk for cohort studies on only three studies. These results should therefore be interpreted with some caution.]

It should be noted that most studies examined the effects of recent drinking patterns (case-control studies) or of the drinking patterns at baseline (cohort studies). The exposure studied most extensively was the frequency of drinking. Other parameters of exposure to alcoholic beverages, such as duration and age at initiation of drinking and the relevant exposure period, were not reported.

(c) *Case-control studies (Table 2.52)*

Twenty-one case-control studies reported tobacco smoking-adjusted odds ratios for total alcoholic beverage consumption and the risk for lung cancer. Four of the seven population-based studies (Carpenter *et al.*, 1998; Hu *et al.*, 2002; Freudenheim *et al.*, 2003; Benedetti *et al.*, 2006) reported no significant association between any level of alcoholic beverage consumption examined and the risk for lung cancer. However, most of them used categories that reflected a relatively low level of drinking (e.g. 1 drink/day or less often; highest level of drinking, > 2 drinks per day, but the median frequency for this category was unclear). Three hospital-based studies (De Stefani *et al.*, 1993; Dosemeci *et al.*, 1997; Rachtan, 2002) that used non-drinkers as the baseline comparison group found a significant association between consumption of more than one drink per day and the risk for lung cancer. Dosemeci *et al.* (1997) found an elevated risk for lung cancer and a dose-response with increasing frequency of consumption, duration of drinking and cumulative measures in bottle-years. One hospital-based study (Zang & Wynder, 2001) did not find an association for cumulative alcoholic beverage intake (frequency \times duration), or for ≥ 7 oz of 'whiskey-equivalents' of alcohol per day [approximately ≥ 68 g of ethanol per day] (odds ratio, 1.1; 95% CI, 1.0–1.4). [The Working Group noted that the baseline comparison group in this study included people who consumed less than one alcoholic beverage per day.] De Stefani *et al.* (2002) also reported a null association for adenocarcinoma of the lung.

In addition, among nine case-control studies of lung cancer published in the Chinese literature, five adjusted for or stratified by tobacco smoking. Five studies reported a positive association between alcoholic beverage consumption and the risk for lung cancer and point estimates that ranged from 1.5 to 6.6 but none reported the levels of consumption.

Table 2.52 Case-control studies of total alcoholic beverage consumption and lung cancer risk in the general population

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Williams & Horm (1977), USA, 1969–71	7518 (3436 men, 3856 women for the alcohol and tobacco smoking analysis) from Third National Cancer Survey (TNCS); age range not given; histological confirmation unclear; response rate, 57%	Intracancer controls from TNCS; patients with cancers thought to be unrelated to tobacco and alcohol use	Personal interview	Oz/week × years		Age, race, smoking	Controls included colon and liver cancer; non-drinkers defined as those who never drank at least once a week for 1 year; odds ratios for alcoholic beverage types reported
				<i>Men</i>			
				Non-drinker	1.0 $p>0.05$		
				<51	0.9 $p>0.05$		
				≥51	1.0 $p>0.05$		
				<i>Women</i>			
Non-drinker	1.0 $p>0.05$						
<51	1.1 $p>0.05$						
≥51	0.7 $p>0.05$						
Herity <i>et al.</i> (1982), Ireland	59 men [patients at St Luke's hospital in Dublin], aged 44–83 years; histological confirmation unclear; response rate not given	152 male cancer patients, source not described, aged 21–83 years; response rate not described	Structured questionnaire in interview	Non-drinkers or ≤90 g of alcohol/day for 10 years >90 g of alcohol/day for 10 years	1.0 1.5 (0.4–5.2)	Stratified for non- or light smokers (≤20 cigs/day for 43 years)	Controls included cancer of gastrointestinal tract; interaction between alcohol drinking and smoking reported

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Kabat & Wynder (1984), USA, 1971–80	134 (37 men, 97 women) never-smoking patients; 100% histologically confirmed; response rate not given	134 (37 men, 97 women) hospitalized with non-tobacco-related diseases; individually matched to cases by age, sex, race, hospital, date of interview (± 2 years), non-smoking status; response rate not given	In-hospital interview with a standardized questionnaire	No significant differences in alcohol intake were found between cases and controls of either sex (no numbers reported)			Nonsmoker defined as someone who had never smoked as much as one cigarette, pipe or cigar per day for a year; most controls had a cancer diagnosis (~60%).
Koo (1988), Hong Kong, China, 1981–83	88 never-smoking hospitalized Chinese women; age not given; 100% histologically confirmed; response rate not given	137 never-smoking Chinese women in the community; individually matched by district, house type before the exclusion of ever smokers	In-hospital (cases) or in-home (controls) interview	<1 time/week ≥ 1 time/week	1.0 1.9 (0.9–3.7) <i>p</i> for trend =0.076	Age, no. of live births, schooling	Never smokers were defined as those who had smoked less than 20 cigarettes or pipes in the past; odds ratio by histological type reported.

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mettlin (1989), New York, USA, 1982–87	569 (355 men, 214 women) hospitalized, aged 35–90 years; 100% histologically confirmed; response rate not given	569 cancer-free hospitalized; matched on age, sex, residence	Self-administered questionnaire	Times/week <i>Beer</i> <i>Wine</i> <i>Liquor</i>	See Table 2.56 See Table 2.58 See Table 2.60	Age, residence, sex, smoking history [probably pack-years], β -carotene intake index, education	Odds ratio for total alcoholic beverage consumption not available
Pierce <i>et al.</i> (1989), Melbourne, Australia, 1984–85	71 hospitalized men; mean age, 67.3 years; 100% cytologically or histologically confirmed; response rate; 100%	70 hospitalized cancer-free men; mean age, 66.5 years; individually matched to cases by age (± 5 years); response rate, 100%	In-hospital interview	Drinks/week Duration (years)	1.0 (0.99–1.01) 1.0 (0.96–1.03)	Age; not clear whether smoking was adjusted	[The Working Group noted methodological concerns and inconsistencies in the article]

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Bandera <i>et al.</i> (1992), New York, USA, 1980–84	280 hospitalized white men, aged 35–79 years; 100% histologically confirmed	564 neighbourhood controls; matched on age, sex, neighbourhood; response rate, 42%	In-person interview at home	Total alcohol (1 year prior)		Age, education smoking (pack-years)	Odds ratios for alcoholic beverage types reported; categories of alcoholic beverage consumption were based on distribution in combined sample of cases and controls
				<i>0–40 pack-years</i>	1.0		
				0–21 drinks/month	0.9 (0.6–1.6)		
				≥22 drinks/month	<i>p</i> for trend=0.1		
				<i>≥41 pack-years</i>			
				0–21 drinks/month	1.0		
				≥22 drinks/month	1.6 (1.0–2.5)		
					<i>p</i> for trend=0.03		

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (1993), Uruguay, 1988–90	327 hospitalized men, aged 25–84 years; 100% histologically confirmed; response rate, 100%	350 men hospitalized with non-neoplastic condition (non-alcohol-related) as well as non-tobacco-related cancer, aged 25–84 years; response rate, 100%	Interviewer-administered questionnaire	<i>Ethanol (mL/day)</i> Lifetime abstainers 1–60 61–176 >176	1.0 1.4 (0.9–2.0) 1.6 (0.9–2.0) 2.2 (1.3–3.0) <i>p</i> for trend =0.002	Age, residence, education, smoking (pack-years); for specific alcoholic beverages, other types of alcoholic beverage also controlled for	Histological type examined but data not reported; odds ratios for alcoholic beverage types reported; odds ratios for alcohol drinking by smoking status reported; tertile cut-off points for alcohol consumption based on the distribution in the combined sample of cases and controls; only one nonsmoking case

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Mayne <i>et al.</i> (1994), New York, USA, 1982–85	413 (212 men, 201 women) nonsmokers identified via the medical records department, pathology department and the tumour registry, aged 31–80 years; 99% histologically confirmed; interview conducted for 76% of all eligible	413 population selected from driving license files; individually matched on age, sex, county of residence, smoking history; response rate: two potential controls had to be contacted to obtain one control for the case, on average	Interviewer-administered questionnaire (home interview, food-frequency questionnaire for alcohol use)	Beer /month Q1 Q2 Q3 Q4	1.0 (ref) 1.1 ($p>0.05$) 0.9 ($p>0.05$) 1.2 ($p>0.05$)	Age, sex, county of residence, smoking history, cigs/day smoked by former smokers, religion, education, body-mass index, income	Nonsmokers included never smokers and former smokers; 44% of cases were never smokers; one-third of case–control pairs used proxy respondents; passive smoking was found not to confound the dietary association and was therefore not included in the final model; odds ratio for total alcoholic beverage consumption not available

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Dosemeci <i>et al.</i> (1997), Istanbul, Turkey, 1979–84	1210 hospitalized men; 67% histologically confirmed; response rate not given (information obtained by hospital at time of admission)	829 hospitalized men including selected cancers reported not to be related to smoking or alcohol use, and subjects found to have no cancer	Standardized data-collection instrument at time of admission	Never drinker	1.0	Age, smoking (pack-years)	Interaction between alcoholic beverage drinking and smoking reported; odds ratio for specific histological type reported; odds ratio among smokers only reported
				Ever drinker	1.6 (1.2–2.1)		
				<i>Alcohol/week</i>			
				1–35 cL	1.6 (0.8–2.9)		
				36–140 cL	1.7 (1.1–2.7)		
				>140 cL	1.7 (1.0–2.9)		
					<i>p</i> for trend <0.001		
				<i>Duration</i>			
				1–10 years	1.8 (0.9–3.5)		
				11–20 years	1.6 (1.0–2.7)		
>20 years	2.1 (1.0–4.5)						
	<i>p</i> for trend =0.001						
<i>Bottle-years (35 cL of hard liquor)</i>							
1–34	1.7 (0.9–3.0)						
35–90	1.9 (1.0–3.7)						
>90	1.6 (0.9–3.0)						
	<i>p</i> for trend =0.004						
Rachtan & Sokolowski (1997), Cracow, Poland, 1991–94	118 hospitalized women; age not reported; 100% histologically confirmed; response rate not given	141 healthy women selected among next of kin of patients admitted to the same hospital without tobacco-related cancer; age not given; response rate not given	Interviewer-administered structured questionnaire	Frequency <i>Beer</i> <i>Wine</i> <i>Vodka</i>	See Table 2.56 See Table 2.58 See Table 2.60		Odds ratios for total alcoholic beverage consumption not available; updated analysis in Rachtan (2002)

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Carpenter <i>et al.</i> (1998), Los Angeles, USA, 1991–94	261 (153 men, 108 women) hospitalized, aged 40–84 years; 100% histologically confirmed; response rate, [69%]	615 (416 men, 199 women) population; frequency matched for age, gender, race; response rate, [50%]	In-person interview	<i>Recent consumption</i>	1.0	Age, gender, race, saturated fat consumption, tobacco smoking (pack–years), years since quitting tobacco smoking; for specific alcoholic beverages, other types of alcoholic beverages also controlled for in the model	Histological type-specific odds ratio reported; odds ratio for alcoholic beverage types reported; subjects were Caucasians and African-Americans; study restricted to subjects who had complete information on smoking, recent alcoholic beverage consumption, past alcohol consumption, diet; period for ‘recent consumption’ not defined
				Never to 3 drinks/month 1–6 drinks/week 1–2 drinks/day >2 drinks/day	0.5 (0.3–0.8) 0.9 (0.5–1.5) 1.1 (0.5–2.5) <i>p</i> for trend =0.06		
				<i>Consumption between age 30 and 40 years</i>	1.0		
				Never to 3 drinks/month 1–6 drinks/week 1–2 drinks/day >2 drinks/day	0.6 (0.4–1.0) 0.7 (0.4–1.2) 0.7 (0.3–1.4) <i>p</i> for trend =0.54		

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments	
Zang & Wynder (2001), 8 metropolitan areas, USA, 1969–94	1763 hospitalized men; age not given [probably <50–≥70 years]; histological confirmation not clear, > [87%] if not 100%; response rate not given	4436 hospitalized men (included non-tobacco-related cancers and non-neoplastic diseases; excluded patients diagnosed with alcohol-related illness); age not given; pair-matched on age, sex, race, hospital, time of hospital admission before applying the exclusion criteria; response rate not given	Interviewer-administered questionnaire (exposure starting at least 1 year prior to the current illness)	<i>Current pattern</i>			Body-mass index, current no. of cigarettes smoked per day; for lifetime exposure to alcohol, age also adjusted	Caucasian only; odds ratios for specific histology reported; odds ratios for alcohol drinking by smoking categories reported
				(<i>'whiskey-equivalent' oz alcohol/day</i>)	<1	1.0		
					1–3.9	1.1 (0.9–1.3)		
					4–6.9	1.2 (0.9–1.4)		
					≥7	1.1 (1.0–1.4)		
					Continuous variable	1.1 (1.0–1.1)		
				<i>Lifetime exposure</i>				
				(<i>'whiskey-equivalent' oz alcohol drink per day × years of drinking</i>)				
					<4	1.0		
					4–16	1.0 (0.8–1.2)		
	17–27	1.2 (0.9–1.5)						
	28–64	1.1 (0.9–1.4)						
	65–103	1.2 (0.9–1.5)						
	≥104	1.1 (0.9–1.3)						
	Continuous variable	1.0 (1.0–1.1)						

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
De Stefani <i>et al.</i> (2002), Montevideo, Uruguay, 1998–2000	160 hospitalized men, aged 30–89 years; 100% histologically confirmed adenocarcinomas; response rate, 97%	520 men hospitalized for non-tobacco-, non-alcohol-related non-neoplastic conditions; frequency-matched on age, residence, urban/rural status; response rate, 93%	In-person interview	<i>Ethanol (mL/day)</i> Non-drinkers 1–60 61–120 >120	1.0 0.8 (0.4–1.5) 1.1 (0.6–2.1) 1.2 (0.6–2.1) <i>p</i> for trend =0.34	Age, residence, urban/rural status, education, family history of lung cancer in first-degree relatives, body mass index, smoking status, cigarettes per day, years since quit, age started smoking	Adenocarcinoma only; drinkers were defined as those who ingested alcohol at least 1 day per week regularly; odds ratios for alcoholic beverage types reported
Hu <i>et al.</i> (2002), 8 provinces, Canada, 1994–97	161 never-smoking women from the Provincial Cancer Registry, aged 20–>70 years; 100% histologically confirmed; response rate, 62%	483 population-based cancer-free; frequency-matched by age, sex, province; response rate, 71%	Questionnaire mailed to cases and controls	<i>Servings/week</i> 0 1 >1	1.0 0.8 (0.5–1.4) 0.8 (0.5–1.2) <i>p</i> for trend =0.25	10-year age groups, province, education, social class	Study restricted to never smokers; definition for never smoking not described; odds ratios for alcoholic beverage types reported

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Korte <i>et al.</i> (2002)	Meta-analysis on alcoholic beverage consumption and risk for lung cancer		No. of studies	<i>Ethanol (g/month)</i>	Pooled odds ratio	Smoking	Pooled odds ratios from case-control studies only (including studies presented in this table)
			3	Non-drinker	1.0		
			5	1–499	0.6 (0.5–0.8)		
			2	500–999	1.3 (1.0–1.7)		
			1	1000–1999	1.1 (0.5–2.8)		
7	≥2000	1.9 (1.4–2.5)					
Pacella-Norman <i>et al.</i> (2002), Johannesburg, South Africa, 1995–99	146 (105 men, 41 women) hospitalized, aged 18–74 years; 90% confirmed by histology, heamotology or cytology; response rate not given	2174 (804 men, 1370 women) hospitalized with non-tobacco-related cancer, aged 18–74 years; response rate not given	Nurse-administered interview (questionnaire)	<i>Men</i>		Age, place of birth, education, work category, missing values, heating fuel, smoking and snuff use (smoking adjusted for past-current smoking, current smoking by cigs/day)	Subjects were black; controls included patients with colon cancer
				Non-drinkers	1.0		
				<1 time/week	0.3 (0.1–1.1)		
				1–3 times/week	0.7 (0.3–1.5)		
				Most days/week	0.7 (0.4–1.3)		
<i>Women</i>							
Non-drinkers	1.0						
<1 time/week	1.3 (0.5–3.3)						
1–3 times/week	0.8 (0.3–2.6)						
Most days/week	0.8 (0.3–2.1)						

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Rachtan (2002), Cracow, Poland, 1991–97	242 hospitalized women; age range not given; 100% histologically confirmed; response rate not given	352 healthy women from next-of-kin of patients admitted to the same hospital without tobacco-related cancer; age not given; response rate not given	Interviewer-administered structured questionnaire	<i>Average vodka intake (g)</i> Non-drinkers <100 g ≥100 g	1.0 2.2 (1.3–3.8) 7.8 (2.9–21.2) <i>p</i> for trend <0.001	Age, pack–years of smoking, passive smoking, siblings with cancer, tuberculosis, place of residence, occupational exposure to coal and other dusts, rubber, acid mist, solvents, metals, other chemicals, consumption of milk, butter, margarine, cheese, meat, fruit, vegetables, carrots, spinach	Odds ratios for vodka for histological type reported; odds ratios for total alcohol drinking by smoking status reported; estimates unadjusted for smoking for beer and wine intake reported

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Freudenheim <i>et al.</i> (2003), New York, USA, 1996–98	168 hospitalized (111 men, 57 women), aged 35–79 years; 100% histologically confirmed; response rate, 48%	3351 (1546 men, 1805 women) population, aged 35–79 years; frequency-matched for age, sex, race for cases in three case–control studies; response rate, 65%	Interviewer-administered questionnaire	<i>Lifetime consumption (L)</i>	1.0	Age, education, race, sex, body-mass index, vegetable intake, fruit intake, total energy intake excluding alcohol, packs smoked per year, years smoked, index of passive exposure to smoke at home, work and in other settings	Odds ratios for alcoholic beverage types reported; [discrepancy in number and sex of cases in paper]
				0	1.1 (0.5–2.6)		
				≤82	1.1 (0.5–2.7)		
				>82	<i>p</i> for trend =0.44		
				<i>Recent consumption (previous 12–24 months)</i>	1.0		
				0	1.0 (0.4–2.4)		
≤2.5	1.4 (0.5–3.4)						
>2.5	<i>p</i> for trend =0.41						

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Gajalakshmi <i>et al.</i> (2003), Tamil Nadu and Kerala, India, 1993–99	778 men from two cancer centres, aged ≤ 34 – ≥ 75 years; 100% histologically confirmed; response rate not given	3430 men (1503 non-tobacco-related cancers, 1927 healthy) recruited from the two cancer centres, aged ≤ 34 – ≥ 75 years; response rate not given	Interviewer-administered standard questionnaire	<i>Total alcohol</i>	1.0	Age, education, centre, smoking pack–years	Cancer controls included colon cancer; alcohol drinkers defined as people who drink alcohol at least once a day for at least 6 months; former drinker defined as drinkers who had stopped drinking for more than 1 year before interview; odds ratios restricted to never smokers reported
				Never	0.9 (0.7–1.3)		
				Former	1.7 (1.3–2.1)		
				Current			
				<i>Non-Indian alcohol</i>	1.0		
				Never	0.8 (0.5–1.2)		
				Former	1.3 (1.0–1.7)		
				Current			
<i>Indian alcohol</i>	1.0						
Never	0.9 (0.6–1.3)						
Former	1.8 (1.4–2.4)						
Current							

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Ruano-Ravina <i>et al.</i> (2004), Northwest Spain, 1999–2000	132 (118 men, 14 women) hospitalized, mean age, 64.2 years; 100% histologically confirmed; response rate, 100%	187 (164 men, 23 women) hospitalized (non-tobacco-related minor surgery); mean age, 62.5 years; frequency-matched on sex; response rate, 100%	Interviewer-administered questionnaire	<i>Beer</i> <i>Wine</i> <i>Liquor</i>	See Table 2.56 See Table 2.58 See Table 2.60	Age, sex, occupation, smoking habit (total lifetime tobacco consumption in thousands of packs), total alcoholic beverage intake	Odds ratio for total alcoholic beverage consumption not available

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Benedetti <i>et al.</i> (2006), Montreal, Canada, Study I: early 1980s Study II: mid 1990s	Study I: 699 hospitalized men, aged 35–70 years; [100% histologically confirmed]; response rate, 65% Study II: 1094 (640 men, 454 women) hospitalized, aged 35–75 years; [100% histological confirmation]; response rate, 76%	Study I: 507 men population-based; frequency-matched by age, residence to all cancer cases (all cancer cases arise from the hospitals); response rate, 69% Study II: 1468 (861 men, 607 women) population-based; stratified to the age and sex distribution of cases; response rate, 67%	Interview (proxy was allowed)	<i>Study I men</i> <1 drink/week 1–6 drinks/week ≥7 drinks/week <i>Study II men</i> <1 drink/week 1–6 drinks/week ≥7 drinks/week <i>Study II women</i> <1 drink/week 1–6 drinks/week ≥7 drinks/week	1.0 1.2 (0.8–1.8) 1.3 (0.9–1.9) 1.0 1.0 (0.7–1.4) 1.2 (0.9–1.8) 1.0 0.4 (0.2–0.5) 0.7 (0.5–1.1)	Age, smoking status, cigarette–years, time since quitting, respondent status, ethnicity, census tract income, years of schooling	Odds ratios for specific histological type reported; odds ratios for alcoholic beverage types reported; odds ratios for alcohol drinking by smoking categories reported (light, moderate, heavy); odds ratios based on median drink–year cut-off reported

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Studies in the Chinese literature							
Zhang <i>et al.</i> (1989), JinZhou, Liaoning, 1988–89	105 hospitalized; age, sex distribution not given; histological confirmation not given; response rate not given	210 hospitalized (105 cancer, 5 cancer-free); age, sex distribution not given; response rate: not given	In-hospital interview	<i>Alcohol drinking</i> No Yes		Alcohol drinking variable no longer significant after adjusting for smoking, chronic bronchitis, exposure to toxic substances, coal burning, depression, cooking, education, family history of cancer	No adjusted odds ratio for alcohol use reported
Zhang <i>et al.</i> (1990), Dandong, Liaoning, 1987–88	Six cause of deaths (including lung cancer) identified between 1987 and 1988, aged >17 years; proxy probably used for cases; response rate not given	Random sample of 2500–3000 from general population; source not well described; age not given; response rate not given	[Interview?]	<i>Drinking/smoking</i> No/No Yes/No No/Yes Yes/Yes	1.0 2.2 (0.5–10.3) 6.2 (1.8–20.9) 10.6 (3.3–34.5)	Urban/rural, sex, age	

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zhang <i>et al.</i> (1992), Lanzhou, Gansu, 1982–88	70 (58 men, 12 women) hospitalized from 8 hospitals in Lanzhou for over 10 years, aged 21–77 years; 100% histologically confirmed; response rate not given	70 hospitalized; 1:1 matched on age, sex, occupation; response rate not given	Interviewer-administered questionnaire	<i>Alcohol drinking</i> No Yes	1.0 2.3	Smoking, coal burning	95% CI or <i>p</i> -value not provided [although probably significant]
Cui <i>et al.</i> (2001b), Jiangyan, Jiangsu, 1995–96	181 male [hospitalized] survivors, aged 24–86 years; 76% histologically confirmed; response rate not given	181 men selected from the healthy relatives or neighbours who had lived in the same area or worked with cases; matched on age	Interviewer-administered questionnaire	<i>Alcohol drinking</i> No Yes	1.0 2.3 (1.2–8.4)	Smoking, respiratory disease, depression, body-mass index	

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zhang <i>et al.</i> (2002), Kunmin, Yunnan, NR	118 (91 men, 27 women) hospitalized, mean age, 58 years; 100% histologically confirmed; response rate not given	118 healthy; matched on sex, occupation, ethnic group, age, residence	Interviewer-administered questionnaire	<i>Alcohol drinking</i> No Yes		[Alcohol drinking variable not significant in multivariate analysis]	No adjusted odds ratio for alcohol use reported
Chen <i>et al.</i> (2003b), Tianjin, before 1996	193 (sex not given) hospitalized, aged 30–76 years; 68% histologically confirmed; response rate: not given	259 (sex not given) randomly selected from a community in Tianjin, aged 30–75 years; response rate not given	Interviewer-administered questionnaire	<i>Alcohol drinking</i> No Yes		Alcohol drinking variable no longer significant after adjusting for smoking	No adjusted odds ratio for alcohol use reported

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Chen <i>et al.</i> (2003c); Huang <i>et al.</i> (2004), Guangzhou, Guangdong, 2000–02	91 hospitalized; age and sex distribution not given; 100% histologically confirmed; response rate not given	138 (91 hospitalized non-cancers and 47 healthy employees of Guangdong Pharmacy School); residents of Guangdong; matched on age, sex; response rate not given	Questionnaire	<i>Alcohol drinking</i> No Yes No Yes No Yes	<i>All lung</i> 1.0 3.3 (1.7–6.4) <i>SCC</i> 1.0 3.9 (1.8–8.2) <i>AC</i> 1.0 2.5 (1.0–6.3)	Crude odds ratio	Subjects overlapped with Chen <i>et al.</i> (2004).
Wu <i>et al.</i> (2003); Chen <i>et al.</i> (2004), Guangzhou, Guangdong, 2000–01	91 (60 men, 31 women) incident hospitalized, aged 22–84 years; histological confirmation not given; response rate not given	91 (60 men, 31 women) hospitalized without cancer or pulmonary diseases; matched by age; response rate not given	Questionnaire	<i>Alcohol drinking</i> No Yes	1.0 6.6 (1.5–28.3)	Education, smoking (cigs/day), ventilation for cooking fume, consumption of animal oil, carrot intake, family history of lung cancer	Same subjects as in Chen, M.-X. <i>et al.</i> (2003)

Table 2.52 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment factors	Comments
Zou <i>et al.</i> (2005), Dayao, Yunan, 1987–2001	53 cases (46 men, 7 women) identified by retrospective cohort, mean age, 62 years; histological confirmation not clear (all confirmed with histological or image diagnosis); response rate not given	159 from the cohort, aged ≥ 30 years; local residents; men age, 65 years; matched to cases (1:3 ratio) on age, sex, residence, education; response rate not given	Interviewer-administered questionnaire	<i>Alcohol drinking</i> No Yes	1.0 1.2 (0.5–2.7)	Using asbestos stove, cigarette smoking, tea drinking	Nested case–control study Proxy respondent used for subjects who died; alcohol drinking variable not defined

AC, adenocarcinoma; CI, confidence interval; NR, non reported; SCC, squamous-cell carcinoma

2.10.2 *Histological type (Tables 2.53 and 2.54)*

Two cohort studies, one pooled analysis and seven case–control studies presented smoking-adjusted risk estimates for alcoholic beverages by histological type of lung cancer. There appears to be no consistent pattern for the effect estimates of alcoholic beverages on the main lung cancer types: squamous-cell carcinoma, adenocarcinoma and small-cell lung cancer (Tables 2.53 and 2.54). A positive association with squamous-cell carcinoma was reported in three case–control studies (Dosemeci *et al.*, 1997; Zang & Wynder, 2001; Rachtan, 2002). A positive relationship between alcoholic beverage consumption and adenocarcinoma was reported in four case–control studies (Carpenter *et al.*, 1998; Zang & Wynder, 2001 [lifetime exposure]; Rachtan, 2002; Benedetti *et al.*, 2006 [only in men]). In a study in which only the cases of adenocarcinoma were included (De Stefani *et al.*, 2002), no association was observed between alcoholic beverage consumption and this histological type, despite the large number of cases.

In a pooled analysis of seven cohort studies (Freudenheim *et al.*, 2005), some association was found for adenocarcinoma and small-cell lung cancer among men, and for adenocarcinoma among women. In a more recent study that was not included in the pooled analysis (Rohrmann *et al.*, 2006), virtually no association was observed for any lung cancer type among both men and women. [Estimates for lung cancer subtype were mostly based on small numbers of cases, which leads to difficulties in interpreting results due to wide confidence intervals and the possibility of chance findings.] Currently available data do not provide any conclusive evidence for the risk of alcoholic beverage intake on lung cancer subtype.

2.10.3 *Types of alcoholic beverage*

Findings from studies examining risk estimates for the consumption of different types of alcoholic beverages (i.e. beer, wine, and hard liquor) indicate that they may have different effects on lung cancer risk.

(a) *Beer (Tables 2.55 and 2.56)*

Among the six cohort studies that examined the effects of beer drinking on risk for lung cancer, two found a positive association for drinking one serving of beer per day in women (Potter *et al.*, 1992) or two or more servings per day in men (Prescott *et al.*, 1999) (Table 2.55). In the latter study, the point estimate for women was of similar magnitude as that in men (relative risk, 1.4 for men and 1.5 for women), but the confidence interval was wide (95% CI, 0.7–3.1).

In a pooled analysis that combined data from seven prospective cohort studies (Freudenheim *et al.*, 2005), a positive association with a significant dose–response relationship was found between beer drinking and the risk for lung cancer among women, but not among men. The risk almost doubled for women who consumed ≥ 15 g ethanol

Table 2.53 Cohort studies of alcoholic beverage consumption and lung cancer by histological type

Reference	Subject and histology	Exposure categories	Risk ratio (95% CI)	Comments	
Boffetta <i>et al.</i> (2001)	<i>Men</i>	Alcoholic	SIR	Adjusted for age, gender, calendar year; estimates not adjusted for smoking; SIR reference, national incidence rates; SCLC cases also included in 'other and unspecified type'	
			SCC		2.4 (2.3–2.6)
			AC		2.1 (1.9–2.4)
			SCLC		1.1 (0.5–2.1)
	Other and unspecified type	Alcoholic	2.1 (2.0–2.3)		
			<i>Women</i>		5.3 (4.1–6.8)
			SCC		
			AC		
	SCLC	1.9 (0.4–5.6)			
	Other and unspecified type	Alcoholic	4.4 (3.7–5.3)		
			<i>Both genders</i>		2.6 (2.4–2.8)
			SCC		
AC			2.3 (2.1–2.5)		
SCLC	1.2 (0.6–2.2)				
Other and unspecified type	Alcoholic	2.3 (2.2–2.5)			

Table 2.53 (continued)

Reference	Subject and histology	Exposure categories	Risk ratio (95% CI)					<i>p</i> for trend	Comments
			>0-<5	5-<15	15-<30	≥30			
Freudenheim <i>et al.</i> (2005)	<i>Men</i> SCC AC SCLC	Alcohol g/day							Reference, 0 g/day; adjusted for education, body-mass index, energy intake, smoking status, smoking duration, cigarettes/day
			0.9 (0.7–1.2)	1.0 (0.8–1.3)	0.8 (0.6–1.2)	1.1 (0.5–2.1)	0.64		
			1.1 (0.8–1.4)	1.2 (0.9–1.6)	1.0 (0.7–1.5)	1.4 (1.0–2.1)	0.10		
	<i>Women</i> SCC AC SCLC		1.1 (0.8–1.5)	1.2 (0.9–1.6)	1.1 (0.8–1.5)	1.7 (1.2–2.3)	<0.01		
			0.7 (0.5–1.1)	0.8 (0.6–1.0)	0.8 (0.6–1.2)	0.9 (0.6–1.5)	0.99		
			0.9 (0.8–1.1)	0.9 (0.7–1.2)	1.0 (0.7–1.3)	1.4 (1.0–2.0)	<0.01		
Rohrmann <i>et al.</i> (2006)	<i>Men and women</i> SCC AC SCLC	Ethanol (g/day)	Non-drinker	5–14.9	15–29.9	30–59.9	≥60	<i>p</i> for trend	Reference, 0.1–4.9 g/day; all results stratified by age, sex, study centre; adjusted for smoking status, smoking duration, height, weight, consumption of fruit, red meat, processed meat, education, total non-ethanol energy intake
		Baseline intake	1.9 (1.2–2.9)	0.8 (0.6–1.2)	0.8 (0.5–1.3)	1.0 (0.6–1.5)	0.9 (0.5–1.6)	0.30	
			1.1 (0.8–1.7)	0.9 (0.7–1.2)	1.1 (0.8–1.5)	1.3 (0.9–1.8)	1.2 (0.7–2.0)	0.19	
			0.9 (0.5–1.6)	0.8 (0.5–1.2)	0.7 (0.4–1.1)	0.9 (0.5–1.4)	0.9 (0.5–1.7)	0.85	
	SCC AC SCLC	Mean lifelong intake	1.2 (0.5–2.8)	0.6 (0.4–0.9)	0.7 (0.5–1.2)	0.7 (0.4–1.2)	0.9 (0.5–1.8)	0.87	
			1.0 (0.5–2.2)	0.9 (0.6–1.2)	1.3 (0.9–1.9)	1.1 (0.7–1.8)	1.4 (0.8–2.6)	0.16	
			0.6 (0.1–2.6)	1.0 (0.6–1.6)	0.9 (0.6–1.6)	1.0 (0.5–1.9)	1.4 (0.7–2.8)	0.38	

AC, adenocarcinoma; CI, confidence interval; SCC, squamous-cell carcinoma; SCLC, small-cell lung cancer; SIR, standardized incidence ratio

Table 2.54 Case-control studies of alcoholic beverage consumption and lung cancer by histological type

Reference	Subject and histology	Exposure categories	Odds ratio (95% CI)				Comments		
Koo (1988)	<i>Women</i> SCC + SCLC AC + LCLC	Times/ week	≥1	<i>p</i> for trend			Reference, <1 time/week; adjusted for age, no. of live births, schooling; restricted to never smokers		
		2.1	0.141						
		1.4	0.460						
Dosemeci <i>et al.</i> (1997)	<i>Men</i> SCC SCLC Others	Ever drank	1.6 (1.1–2.2)				Reference, never drinkers; adjusted for age, smoking		
			1.3 (0.8–2.1)						
			1.9 (1.2–2.9)						
	SCC SCLC Others	Alcohol (cL/week)	1–35	36–140	≥141	<i>p</i> for trend			
			1.7 (0.8–3.5)	1.6 (0.9–2.8)	1.8 (1.0–3.6)	0.003			
			1.8 (0.7–4.6)	1.2 (0.6–2.6)	0.8 (0.2–2.3)	0.419			
			2.0 (0.8–5.0)	1.9 (0.9–3.8)	1.8 (0.8–4.3)	0.008			
			SCC SCLC Others	Duration (years)	1–10	11–20	≥21	<i>p</i> for trend	
					1.6 (0.7–4.0)	1.7 (1.0–3.1)	2.7 (1.2–6.2)	< 0.001	
	2.0 (0.7–5.8)	1.2 (0.5–2.7)			1.6 (0.5–5.3)	0.139			
	SCC SCLC Others	Bottle- years	1–34	35–90	≥91	<i>p</i> for trend			
			1.9 (1.0–3.9)	1.7 (0.8–3.9)	1.9 (1.0–3.9)	0.003			
1.7 (0.6–4.5)			1.8 (0.7–4.6)	0.7 (0.2–2.4)	0.298				
Others	1.6 (0.6–4.3)	2.6 (1.1–6.3)	1.4 (0.5–3.7)	0.025					

Table 2.54 (continued)

Reference	Subject and histology	Exposure categories	Odds ratio (95% CI)			Comments	
Carpenter <i>et al.</i> (1998)	<i>Men and women</i>	Intake	1–6 drinks/ week	≥1 drink/day	<i>p</i> for trend	Reference, never to 3 drinks/month; adjusted for age, sex, race, saturated fat, pack–years smoked, years since quitting smoking; alcoholic beverage types mutually adjusted	
		AC	<i>Beer</i>	0.7 (0.4–1.3)	0.8 (0.4–1.6)		0.35
		SCC + SCLC		1.0 (0.5–1.8)	0.8 (0.4–1.7)		0.32
		Other cell types		1.0 (0.5–1.8)	0.6 (0.3–1.3)		0.13
		AC	<i>Wine</i>	1.0 (0.5–1.8)	0.5 (0.2–1.6)		0.22
		SCC + SCLC		0.6 (0.3–1.1)	0.5 (0.2–1.3)		0.11
		Other cell types		0.8 (0.4–1.6)	0.8 (0.3–2.0)		0.49
		AC	<i>Liquor</i>	1.0 (0.6–1.9)	1.4 (0.6–3.2)		0.54
		SCC + SCLC		0.9 (0.5–1.6)	1.8 (0.9–4.0)		0.16
		Other cell types		1.1 (0.6–1.9)	2.1 (0.9–4.5)		0.20

Table 2.54 (continued)

Reference	Subject and histology	Exposure categories					Odds ratio (95% CI)		Comments
		1-3.9	4-6.9	≥7	Continuous				
Zang & Wynder (2001)	‘Whiskey-equivalent’ (oz alcohol/day)	1-3.9	4-6.9	≥7	Continuous				Reference for current drinking, <1 oz alcohol/day; reference for lifelong exposure, <4 oz/day-year; adjusted for body-mass index, current cigarettes per day; dose-response used oz/day-year as continuous variable.
	<i>Men</i>								
	SCC	1.1 (0.9-1.5)	0.9 (0.7-1.3)	1.4 (1.1-1.8)	1.1 (1.0-1.2)				
	AC	1.1 (0.9-1.4)	1.3 (1.0-1.7)	1.0 (0.8-1.3)	1.0 (0.9-1.1)				
	SCLC	1.2 (0.8-1.7)	1.4 (0.9-2.2)	1.4 (1.0-2.0)	1.1 (1.0-1.3)				
	LCLC	1.2 (0.7-1.8)	0.7 (0.4-1.5)	1.2 (0.7-1.9)	1.0 (0.9-1.2)				
	Lifelong exposure (oz/day ‘whiskey-equivalent’ × years of drinking)	4-16	17-27	28-64	65-103	≥104	Continuous		
	SCC	1.0 (0.7-1.4)	0.8 (0.5-1.2)	1.1 (0.8-1.6)	1.1 (0.8-1.7)	1.2 (0.9-1.6)	1.0 (1.0-1.1)		
	AC	1.1 (0.8-1.5)	1.6 (1.1-2.3)	1.1 (0.8-1.5)	1.4 (1.0-2.0)	1.1 (0.8-1.5)	1.1 (1.0-1.1)		
	SCLC	1.1 (0.7-1.9)	1.0 (0.5-1.9)	1.0 (0.6-1.7)	1.5 (0.9-2.5)	1.3 (0.9-1.9)	1.0 (1.0-1.1)		
LCLC	1.1 (0.6-2.0)	1.4 (0.7-2.8)	1.1 (0.6-2.0)	0.9 (0.4-1.8)	[0.9] (0.5-1.5)	1.0 (0.9-1.1)			

Table 2.54 (continued)

Reference	Subject and histology	Exposure categories	Odds ratio (95% CI)				Comments
			1-60	61-120	>120	<i>p</i> for trend	
De Stefani <i>et al.</i> (2002)	Men AC	Ethanol (mL/day)	1-60	61-120	>120	<i>p</i> for trend	Reference, non-drinker; adjusted for age, residence, urban/rural status, education, family history of lung cancer in first-degree relatives, body-mass index, smoking status, cigarettes per day, years since quitting, age at start of smoking
		Beer	0.8 (0.4-1.5)	1.1 (0.6-2.1)	1.2 (0.6-2.1)	0.34	
		Wine	1.1 (0.5-2.5)	0.6 (0.3-1.6)	0.4 (0.2-1.1)	0.31	
		Hard liquor	0.6 (0.3-1.2)	0.6 (0.3-1.2)	1.4 (0.7-3.0)	0.29	
			1.5 (0.8-2.6)	2.9 (1.4-6.2)		0.09	
Djousse <i>et al.</i> (2002)	Alcohol (g/day) Men and women SCC AC Others		0.1-12	12.1-24	>24		Reference, 0 g/day; adjusted for age, sex, smoking status, pack-years of smoking, year of birth
		SCC	0.4 (0.1-2.0)	0.4 (0.1-2.6)	0.3 (0.1-1.7)		
		AC	2.9 (0.8-10.9)	1.5 (0.3-8.1)	2.3 (0.5-10.5)		
		Others	0.7 (0.2-2.3)	0.8 (0.2-2.9)	0.8 (0.2-2.7)		

Table 2.54 (continued)

Reference	Subject and histology	Exposure categories	Odds ratio (95% CI)			Comments
Rachtan (2002)	Average vodka intake (g) <i>Women</i>	<100	≥100	<i>p</i> for trend		Reference, non-drinkers; adjusted for age, pack-years of smoking, passive smoking, consumption of milk, butter, margarine, cheese, meat, fruit, vegetables, carrots, spinach, siblings with cancer, tuberculosis, residence, occupational exposure
	SCC	1.3 (0.6–2.9)	3.9 (1.0–15.2)	<0.001		
	AC	2.6 (1.2–6.1)	8.0 (1.7–37.7)	0.003		
	SCLC	1.9 (0.8–4.5)	11.8 (3.0–45.9)	<0.001		

Table 2.54 (continued)

Reference	Subject and histology	Exposure categories	Odds ratio (95% CI)		Comments
Benedetti <i>et al.</i> (2006)	Drinks/week		1–6	≥7	Reference, never weekly; adjusted for age, respondent status, ethnicity, smoking status, cigarette–years, socioeconomic status, years of schooling, years since quitting
	<i>Men (Study I)</i>				
	SCC		1.3 (0.8–2.2)	1.4 (0.9–2.2)	
	AC		1.8 (0.9–3.5)	2.0 (1.1–3.6)	
	SCLC		1.1 (0.6–2.1)	1.1 (0.6–2.0)	
	LCLC		0.9 (0.4–2.3)	0.5 (0.2–1.3)	
	<i>Men (Study II)</i>				
	SCC		1.3 (0.7–2.2)	1.4 (0.8–2.3)	
	AC		1.0 (0.6–1.7)	1.5 (1.0–2.5)	
	SCLC		1.1 (0.6–2.2)	1.3 (0.7–2.4)	
	LCLC		1.9 (0.7–4.6)	2.0 (0.8–4.9)	
	<i>Women (Study II)</i>				
	SCC		0.2 (0.1–0.4)	1.0 (0.5–2.1)	
	AC		0.5 (0.3–0.8)	0.9 (0.5–1.5)	
SCLC		0.3 (0.2–0.7)	0.9 (0.4–2.1)		
LCLC		0.3 (0.1–0.8)	0.4 (0.1–1.2)		

AC, adenocarcinoma; CI, confidence interval; LCLC, large cell lung cancer; SCC, squamous-cell carcinoma; SCLC, small-cell lung cancer

Table 2.55 Cohort studies of beer consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Pollack <i>et al.</i> (1984)	Men	<i>oz/month</i> Non-beer drinker 1–9 10–99 [100]–499 ≥500	1.0 [0.7] [0.3–1.5] [0.5] [0.2–1.4] [1.1] [0.7–2.1] [1.1] [0.7–2.1]	Adjusted for age, cigarette smoking status (never, former and current smokers), alcohol content of the other two types of beverage (if significant) [values read from graph]
Chow <i>et al.</i> (1992)	Men	<i>Times/month</i> Never drank <3 3–5 6–13 >13 Former drinker	1.0 1.2 (0.8–1.9) 1.4 (0.8–2.3) 1.7 (1.0–2.9) 1.1 (0.6–1.9) 1.8 (1.1–3.0)	Adjusted for age, industry/occupation, smoking status (never any tobacco, other tobacco only, occasional/past use of 1–19, 20–29, ≥30 cigarettes/day, current use of 1–19, 20–29, ≥30 cigarettes/day)
Potter <i>et al.</i> (1992)	Women	Non-drinker <1 glass/day ≥1 glass/day	1.0 0.6 (0.3–1.2) 1.9 (0.96–3.9)	Adjusted for smoking (pack–years)
Woodson <i>et al.</i> (1999)	Men	<i>Ethanol (g/day)</i> Non-drinker Q1 0.01–1.6 Q2 1.7–4.5 Q3 4.6–11.5 Q4 11.6–242.6	1.0 (0.9–1.2) 1.0 (1.0) 0.8 (0.6–1.0) 0.9 (0.7–1.1) 0.9 (0.7–1.1) <i>p</i> for trend=0.19	Adjusted for age, body mass index, years smoked, cigarettes per day, intervention group
Prescott <i>et al.</i> (1999)	Men Women	<i>Drinks/week</i> <1 1–13 >13 <1 1–13 >13	1.0 (1.0) 1.1 (0.8–1.4) 1.4 (1.0–1.8) 1.0 (1.0) 0.9 (0.6–1.3) 1.5 (0.7–3.1)	Adjusted for age, study cohort, education, smoking (current smoking: pack–years, duration of smoking), other types of alcoholic beverage

Table 2.55 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Freudenheim <i>et al.</i> (2005) Pooled analysis of 7 prospective studies	Men	<i>g/day</i> None	1.0	Adjusted for education, body-mass index, energy intake, other types of alcoholic beverage, smoking status (never, past, current), smoking duration for past and current smokers, cigarettes smoked daily for current smokers
		>0-<5	0.9 (0.8-1.1)	
		5-<15	0.8 (0.7-1.0)	
		≥15	1.1 (0.9-1.4)	
	Women	None	<i>p</i> for trend=0.47	
		>0-<5	1.0	
		5-<15	0.8 (0.6-0.9)	
		≥15	1.2 (1.0-1.5)	
			1.9 (1.5-2.4)	
			<i>p</i> for trend <0.001	

CI, confidence interval

from beer per day (approximately ≥ 1 beer per day; odds ratio, 1.9; 95% CI, 1.5–2.4), but the relative risk was 0.8 (95% CI, 0.6–0.9) for those with the lowest level of beer consumption (< 5 g ethanol/day). A null association was reported in three studies (Pollack *et al.*, 1984; Chow *et al.*, 1992; Woodson *et al.*, 1999), all of which were restricted to men. Chow *et al.* (1992) reported a relative risk of 1.7 (95% CI, 1.0–2.9) for drinking beer 6–13 times per month, and of 1.1 (95% CI, 0.6–1.9) for drinking beer more than 13 times per month.

Among 11 case–control studies that presented tobacco smoking-adjusted odds ratios for beer drinking compared with non-drinkers, three reported a positive association for the highest level of beer drinking used in the analyses (Bandera *et al.*, 1992; De Stefani *et al.*, 1993; Benedetti *et al.*, 2006, in the first study in men only (Table 2.56).

(b) *Wine (Tables 2.57 and 2.58)*

Among 10 case–control studies (Table 2.58) that provided tobacco smoking-adjusted risk estimates for wine intake, only one reported a positive association for white wine intake (relative risk, 1.5; 95% CI, 0.5–4.4) but not for red wine or rosé (Ruano-Ravina *et al.*, 2004). In contrast, a significant inverse association was observed between red wine consumption and risk for lung cancer in this study. Six other case–control studies reported odds ratios below 1 for wine consumption, although these were not always statistically significant.

Among the three cohort studies that reported risk estimates for wine drinking (Table 2.57), two reported a significant inverse association in men (Prescott *et al.*, 1999; Woodson *et al.*, 1999 [trend test]). In another study, drinking ≥ 50 oz of wine per month (approximately ≥ 10 glasses of wine per month) was associated with a twofold increased risk for lung cancer compared with non-wine drinkers (Pollack *et al.*, 1984).

In a pooled analysis based on seven cohort studies (Freudenheim *et al.*, 2005), an inverse association was detected by the trend test for men, but not for women.

None of the cohort studies reported relative risk estimates adjusted for dietary factors such as vegetable/fruit intake. Confounding by dietary factors may explain to current observations.

(c) *Liquor (Tables 2.59 and 2.60)*

Two of five cohort studies reported a positive association between liquor drinking and risk for lung cancer, adjusted for tobacco smoking (Table 2.59) (Pollack *et al.*, 1984; Prescott *et al.*, 1999 in men only). The strongest association was identified by Pollack *et al.* (1984), in which men who consumed ≥ 1 measure of whiskey per day were found to have a relative risk of 2.6 [95% CI, 1.3–5.0]. Prescott *et al.* (1999) found a borderline significant 50% increase in risk among men who consumed at least two drinks of liquor per day; no association was observed among women.

Table 2.56 Case-control studies of beer consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Williams & Horm (1977)	Men	Non-drinker	1.0 (not given)	Adjusted for age, race, smoking; 'controls' were 'tobacco- and alcohol-unrelated' cancer; however, included colon and liver cancer
		<51 can-years	1.2	
		≥51 can-years	1.1	
	Women	Non-drinker	1.0	
		<51 can-years	0.8	
Mettlin (1989)	Men and women	<i>Times/week</i>		Adjusted for age, residence, sex, smoking history [pack-years or similar index of exposure], β-carotene intake index, education
		Never	1.0	
		<1	0.5 (0.4–0.8)	
		1–3	0.7 (0.5–1.1)	
		4–9	0.7 (0.5–1.2)	
		≥10	1.3 (0.8–2.1)	
Bandera <i>et al.</i> (1992)	Men	Drink/month		Adjusted for age, education, smoking (pack-years); no obvious interaction between beer consumption and smoking observed
		0	1.0	
		1–11	1.1 (0.7–1.7)	
		≥12	1.6 (1.0–2.4)	
		0	1.0	Also adjusted for carotenoids and fat
		1–11	1.0 (0.7–1.6)	
		≥12	1.5 (1.0–2.2)	
			<i>p</i> for trend=0.009	
De Stefani <i>et al.</i> (1993)	Men	<i>Ethanol (mL/day)</i>		Adjusted for age, residence, education, smoking (pack-years), other types of alcoholic beverage
		Lifetime abstainers	1.0	
		1–9	0.7 (0.3–2.5)	
		10–59	1.4 (0.4–6.2)	
		>59	3.4 (1.3–15.2)	
		<i>p</i> for trend=0.02		

Table 2.56 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Mayne <i>et al.</i> (1994)	Men and Women	<i>Monthly frequency</i>	(not given)	<i>p</i> value >0.05 for odds ratios of quartiles 2–4; adjusted for age, sex, county of residence, smoking history (never and former), cigarettes/day smoked in former smokers, religion, education, body mass index, income; ranges for quartiles not provided
		Q1	1.0 (ref)	
		Q2	1.1	
		Q3	0.9	
		Q4	1.2	
			<i>p</i> for trend=NS	
Rachtan & Sokolowski (1997)	Women	Non-drinker	1.0	Estimates only adjusted for age, not for smoking; updated analysis given in Rachtan (2002)
		Rarely	1.1 (0.5–2.3)	
		1–2/month	1.8 (0.5–6.7)	
		At least once/week	3.3 (0.6–17.5)	
			<i>p</i> for trend=0.126	
Carpenter <i>et al.</i> (1998)	Men and women	<i>Recent consumption</i>		Adjusted for age, gender, race, saturated fat consumption, tobacco smoking (pack-years), years since quitting tobacco smoking, other types of alcoholic beverage
		Never to 3 drinks/mth	1.0	
		1–6 drinks/week	0.4 (0.2–0.7)	
		≥1 drink/day	0.9 (0.4–1.8)	
			<i>p</i> for trend=0.45	
		<i>Consumption between age 30 and 40 years</i>		
		Never to 3 drinks/mth	1.0	
		1–6 drinks/week	0.9 (0.6–1.4)	
≥1 drink/day	0.7 (0.4–1.2)			
			<i>p</i> for trend=0.09	
De Stefani <i>et al.</i> (2002)	Men	<i>Ethanol (mL/day)</i>		Adenocarcinoma only; adjusted for age, residence, urban/rural status, education, family history of lung cancer in first-degree relatives, body mass index, smoking status, cigarettes per day, years since quitting, age at start of smoking, other types of alcoholic beverage; [for exclusive consumption of a specific alcoholic beverage, total alcohol intake might also be adjusted for].
		Non-drinker	1.0	
		1–60	1.1 (0.5–2.5)	
		>60	0.6 (0.3–1.6)	
			<i>p</i> for trend=0.31	
	Abstainer	1.0		
	Beer only	0.9 (0.1–5.6)		

Table 2.56 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Hu <i>et al.</i> (2002)	Women	<i>Servings/week</i>		Never smokers only; adjusted for age, province, education, social class
		0	1.0	
		≤0.5	1.2 (0.6–2.4)	
Rachtan (2002)	Women	>0.5	0.5 (0.2–1.1)	Adjusted for age only; estimates not adjusted for smoking [Unit of time not given]
			<i>p</i> for trend=0.17	
		<i>Frequency</i>		
		Non-drinker	1.0	
		Rarely	1.0 (0.6–1.8)	
		≥3 times/month	2.6 (1.5–4.5)	
			<i>p</i> for trend=0.002	
		<i>Average amount (g)</i>		
		Non-drinker	1.0	
		≥250	1.3 (0.8–2.0)	
>250	9.0 (2.6–31.6)			
	<i>p</i> for trend<0.001			
	<i>Drinking duration (years)</i>			
Non-drinker	1.0			
≤29	1.0 (0.5–1.9)			
≥30	2.0 (1.3–3.3)			
	<i>p</i> for trend=0.005			

Table 2.56 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Freudenheim <i>et al.</i> (2003)	Men and women	<i>Lifetime consumption (L)</i>		Adjusted for age, education, race, sex, body mass index, vegetable intake, fruit intake, total energy intake excluding alcohol, packs smoked per year, years smoked, index of passive exposure to smoke at home, work, in other settings
		0	1.0	
		≤62	1.2 (0.7–1.9)	
		>62	1.4 (0.8–2.3)	
			<i>p</i> for trend=0.30	
		<i>Consumption in previous 12–24 months (L)</i>		
0	1.0			
≤1.6	0.8 (0.4–1.4)			
>1.6	1.7 (1.0–2.9)			
		<i>p</i> for trend=0.05		
Ruano-Ravina <i>et al.</i> (2004)	Men and women	Non-drinker	1.0 (0.6–2.1)	Adjusted for age, sex, occupation, smoking habit (total lifetime tobacco consumption in thousands of packs), total alcoholic beverage intake
		Drinker	1.1 (0.97–1.02)	
		<i>Continuous variable</i>		
Benedetti <i>et al.</i> (2006)	Men (Study I)	Beer (weekly unit)	0.99	Adjusted for age, smoking status, cigarette–years, time since quitting, respondent status, ethnicity, census tract income, years of schooling
		Never weekly	1.0	
		1–6 drinks/week	1.2 (0.9–1.7)	
	Men (Study II)	≥7 drinks/week	1.5 (1.1–2.1)	
		Never weekly	1.0	
		1–6 drinks/week	1.0 (0.7–1.4)	
	Women (Study II)	≥7 drinks/week	1.0 (0.7–1.4)	
		Never weekly	1.0	
		1–6 drinks/week	0.3 (0.2–0.5)	
		≥7 drinks/week	0.9 (0.5–1.6)	

CI, confidence interval; NS, not significant

Table 2.57 Cohort studies of wine consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Pollack <i>et al.</i> (1984)	8006 Men	<i>oz/month</i> Non-wine drinker	1.0	Adjusted for age, cigarette-smoking status (never, former, current smokers), alcohol content of the other two types of beverage (if significant) [read from graph]
		1	[1.2] [0.6–2.6]	
		2–49	[0.8] [0.2–2.6]	
		≥50	2.2 [1.0–4.4]	
Prescott <i>et al.</i> (1999)	17 669 Men	<i>Drinks/week</i> <1	1.0	Adjusted for age, study cohort, education, smoking (current smoking: pack-years, duration of smoking), other types of alcoholic beverage
		1–13	0.8 (0.6–1.0)	
		>13	0.4 (0.2–0.9)	
	13 525 Women	<1	1.0	
		1–13	0.9 (0.6–1.3)	
		>13	0.2 (0.0–1.3)	
Woodson <i>et al.</i> (1999)	27 111 Men	<i>Ethanol (g/day)</i> Non-drinker	1.1 (0.9–1.3)	Adjusted for age, body mass index, years smoked, cigarettes per day, intervention group
		0.09–2.0	1.0	
		2.1–67.5	0.8 (0.6–1.1)	
			<i>p</i> for trend=0.02	
Freudenheim <i>et al.</i> (2005)	Men	<i>g/day</i> None	1.0	Adjusted for education, body mass index, energy intake, other types of alcoholic beverage, smoking status (never, past, current), smoking duration for past and current smokers, cigarettes smoked daily for current smokers
Pooled analysis of 7 prospective studies		>0–<5	0.9 (0.8–1.1)	
		5–<15	0.7 (0.5–0.9)	
		≥15	0.9 (0.6–1.4)	
		<i>p</i> for trend=0.04		
	Women	None	1.0	
	>0–<5	0.9 (0.7–1.1)		
	5–<15	0.8 (0.5–1.1)		
	≥15	1.1 (0.8–1.5)		
			<i>p</i> for trend=0.99	

CI, confidence interval

Table 2.58 Case-control studies of wine consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Williams & Horm (1977)	Men	Non-drinker	1.0 (not given)	Adjusted for age, race, smoking; 'controls' had 'tobacco- and alcohol-unrelated' cancer; however, controls included colon and liver cancer.
		<51 glass-years	0.6	
	≥51 glass-years	1.1		
	Women	Non-drinker	1.0	
<51 glass-years		0.7		
Mettlin (1989)	Men and women	≥51 glass-years	1.1	Adjusted for age, residence, sex, smoking history [pack-years or similar index of exposure], β-carotene intake index, education
		<i>Times/week</i>		
		Never	1.0	
		<1	0.6 (0.4–0.8)	
		1–3	0.5 (0.3–0.8)	
Bandera <i>et al.</i> (1992)	Men	4–9	0.8 (0.5–1.5)	Adjusted for age, education, smoking (pack-years); no obvious interaction between wine consumption and smoking observed
		≥10	1.0 (0.4–2.5)	
		<i>Drinks/month</i>		
		0	1.0	
		1	1.0 (0.7–1.4)	
De Stefani <i>et al.</i> (1993)	Men	≥2	0.7 (0.5–1.1)	Adjusted for age, residence, education, smoking (pack-years), other types of alcoholic beverage
		<i>Ethanol (mL/day)</i>		
		Lifetime abstainer	1.0	
		1–36	1.2 (0.7–2.2)	
		37–120	1.3 (0.7–3.1)	
Rachtan & Sokolowski (1997)	Women	>120	1.5 (0.9–3.3)	Estimates only adjusted for age, not for smoking; updated analysis given in Rachtan (2002)
		<i>p</i> for trend=0.09		
		Non-drinker	1.0	
		Rarely	0.9 (0.5–1.8)	
		1–2/month	1.1 (0.5–2.5)	
At least 1/week	1.2 (0.2–8.5)			
		<i>p</i> for trend=0.958		

Table 2.58 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Carpenter <i>et al.</i> (1998)	Men and women	<i>Recent consumption</i>		Adjusted for age, gender, race, saturated fat consumption, tobacco smoking (pack-years), years since quitting tobacco smoking, other types of alcoholic beverage
		Never to 3 drinks/month	1.0	
		1–6 drinks/week	0.7 (0.4–1.3)	
		≥1 drink/day	0.8 (0.3–1.9)	
			<i>p</i> for trend=0.66	
		<i>Consumption between age 30 and 40 years</i>		
		Never to 3 drinks/month	1.0	
		1–6 drinks/week	0.8 (0.5–1.3)	
		≥1 drink/day	0.6 (0.3–1.3)	
			<i>p</i> for trend=0.16	
De Stefani <i>et al.</i> (2002)	Men	<i>Alcohol (mL/day)</i>		Adenocarcinoma only; adjusted for age, residence, urban/rural status, education, family history of lung cancer in first-degree relatives, body mass index, smoking status, cigarettes per day, years since quitting, age at start of smoking, other types of alcoholic beverage; [for exclusive consumption of a specific alcoholic beverages, total alcohol intake might also be adjusted for].
		Non-drinker	1.0	
		1–60	0.6 (0.3–1.2)	
		61–120	0.6 (0.3–1.2)	
		>120	0.4 (0.2–1.1)	
			<i>p</i> for trend=0.09	
	Abstainer	1.0		
	Wine only	0.7 (0.4–1.4)		
Hu <i>et al.</i> (2002)	Women	<i>Servings/week</i>		Never smokers only; adjusted for age, province, education, social class
		0	1.0	
		≤0.5	0.7 (0.4–1.2)	
		>0.5	0.7 (0.4–1.2)	
			<i>p</i> for trend=0.10	

Table 2.58 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Rachtan (2002)	Women	<i>Frequency</i>		Adjusted for age only; estimates not adjusted for smoking [Unit of time not given]
		Non-drinker	1.0	
		Rarely	1.3 (0.9–1.9)	
		≥3 times/month	2.0 (1.2–3.3)	
			<i>p</i> for trend=0.007	
		<i>Average amount (g)</i>		
		Non-drinker	1.0	
		≤70	1.1 (0.8–1.7)	
		>70	2.6 (1.6–4.4)	
			<i>p</i> for trend=0.001	
		<i>Drinking duration (years)</i>		
		Non-drinker	1.0	
≤29	1.4 (0.8–2.4)			
≥30	1.6 (1.1–2.3)			
	<i>p</i> for trend=0.021			
Freudenheim <i>et al.</i> (2003)	Men and women	<i>Lifetime consumption (L)</i>		Adjusted for age, education, race, sex, body mass index, vegetable intake, fruit intake, total energy intake excluding alcohol, packs smoked per year, years smoked, index of passive smoking exposure to smoke at home, work, in other settings
		0	1.0	
		≤19	0.9 (0.5–1.4)	
		>19	0.8 (0.5–1.3)	
			<i>p</i> for trend=0.06	
		<i>Consumption in previous 12–24 months (L)</i>		
		0	1.0	
		≤1.0	0.7 (0.4–1.3)	
		>1.0	0.7 (0.4–1.3)	
			<i>p</i> for trend=0.10	

Table 2.58 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Ruano-Ravina <i>et al.</i> (2004)	Men and women	Non-drinker	1.0	Adjusted for age, sex, occupation, smoking habit (total lifetime tobacco consumption in thousands of packs), total alcohol intake
		White	1.5 (0.5–4.4)	
		Red	0.4 (0.2–1.0)	
		Rosé	0.4 (0.1–1.4)	
		All types	0.5 (0.2–1.4)	
		<i>Continuous variable</i>		
		Red (glasses/day)	0.9 (0.8–1.0)	
Benedetti <i>et al.</i> (2006)	Men (Study I)	Never weekly	1.0	Adjusted for age, smoking status, cigarette–years, time since quitting, respondent status, ethnicity, census tract income, years of schooling
		1–6 drinks/week	1.4 (1.0–1.9)	
		≥7 drinks/week	0.7 (0.4–1.1)	
	Men (Study II)	Never weekly	1.0	
		1–6 drinks/week	0.6 (0.4–0.8)	
		≥7 drinks/week	0.8 (0.5–1.1)	
	Women (Study II)	Never weekly	1.0	
		1–6 drinks/week	0.3 (0.2–0.4)	
		≥7 drinks/week	0.7 (0.4–1.2)	

CI, confidence interval

In a pooled analysis (Freudenheim *et al.*, 2005), a positive association was detected among men who drank one measure of liquor per day or more, with a significant dose–response relationship. No association was observed among women.

Liquor consumption was found to be positively associated with the risk for lung cancer in three (Carpenter *et al.*, 1998; De Stefani *et al.*, 2002; Rachtan, 2002) of 11 case–control studies that reported tobacco smoking-adjusted odds ratio estimates for liquor consumption (Table 2.60). The strongest association was found in the study by Rachtan (2002), in which Polish women who consumed ≥ 100 g alcohol from liquor per week (approximately one measure per day) had an eightfold greater risk for lung cancer than non-drinking women (95% CI, 2.9–21.2).

2.10.4 *Studies stratified by tobacco-smoking status (Tables 2.61 and 2.62)*

Studies based on never smokers may be the most valid approach to study the carcinogenicity of alcoholic beverages in the lung. In smokers, tobacco smoking may modify the effect of alcohol consumption and heterogeneity of risk may exist between populations with different smoking patterns. One of the proposed mechanisms for the carcinogenic effect of alcoholic beverages is that they may act as a solvent for tobacco-associated carcinogens. It is therefore important to examine the effect of alcoholic beverage consumption among both never smokers and smokers, and to study the interaction between these two risk factors. Tables 2.61 and 2.62 summarize the results from cohort and case–control studies that presented relative risks for alcoholic beverage use by smoking category.

Results from two cohort studies (Nishino *et al.*, 2006; Rohrmann *et al.*, 2006) did not seem to suggest an interaction between smoking status (never, former and current) and alcoholic beverage consumption, although a *p*-value for a formal test of interaction was not available. [These analyses may have the limitation that most of the cases of lung cancer were smokers.]

In a pooled analysis (Freudenheim *et al.*, 2005), no obvious interaction was suggested following stratification by smoking status among women. A positive association was only found among male never smokers but not among male former or current smokers, which suggests a heterogeneity of the effect of alcoholic beverages by smoking status in men.

Since most cases of lung cancer are smokers, several cohort and case–control studies examined the effect of alcoholic beverages according to the amount smoked. Woodson *et al.* (1999) conducted a cohort study with detailed analyses of the effect of alcoholic beverage according to intake by smoking behaviour, characterized by the number of cigarettes per day, duration of smoking, frequency of inhaling and time since quitting. No obvious differences in the relative risks were found across these smoking categories. Most of the case–control studies reported significant positive associations only among smokers or greater risk estimates among heavier smokers than among lighter smokers (Herity *et al.*, 1982; De Stefani *et al.*, 1993; Dosemeci *et al.*, 1997; Zang & Wynder, 2001; Benedetti *et al.*, 2006 [men only]).

Table 2.59 Cohort studies of liquor consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Pollack <i>et al.</i> (1984)	Men	<i>oz/month</i> Non-whiskey drinker 1–4 5–49 ≥50	1.0 [1.1] [0.6–2.0] [1.0] [0.5–2.1] 2.6 [1.3–5.0]	Adjusted for age, cigarette-smoking status (never, former, current smokers), alcohol content of the other two types of beverage (if significant); [read from graph]
Chow <i>et al.</i> (1992)	Men	<i>Times/month</i> Never drank <3 3–5 6–13 >13 Former drinker	1.0 1.3 (0.9–2.0) 1.3 (0.8–2.1) 1.3 (0.7–2.2) 1.0 (0.5–1.8) 1.9 (1.1–3.1)	Adjusted for age, industry/occupation, smoking status (never any tobacco, other tobacco only, occasional/past use of 1–19, 20–29, ≥30 cigarettes/day, current use of 1–19, 20–29, ≥30 cigarettes/day)
Potter <i>et al.</i> (1992)	Women	Non-drinker ≥1/day	1.0 1.1 (0.6–2.3)	Adjusted for smoking (pack–years)
Woodson <i>et al.</i> (1999)	Men	<i>Ethanol (g/day)</i> Non-drinker Q1 0.01–2.6 Q2 2.7–10.6 Q3 10.7–22.7 Q4 22.8–160.0	1.1 (0.9–1.3) 1.0 1.0 (0.9–1.3) 1.1 (0.9–1.3) 1.1 (0.9–1.3) <i>p</i> for trend=0.12	Adjusted for age, body mass index, years smoked, cigarettes per day, intervention group
Prescott <i>et al.</i> (1999)	Men	<i>Drinks/week</i> <1 1–13 >13	1.0 1.2 (0.97–1.5) 1.5 (0.99–2.1)	Adjusted for age, study cohort, education, smoking (current smoking: pack–years, duration of smoking), other types of alcoholic beverage
	Women	<1 1–13 >13	1.0 0.8 (0.6–1.2) 0.7 (0.2–2.2)	

Table 2.59 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments	
Freudenheim <i>et al.</i> (2005) Pooled analysis of 7 prospective studies	Men	<i>g/day</i>		Adjusted for education, body mass index, energy intake, other types of alcoholic beverage, smoking status (never, past, current), smoking duration for past and current smokers, cigarettes smoked daily for current smokers	
		None	1.0		
		>0-<5	1.2 (0.98-1.4)		
		5-<15	1.0 (0.8-1.2)		
	Women	≥15	1.3 (1.1-1.7)		<i>p</i> for trend=0.04
		None	1.0		
		>0-<5	0.9 (0.7-1.0)		
		5-<15	0.8 (0.6-1.1)		
		≥15	1.0 (0.8-1.2)	<i>p</i> for trend=0.52	

CI, confidence interval

Table 2.60 Case-control studies of liquor consumption and lung cancer

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Williams & Horm (1977)	Men	Non-drinker	1.0 (not given)	Adjusted for age, race, smoking; controls included colon and liver cancer
		<51 jigger-years	0.9	
		≥51 jigger-years	1.1	
	Women	Non-drinker	1.0	
		<51 jigger-years	1.2	
		≥51 jigger-years	0.6	
Mettlin (1989)	Men and women	<i>Times/week</i>		Adjusted for age, residence, sex, smoking history [pack-years or similar index of exposure], β-carotene intake index, education
		Never	1.0	
		<1	0.7 (0.5–1.0)	
		1–3	0.9 (0.6–1.5)	
		4–9	0.6 (0.4–0.9)	
		≥10	0.7 (0.4–1.1)	
Bandera <i>et al.</i> (1992)	Men	<i>Drinks/month</i>		Adjusted for age, education, smoking (pack-years); no obvious interaction between liquor consumption and smoking was observed.
		0	1.0	
		1–8	0.6 (0.4–1.0)	
		≥9	1.1 (0.7–1.6)	
			<i>p</i> for trend=0.1	
De Stefani <i>et al.</i> (1993)	Men	<i>Ethanol (mL/day)</i>		Adjusted for age, residence, education, smoking (pack-years), other types of alcoholic beverage
		Lifetime abstainer	1.0	
		1–34	0.9 (0.6–1.6)	
		35–115	1.3 (0.8–2.6)	
		>115	1.1 (0.6–1.4)	
	<i>p</i> for trend=0.50			
Rachtan & Sokolowski (1997)	Women	<i>Vodka</i>		Adjusted for pack-years smoked, carrot intake, margarine on bread
		Non-drinker	1.0	
		1–2/month	2.6 (1.3–5.5)	
	At least 1/week	7.5 (0.8–71.0)		

Table 2.60 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Carpenter <i>et al.</i> (1998)	Men and women	<i>Recent consumption</i>		Adjusted for age, gender, race, saturated fat consumption, tobacco smoking (pack-years), years since quitting tobacco smoking, other types of alcoholic beverage
		Never to 3 drinks/month	1.0	
		1–6 drinks/week	1.2 (0.7–2.2)	
		≥1 drink/day	1.9 (1.0–3.4)	
			<i>p</i> for trend=0.06	
		<i>Consumption between age 30 and 40 years</i>		
	Never to 3 drinks/month	1.0 (0.7–1.5)		
	1–6 drinks/week	1.0 (1.1–3.2)		
	≥1 drink/day	1.8		
		<i>p</i> for trend=0.06		
De Stefani <i>et al.</i> (2002)	Men	<i>Ethanol (ml/day)</i>		Adenocarcinoma only; adjusted for age, residence, urban/rural status, education, family history of lung cancer in first-degree relatives, body mass index, smoking status, cigarettes per day, years since quit, age at start of smoking, other types of alcoholic beverage; [for exclusive consumption of a specific alcoholic beverage, total alcohol intake might also be adjusted for].
		Non-drinker	1.0	
		1–60	1.5 (0.8–2.6)	
		61–120	2.9 (1.4–6.2)	
		>120	1.4 (0.7–3.0)	
	<i>p</i> for trend=0.09			
	Abstainer	1.0		
	Liquor only	2.1 (0.9–4.9)		
Hu <i>et al.</i> (2002)	Women	<i>Servings/week</i>		Never smokers only; adjusted for age, province, education, social class
		0	1.0	
		≤0.5	1.1 (0.6–2.1)	
		>0.5	1.1 (0.6–2.1)	
		<i>p</i> for trend=0.58		
Rachtan (2002)	Women	<i>Average amount (g)</i>		Adjusted for age, pack-years of smoking, passive smoking, siblings with cancer, tuberculosis, place of residence, occupational exposure, dietary factors [unit of time not given]
		Non-drinker	1.0	
		<100	2.2 (1.3–3.8)	
		≥100	7.8 (2.9–21.2)	
		<i>p</i> for trend<0.0001		

Table 2.60 (continued)

Reference	Subjects	Exposure categories	Relative risk (95% CI)	Comments
Freudenheim <i>et al.</i> (2003)	Men and women	<i>Lifetime consumption (L)</i>		Adjusted for age, education, race, sex, body mass index, vegetable intake, fruit intake, total energy intake excluding alcohol, packs smoked per year, years smoked, index of passive smoking exposure to smoke at home, work, in other settings
		0	1.0	
		≤28	1.2 (0.8–1.9)	
		>28	0.8 (0.5–1.2)	
			<i>p</i> for trend=0.44	
		<i>Consumption in previous 12–24 months (L)</i>		
0	1.0			
≤1.0	0.6 (0.3–1.2)			
>1.0	0.9 (0.5–1.5)			
	<i>p</i> for trend=0.47			
Ruano-Ravina <i>et al.</i> (2004)	Men and women	Non-drinker	1.0	Adjusted for age, sex, occupation, smoking habit (total lifetime tobacco consumption in thousands of packs), total alcoholic beverage intake
		Drinker	1.6 (0.8–3.4)	
		<i>Continuous variable</i>		
		Liquor (weekly unit)	1.0 (1.0–1.1)	
Benedetti <i>et al.</i> (2006)	Men (Study I)	Never weekly	1.0	Adjusted for age, smoking status, cigarette–years, time since quitting, respondent status, ethnicity, census tract income, years of schooling
		1–6 drinks/week	1.4 (1.0–1.9)	
		≥7 drinks/week	1.2 (0.8–1.7)	
	Men (Study II)	Never weekly	1.0	
		1–6 drinks/week	0.9 (0.7–1.2)	
		≥7 drinks/week	0.9 (0.7–1.3)	
Women (Study II)	Never weekly	1.0		
	1–6 drinks/week	0.4 (0.3–0.6)		
	≥7 drinks/week	1.7 (0.8–3.5)		

CI, confidence interval

Table 2.61 Cohort studies of alcoholic beverage consumption and lung cancer stratified by smoking status

Reference	Subjects and smoking status	Exposure categories	Risk ratio (95% CI)					Comments
Murata <i>et al.</i> (1996)	Ethanol (ml/day) <i>Men</i> Never smokers + former smokers Current smokers	>0 and ≤27	>27				Reference, 0 mL/day; crude CI from data matched on age	
		1.3 [(0.5–3.2)]	2.2 [(0.8–6.1)]					
Woodson <i>et al.</i> (1999)	Alcohol (g/day) Men <i>Cigarettes/day</i> <20 20–29 ≥30 <i>Years smoked</i> <32 32–40 >40 <i>Inhaled</i> Seldom Often Always <i>Cessation</i> <3 years >3 years Never	Non-drinker	5.3–13.3	13.4–27.6	≥27.7	<i>p</i> for trend	Reference, 0–5.2 g/day; all smokers; smokers defined as men who smoked 5 or more cigarettes per day; cut-offs for alcohol based on quartiles; adjusted for age, body mass index, years smoked, cigarettes per day, treatment group	
		1.2 (0.8–1.7)	0.9 (0.7–1.3)	0.9 (0.6–1.3)	1.2 (0.8–1.7)	0.59		
		1.2 (0.9–1.6)	1.1 (0.8–1.4)	1.0 (0.7–1.3)	1.0 (0.8–1.4)	0.99		
		1.0 (0.6–1.6)	0.9 (0.6–1.3)	0.8 (0.5–1.2)	0.8 (0.5–1.2)	0.26		
		1.4 (0.7–2.9)	1.1 (0.6–2.1)	1.1 (0.6–2.1)	1.0 (0.5–1.9)	0.87		
		1.4 (1.0–2.0)	1.1 (0.8–1.5)	1.1 (0.8–1.5)	1.3 (0.9–1.7)	0.16		
		1.0 (0.8–1.3)	0.9 (0.7–1.2)	0.8 (0.6–1.0)	0.9 (0.7–1.1)	0.13		
		1.4 (0.7–2.8)	0.8 (0.4–1.7)	0.7 (0.3–1.5)	0.7 (0.3–1.7)	0.37		
		1.4 (1.0–2.0)	1.2 (0.9–1.5)	1.1 (0.8–1.5)	1.1 (0.8–1.5)	0.81		
		1.0 (1.0–1.3)	0.9 (0.7–1.1)	0.8 (0.7–1.1)	1.0 (0.8–1.2)	0.84		
1.2 (0.7–2.0)	0.8 (0.5–1.4)	1.1 (0.6–2.0)	0.9 (0.5–1.8)	0.67				
1.2 (0.6–2.6)	0.9 (0.4–1.8)	0.8 (0.4–1.7)	1.5 (0.7–3.2)	0.81				
1.2 (0.9–1.5)	1.0 (0.8–1.2)	0.9 (0.7–1.1)	1.0 (0.8–1.2)	0.16				

Table 2.61 (continued)

Reference	Subjects and smoking status	Exposure categories	Risk ratio (95% CI)			<i>p</i> for trend	Comments
			>0–<5	5–<15	≥15		
Freudenheim <i>et al.</i> (2005)	Alcohol (g/day)						Reference, 0 g/day; adjusted for education, body mass index, energy intake; for former smokers, also adjusted for smoking duration; for current smokers, also adjusted for smoking duration and cigs/day
	<i>Men</i>						
	Nonsmoker		1.5 (0.6–3.5)	2.5 (1.1–5.8)	6.4 (2.7–14.9)	<0.01	
	Former smoker		0.7 (0.5–1.0)	0.9 (0.7–1.2)	0.9 (0.7–1.3)	0.27	
	Current smoker		0.9 (0.5–1.4)	1.0 (0.8–1.4)	0.9 (0.7–1.2)	0.92	
	Current smoker (<20 cigs/day)		0.8 (0.4–1.7)	1.0 (0.7–1.5)	0.8 (0.5–1.1)	0.12	
	<i>Women</i>						
	Nonsmoker		1.0 (0.7–1.4)	0.9 (0.5–1.5)	1.4 (0.6–2.9)	0.98	
	Former smoker		0.7 (0.4–1.2)	0.9 (0.6–1.2)	1.1 (0.7–1.8)	0.26	
	Current smoker		0.8 (0.6–1.0)	0.9 (0.7–1.1)	1.1 (0.9–1.3)	0.02	
Current smoker (<20 cigs/day)		0.6 (0.4–0.9)	0.8 (0.6–1.1)	0.9 (0.7–1.3)	0.42		

Table 2.61 (continued)

Reference	Subjects and smoking status	Exposure categories	Risk ratio (95% CI)				<i>p</i> for trend	Former drinker	Comments
Nishino <i>et al.</i> (2006)	Ethanol (g/day)	Ever drinker	≤24.9	25.0–49.9	≥50				Reference, never drinker; adjusted for age, family history of lung cancer, intake of green leafy vegetables, oranges, other fruits
	Men								
	Never smoker		1.2 (0.4–3.5)	1.1 (0.4–3.5)	0.4 (0.0–3.2)	1.2 (0.1–10.0)	0.61	4.2 (1.1–15.7)	
	Former smoker		0.7 (0.4–1.3)	0.6 (0.4–1.2)	0.7 (0.3–1.3)	0.3 (0.1–1.5)	0.13	1.4 (0.7–2.6)	
	<i>Current smoker</i>								
	≤20 cigs/day		0.9 (0.6–1.3)	0.8 (0.5–1.2)	0.8 (0.5–1.3)	1.1 (0.6–2.0)	0.99	1.3 (0.7–2.4)	
	>20 cigs/day		1.3 (0.7–2.5)	0.7 (0.3–1.7)	1.5 (0.7–3.0)	1.3 (0.6–2.9)	0.20	2.6 (1.1–6.1)	

Table 2.61 (continued)

Reference	Subjects and smoking status	Exposure categories	Risk ratio (95% CI)					<i>p</i> interaction	Comments	
Rohrmann <i>et al.</i> (2006)	Ethanol (g/day) <i>Men and women</i>	Baseline intake	Non-drinker	5–14.9	15–29.9	30–59.9	≥60		Reference, 0.1–4.9 g/day; all results stratified by age, sex, study centre; adjusted for height, weight, consumption of fruit, red meat, processed meat, education, total non-ethanol energy intake; for former smokers, also adjusted for smoking duration, time since quitting; for current smokers, also adjusted for smoking duration, cigs/day	
			Never smoker	0.6 (0.3–1.2)	0.9 (0.6–1.5)	0.7 (0.3–1.4)	0.6 (0.2–1.8)			
			Former smoker	1.5 (1.0–2.2)	0.7 (0.5–1.0)	0.7 (0.5–1.0)	0.9 (0.6–1.3)	0.9 (0.5–1.7)		0.64
		Current smoker	1.3 (1.0–1.7)	0.8 (0.6–1.0)	0.9 (0.7–1.2)	1.0 (0.8–1.3)	0.9 (0.7–1.2)			
		Mean lifelong intake	Never smoker	0.5 (0.2–1.2)	0.5 (0.3–0.8)	0.6 (0.3–1.5)	0.4 (0.1–3.0)	1.2 (0.1–13.6)		
			Former smoker	1.9 (0.9–4.2)	1.1 (0.8–1.6)	1.3 (0.9–2.0)	1.3 (0.8–2.2)	1.7 (0.9–3.5)		0.22
Current smoker	1.0 (0.6–1.8)		0.8 (0.6–1.0)	0.9 (0.7–1.2)	0.8 (0.6–1.1)	1.2 (0.8–1.7)				

CI, confidence interval

Table 2.62 Case-control studies of alcoholic beverage consumption and lung cancer stratified by smoking status

Reference	Subjects	Smoking status	Exposure categories	Odds ratio (95% CI)			Comments
Herity <i>et al.</i> (1982)	Men	0–<43 pack-years ≥43 pack-years	Intake (g/day for 10 years)	0–<90	≥90		[Assuming 20 cigarettes/pack]
				1.0	1.5 (0.4–5.2)		
Bandera <i>et al.</i> (1992)	Men	0–40 pack-years >40 pack-years	Drinks/month	≥ 21	<i>p</i> for trend		Reference, 0–20 drinks/month; adjusted for age, smoking, education; no obvious interaction between beer, wine or liquor consumption and smoking observed
				0.9 (0.6–1.6)	0.10		
De Stefani <i>et al.</i> (1993)	Men	0–19 cigs/day ≥20 cigs/day	Beer (mL/day)	1–9	10–59	≥60	Reference, non-drinkers; adjusted for age, residence
				0.4 (0.1–2.2)	–	2.9 (0.5–15.7)	
				0.9 (0.4–2.0)	2.4 (0.6–8.9)	4.2 (1.4–12.6)	

Table 2.62 (continued)

Reference	Subjects	Smoking status	Exposure categories	Odds ratio (95% CI)			Comments	
Dosemeci <i>et al.</i> (1997)	Men	Never smoker	Duration (years)	Never drank	1–20	≥21	Reference, never smoker and never drinker	
			1.0	–	–			
			1–20 cigs/day	2.8 (2.1–3.6)	4.4 (2.6–7.3)	5.2 (2.0–14.6)		
			≥21 cigs/day	6.1 (4.0–9.3)	8.5 (2.5–14.3)	14.1 (3.9–61.2)		
Zang & Wynder (2001)	Men	Nonsmoker	'Whiskey-equivalent' oz/day	0	1–5.9	≥6	Reference, non-drinkers and nonsmokers; data for current smokers only also reported	
			<20 cigs/day	1.0	1.2 (0.7–2.1)	0.7 (0.2–2.0)		
			20 cigs/day	6.2 (3.5–11.0)	7.4 (4.8–11.5)	8.3 (5.3–13.1)		
			>20 cigs/day	13.8 (8.2–21.5)	14.6 (10.0–21.5)	15.4 (10.4–22.8)		
Rachtan (2002)	Women	Nonsmoker	Alcohol (g/week)	≥1–4	≥4–8	≥1–8	Reference, <1 g/week; nonsmokers were never smokers	
				3.9 (1.8–8.3)	8.8 (2.8–27.3)	12.1 (3.9–36.9)		
				Current smoker		2.5 (1.2–5.1)		3.7 (1.7–8.2)
				Current + former smoker		2.8 (1.5–5.1)		5.0 (2.5–9.9)
		Nonsmoker	Vodka drinking	Non-drinker	Drinker		Reference, nonsmoker/non-drinker	
				Smoker	1.0	3.5 (1.9–6.4)		20.2 (11.7–35.0)

Table 2.62 (continued)

Reference	Subjects	Smoking status	Exposure categories	Odds ratio (95% CI)		Comments
				1–6	≥7	
Benedetti <i>et al.</i> (2006)		Cigarette–years	Drinks/week	1–6	≥7	Reference, never weekly; adjusted for age, respondent status, ethnicity, smoking status, cigarette–years, socioeconomic status, years of schooling, time since quitting. *Odds ratio for women consuming 1 or more beer weekly compared with women who never consumed beer on a weekly basis
	Study I	<825	<i>Total alcohol</i>	1.0 (0.5–1.8)	1.3 (0.7–2.4)	
	Men	825–1375		1.1 (0.6–2.0)	1.1 (0.6–2.0)	
		>1375		1.8 (0.8–4.3)	1.5 (0.8–3.1)	
			<i>p</i> for interaction	0.26	0.52	
	Study II	<675	<i>Beer</i>	0.3 (0.1–0.6)	0.7 (0.4–1.2)	
	Men	675–1270		1.4 (0.8–2.6)	1.9 (1.1–3.4)	
		>1270		1.9 (1.0–3.7)	1.6 (0.9–2.8)	
			<i>p</i> for interaction	0.00	0.06	
	Women	0	0.2 (0.0–0.6)	1.1 (0.4–3.3)		
		≤861	0.6 (0.3–1.1)	0.9 (0.5–1.8)		
		>861	0.2 (0.1–0.4)	0.5 (0.2–1.0)		
			<i>p</i> for interaction	0.70	0.54	
	Study I	<825	<i>Beer</i>	0.9 (0.5–1.6)	1.3 (0.7–2.3)	
	Men	825–1375		1.4 (0.8–2.5)	1.8 (1.0–3.0)	
		>1375		1.4 (0.7–3.0)	1.4 (0.7–2.6)	
			<i>p</i> for interaction	0.15	0.35	
	Study II	<675	<i>Beer</i>	0.6 (0.3–1.2)	0.9 (0.5–1.8)	
Men	675–1270	1.1 (0.7–1.8)		1.4 (0.8–2.2)		
	>1270	1.3 (0.8–2.4)		0.9 (0.5–1.5)		
		<i>p</i> for interaction	0.00	0.88		
Women	0	0.5 (0.3–0.9)*	–			
	≤861	0.3 (0.2–0.6)	0.7 (0.3–1.7)			
	>861	0.4 (0.2–0.7)	1.0 (0.4–2.7)			
		<i>p</i> for interaction	0.27	1.00		

Table 2.62 (continued)

Reference	Subjects	Smoking status	Exposure categories	Odds ratio (95% CI)		Comments
Benedetti <i>et al.</i> (2006) (contd)		Cigarette– years	Drinks/ week	1–6	≥7	
			<i>Wine</i>	1.1 (0.6–1.7)	1.2 (0.6–2.4)	
	Study I	<825		1.3 (0.8–2.1)	0.3 (0.1–0.7)	**Odds ratio for women consuming 1 or more drinks of spirits weekly compared with women who never consumed spirits on a weekly basis
	Men	825–1375		1.9 (1.0–3.8)	0.6 (0.3–1.5)	
		>1375	<i>p</i> for interaction	0.16	0.19	
	Study II	<675		0.4 (0.2–0.8)	0.6 (0.3–1.2)	
	Men	675–1270		0.5 (0.3–0.8)	0.8 (0.5–1.4)	
		>1270		0.8 (0.5–1.3)	0.8 (0.4–1.6)	
			<i>p</i> for interaction	0.01	0.07	
	Women	0		0.2 (0.1–0.6)	0.7 (0.2–2.5)	
		≤861		0.3 (0.2–0.7)	1.2 (0.5–2.5)	
		>861		0.2 (0.1–0.4)	0.3 (0.1–0.7)	
			<i>p</i> for interaction	0.83	0.27	
			<i>Spirits</i>			
	Study I	<825		1.3 (0.8–2.2)	1.0 (0.5–2.2)	
	Men	825–1375		1.0 (0.7–1.6)	1.0 (0.5–1.8)	
		>1375		2.2 (1.1–4.1)	1.5 (0.7–3.0)	
			<i>p</i> for interaction	0.41	0.67	
Study II	<675		0.6 (0.3–1.3)	1.4 (0.6–3.1)		
Men	675–1270		1.1 (0.7–1.8)	1.2 (0.6–2.1)		
	>1270		0.9 (0.5–1.4)	0.7 (0.4–1.2)		
		<i>p</i> for interaction	0.19	0.25		
Women	0		0.8 (0.5–1.5)**	–		
	≤861		0.5 (0.3–1.0)	1.0 (0.4–2.7)		
	>861		0.3 (0.2–0.6)	1.8 (0.5–6.0)		
		<i>p</i> for interaction	0.92	0.80		

CI, confidence interval

2.10.5 *Studies among nonsmokers (Tables 2.63 and 2.64)*

Residual confounding by tobacco smoking is a concern when interpreting the associations between alcoholic beverage intake and lung cancer. Restricting the analysis to never smokers appears to be an effective strategy to provide further insight on this topic, although secondhand tobacco smoke might still be a concern.

Korte *et al.* (2002) reported the unpublished data from the Cancer Prevention Study (CPS) I and II (Table 2.63). In CPS I, an increased risk for lung cancer was associated with drinking ≥ 500 g alcohol per month among both men and women who had never smoked. This association was not observed in CPS II.

A pooled study (Freudenheim *et al.*, 2005), based on seven cohorts, found an elevated pooled relative risk for alcoholic beverage consumption among never-smoking men (a dose–response was also observed), but not among never-smoking women.

Two cohort studies published subsequently reported a null association among never smokers, with adjustment for dietary factors. Both studies examined higher levels of alcoholic beverage drinking than those studied previously (Nishino *et al.*, 2006: ≥ 50 g of ethanol per day [~ 4 drinks/day]; Rohrmann *et al.*, 2006: ≥ 60 g of ethanol per day [~ 5 drinks/day]), although the number of cases at these levels of drinking was small.

Seven case–control studies included never smokers only as the study subjects or stratified analyses to never smokers (Table 2.64). [Analyses stratified to never smokers often suffer from the small number of lung cancer cases that arise among never smokers and result in wide confidence intervals.] In the three studies based on populations of never smokers (Kabat & Wynder, 1984; Koo, 1988; Hu *et al.*, 2002), no significant differences in alcoholic beverage intake were found between cases and controls. [One limitation of such a design is the lack of power to examine the risk associated with heavy drinking, as it is uncommon to find heavy drinkers among never smokers. For example, Hu *et al.* (2002) compared drinkers of 1 serving/week and >1 serving per week with non-drinkers which reflects the low drinking level in this group of women and which is likely to contribute to the null association observed in this study.] In contrast, Rachtan (2002) identified a significantly elevated risk associated with even a moderate level of alcoholic beverage intake among Polish women who never smoked (e.g. odds ratio, 8.8; 95% CI, 2.8–27.3 for 4–8 g alcohol per week [approximately 0.3–0.6 drinks/week]). A strong dose–response was also observed. [The magnitude of the risk estimates seems unlikely for these levels of alcoholic beverage drinking. This result may represent a chance finding, confounding or population/environmental characteristics that are specific to this study.]

2.10.6 *Population characteristics*

There are currently no sufficient data to examine whether the effect of alcoholic beverages differ among men and women and among populations of different ethnic origins. Studies that consisted of men only or women only are often not comparable due

Table 2.63 Cohort studies of alcoholic beverage consumption and lung cancer among nonsmokers

Reference	Subjects	Exposure category	No. of cases	Risk ratio (95% CI)	Comments	
Murata <i>et al.</i> (1996)	Men	<i>Ethanol (mL/day)</i>	13	1.0	Nonsmokers included never smokers and past smokers; no other adjustment [crude CI calculated from data matched on age]	
		Non-drinker	10	1.3 [0.5–3.2]		
		>0–≤27	8	2.2 [0.8–6.1]		
Korte <i>et al.</i> (2002)	CPS I Men	<i>Ethanol (g/month)</i>	Not provided	1.0	Definition of nonsmokers in CPS I: lifetime never smokers; definition of nonsmokers in CPS II: <1 cigarette-year, pipe-year or cigar-year (<0.05 pack-years)	
		Non-drinker		1.1 (1.0–1.2)		
		1–499		1.4 (1.2–1.5)		
	Women	Non-drinker	1.0			
		1–499	1.2 (0.8–1.6)			
		≥500	2.0 (1.2–3.2)			
	CPS II Men	Non-drinker	1.0			
		1–499	0.95 (0.6–1.6)			
		≥500	1.2 (0.7–2.2)			
		Women	Non-drinker	1.0		
1–499	1.3 (0.9–1.9)					
≥500	0.6 (0.3–1.2)					
Freudenheim <i>et al.</i> (2005)	Men	<i>Alcohol (g/day)</i>	10	1.0	Adjusted for education, body mass index, energy intake	
		0		1.5 (0.6–3.5)		
		>0–<5		16		2.5 (1.1–5.8)
		5–<15		18		6.4 (2.7–14.9)
		≥15		30		<i>p</i> for trend<0.001
	Women	0	90	1.0		
		>0–<5	68	0.98 (0.7–1.4)		
		5–15	17	0.9 (0.5–1.5)		
		≥15	8	1.4 (0.6–2.9)		
				<i>p</i> for trend=0.98		

Table 2.63 (continued)

Reference	Subjects	Exposure category	No. of cases	Risk ratio (95% CI)	Comments	
Nishino <i>et al.</i> (2006)	Men	<i>Ethanol (g/day)</i>				Adjusted for age, family history of lung cancer, intake of green leafy vegetables, oranges, other fruits
		Never drinker	5	1.0		
		Ever drinker	13	1.2 (0.4–3.5)		
		Current drinker				
		<25.0	7	1.1 (0.4–3.5)		
		25.0–49.9	1	0.4 (0.0–3.2)		
		≥50.0	1	1.2 (0.1–10.0)		
				<i>p</i> for trend=0.61		
		Former drinker	4	4.2 (1.1–15.7)		
Rohrmann <i>et al.</i> (2006)	Men and women	Ethanol (g/day)			All results stratified by age, sex, study centre; adjusted for height, weight, consumption of fruit, red meat, processed meat, education, physical activity, total non-ethanol energy intake; definition for never-smoking not provided	
		<i>Baseline intake</i>				
		Non-drinker	14	0.6 (0.3–1.2)		
		0.1–4.9	44	1.0		
		5–14.9	27	0.9 (0.6–1.5)		
		15–29.9	9	0.7 (0.3–1.4)		
		30–59.9	3	0.6 (0.2–1.8)		
		≥60	0			
		<i>Mean lifelong intake</i>				
		Non-drinker	7	0.5 (0.2–1.2)		
		0.1–4.9	43	1.0		
		5–14.9	14	0.5 (0.3–0.8)		
		15–29.9	6	0.6 (0.3–1.5)		
30–59.9	1	0.4 (0.1–3.0)				
≥60	1	1.2 (0.1–13.6)				

CI, confidence interval; CPS, Cancer Prevention Study

Table 2.64 Case-control studies of alcoholic beverage consumption and lung cancer among nonsmokers

Reference	Subjects	Exposure category	Exposed cases	Odds ratio (95% CI)	Comments
Kabat & Wynder (1984)	Men and women	Not specified	Not reported	No significant difference in alcoholic beverage intake found between cases and controls for either sex	No odds ratio reported; nonsmoker defined as someone who had never smoked as much as one cigarette, pipe or cigar per day for 1 year.
Koo (1988)	Women	<1 time/week ≥1 time/week	61 27	1.0 (0.93–3.70) 1.9 <i>p</i> for trend=0.076	Never smokers defined as those who had smoked less than 20 cigarettes or pipes in the past; adjusted for age, no. of live births, schooling.
Mayne <i>et al.</i> (1994)	Men and women	<i>Beer (times/month)</i> Q1 Q2 Q3 Q4	Not given	1.0 (not given) 1.1 0.9 1.2 <i>p</i> for trend=NS	Nonsmokers included never smokers (not smoked more than 100 cigarettes) and former smokers (had smoked at some time but had not smoked more than 100 cigarettes in the past 10 years); adjusted for age, sex, county of residence, smoking history, cigs/day smoked by former smokers, religion, education, body mass index, income
Zang & Wynder (2001)	Men	<i>Current 'whiskey-equivalent' (oz/day)</i> 0 1–5.9 ≥6	23 26 4	1.0 1.2 (0.7–2.1) 0.7 (0.2–2.0)	Nonsmokers were those who had never smoked at least one cigarette per day for at least 1 year; adjusted for body mass index, age

Table 2.64 (continued)

Reference	Subjects	Exposure category	Exposed cases	Odds ratio (95% CI)	Comments	
Hu <i>et al.</i> (2002)	Women	Servings/week				Nonsmokers were never smokers; adjusted for age, province, education, social class
		<i>Total alcohol</i>				
		0	86	1.0		
		1	36	0.8 (0.5–1.4)		
		>1	35	0.8 (0.5–1.2)		
				<i>p</i> for trend=0.25		
		<i>Beer</i>				
		0	127	1.0		
		≤0.5	17	1.2 (0.6–2.4)		
		>0.5	7	0.5 (0.2–1.1)		
				<i>p</i> for trend=0.17		
		<i>Wine</i>				
		0	100	1.0		
		≤0.5	30	0.7 (0.4–1.2)		
		>0.5	25	0.7 (0.4–1.2)		
		<i>p</i> for trend=0.10				
<i>Liquor</i>						
0	116	1.0				
≤0.5	17	1.1 (0.6–2.1)				
>0.5	21	1.1 (0.6–2.1)				
		<i>p</i> for trend=0.58				

Table 2.64 (continued)

Reference	Subjects	Exposure category	Exposed cases	Odds ratio (95% CI)	Comments		
Rachtan (2002)	Women	<i>Total intake (g/week)</i>				Nonsmokers were lifelong nonsmokers; for total alcohol, age was adjusted; for vodka intake, adjusted for age, passive smoking, consumption of milk, butter, margarine, cheese, meat, fruit, vegetables, carrots, spinach, sibilings with cancer, tuberculosis, place of residence, occupational exposures	
		<1	23	1.0			
		≥1–4	15	3.9 (1.8–8.3)			
		≥4–8	7	8.8 (2.8–27.3)			
		≥8	9	12.1 (3.9–36.9)	<i>p</i> for trend<0.001		
		<i>Usual vodka intake(g)</i>					
		Non-drinker	23	1.0			
		<100	25	2.3 (1.1–4.9)			
		≥100	6	15.0 (2.3–96.0)	<i>p</i> for trend<0.001		
		Benedetti et al. (2006)	Women	Drinks/week			
<i>Total alcohol</i>							
Never weekly	25			1.0			
1–6	3			0.2 (0.0–0.6)			
≥7	5			1.1 (0.4–3.3)			
<i>Beer</i>							
Never weekly	31			1.0			
≥1	2			0.5 (0.3–0.9)			
<i>Wine</i>							
Never weekly	27			1.0			
1–6	3			0.2 (0.1–0.6)			
≥7	3			0.7 (0.2–2.5)			
<i>Liquor</i>							
Never weekly	29	1.0					
≥1	4	0.8 (0.5–1.5)					

CI, confidence interval; NS, not significant

to the different levels of alcoholic beverage exposure in these studies. A few studies conducted analyses stratified by gender using the same exposure categories (Williams & Horm, 1977; Bandera *et al.*, 1997; Prescott *et al.*, 1999; Korte *et al.*, 2002 [CPS I and CPS II]; Pacella-Norman *et al.*, 2002; Freudenheim *et al.*, 2005; Benedetti *et al.*, 2006; Rohrmann *et al.*, 2006). There was no obvious heterogeneity between genders based on results of total alcoholic beverage consumption and risk for lung cancer. However, heterogeneity may exist when level of smoking, type of alcoholic beverage and histological type of lung cancer are considered.

2.11 Cancer of the urinary bladder

Information on alcoholic beverage consumption and cancer of the urinary bladder was derived from five cohort (Table 2.65) and 18 case–control (Table 2.66) studies, which included more than 9000 cases in total.

Of the five cohort studies, one investigation in the Netherlands (Zeegers *et al.*, 2001) found a relative risk of 1.6 in men who drank ≥ 30 g ethanol per day, but no trend in risk with dose. The corresponding value for women was 1.0. The other cohort studies, one among Danish brewery workers (Jensen, 1979) and three from selected populations in the USA (Mills *et al.*, 1991; Chyou *et al.*, 1993; Djoussé *et al.*, 2004) found no association between various measures of alcoholic beverage consumption and risk for cancer of the urinary bladder.

In a multicentre case–control study conducted in 1978–79 in 10 areas of the USA (Thomas *et al.*, 1983), which included 2982 incident cases, no association was found between urinary bladder cancer and total alcoholic beverage consumption (relative risk for ≥ 42 drinks per week, 0.99 in men and 0.66 in women) or consumption of beer (relative risk, 0.93 in both sexes combined), wine (relative risk, 0.60) or spirits (relative risk, 1.14). Of the subsequent case–control studies, nine showed some excess risk in (heavy) alcoholic beverage drinkers and eight showed no association. Moreover, the largest studies, conducted in Canada on 1125 cases (Band *et al.*, 2005) and in Italy on 727 cases (Pelucchi *et al.*, 2002a), also showed no association between various measures of alcoholic beverage consumption and risk for cancer of the urinary bladder.

An explanation for some apparently inconsistent epidemiological findings on alcoholic beverage consumption and cancer of the urinary bladder is that there are different correlates (including tobacco, coffee and diet) of alcoholic beverage drinking in various populations. Alcoholic beverage drinking, in part, may be positively correlated with cigarette smoking, a poorer diet or other recognized risk factors (i.e. social or occupational) for bladder cancer. Thus, residual confounding is possible.

A meta-analysis of 11 studies (two cohort and nine case–control) published between 1966 and 2000 (Bagnardi *et al.*, 2001), which included a total of 5997 cases, found relative risks of 1.04 (95% CI, 0.99–1.09) for 25 g, 1.08 (95% CI, 0.98–1.19) for 50 g and 1.17 (95% CI, 0.97–1.41) for 100 g ethanol per day.

Table 2.65 Cohort studies of alcoholic beverage consumption and cancer of the urinary bladder

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Special population								
Jensen (1979), Denmark	14 313 Danish brewery workers employed at least 6 months in 1939–63; followed for cancer incidence and mortality in 1943–73; age not given; workers allowed 2.1 L of free beer/day (77.7 g pure alcohol)	Follow-up 1943–72	Cases and deaths ascertained through Cancer Registry (ICD-7)	All cancers Bladder cancer	1303 75	SIR (1.0–1.2) 0.9 (0.7–1.1)	Age, sex, area, time trends	Cancer morbidity and mortality compared with those in the general population

Table 2.65 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
General population								
Mills <i>et al.</i> (1991), USA, California Seventh-day Adventists	34 198 white, non-Hispanic Seventh-day Adventists, aged ≥ 25 years; followed through to 1982; newly diagnosed cancer cases identified by record linkage with the Los Angeles Cancer Surveillance Program and the Resource for Cancer Epidemiology in San Francisco; follow-up 99% complete	Detailed lifestyle and 51-item food-frequency questionnaire in 1976	Bladder (ICD-0, 188); 52 histologically confirmed (36 men, 16 women); 94% transitional-cell carcinomas	<i>Beer/wine/liquor (frequency/week)</i> <1 ≥ 1	45 3	1.0 (0.6–5.9) 1.5 (0.4–4.9)	Age, sex Age, sex, smoking	

Table 2.65 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chyou <i>et al.</i> (1993), USA, Japanese–American Cohort study (1965–68)	American men of Japanese ancestry, born 1900–19 and residing on Oahu, Hawaii; identified via the Honolulu Heart Program and through Service draft registration files; of 11 148, 8006 interviewed (72%) in 1965–68; data from 7995 men used; incident cancer cases identified via the Hawaii Cancer Registry; follow-up to May 1991	Interview on smoking history, usual frequency of consumption of 17 food items; a diet recall history (24 h) obtained	96 histologically confirmed cancers in the lower urinary tract (bladder, 83; renal pelvis, 8; ureter, 5); 91% transitional-cell carcinomas	<i>Total intake (g/day)</i>				
				0	30	1.0		
				<15	38	1.3 (0.8–2.1)		
				>15	27	1.2 (0.7–2.0)		
				<i>Beer (g/day)</i>				
				0	30	1.0		
				250	29	1.4 (0.8–2.3)		
				>250	29	1.1 (0.7–1.9)		
				<i>Wine</i>				
				None	30	1.0		
Any	18	1.2 (0.7–2.3)						
<i>Spirits (g/day)</i>								
0	30	1.0						
<2	15	0.95 (0.5–1.8)						
>2	29	1.7 (0.98–2.8)						

Table 2.65 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Zeegers <i>et al.</i> (2001), Netherlands Cohort Study (1986–92)	58 279 men and 62 573 women from 204 municipal registries, aged 55–69 years in 1986; follow-up, 6.3 years via record linkage with cancer registries and the Dutch database of pathology reports	Self-administered questionnaire; consumption of beer, red and white wine, sherry and other fortified wines, liqueur and liquor noted	Analysis based on 594 cancer cases (517 men, 77 women) of bladder, renal pelvis, ureter, urethra and 3170 sub-cohort members (1591 men, 1579 women)	<i>Total alcohol intake (g/day)</i>		Men		Age, smoking (status, amount and duration)
				0	62	1.0		
				<5	108	1.5 (1.0–2.2)		
				5–<15	136	1.5 (1.0–2.2)		
				15–<30	109	1.2 (0.8–1.7)		
				≥30	102	1.6 (1.1–2.5)		
				<i>Beer (g/day)</i>				
				0	62	1.0		
				<5	174	1.4 (0.9–2.0)		
				5–<15	89	1.4 (1.0–2.2)		
15–<30	22	1.7 (0.9–3.2)						
≥30	10	1.1 (0.5–2.6)						

Table 2.65 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Zeegers <i>et al.</i> (2001) (contd)				<i>Wine (g/day)</i>				
				0	62	1.0		
				<5	151	1.5 (1.1–2.2)		
				5–<15	67	1.2 (0.8–1.9)		
				15–<30	25	1.1 (0.7–2.0)		
				≥30	11	1.7 (0.7–4.1)		
				<i>Liquor (g/day)</i>				
				0	62	1.0		
				<5	114	1.4 (1.0–2.1)		
				5–<15	89	1.4 (0.9–2.1)		
				15–<30	70	1.3 (0.8–1.9)		
				≥30	50	1.9 (1.2–3.2)		
				<i>Total intake (g/day)</i>				
0	25	1.0						
<5	29	0.97 (0.56–1.69)						
≥5	33	0.75 (0.41–1.37)						

Table 2.65 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Djoussé <i>et al.</i> (2004), USA, Framingham Heart Study	Population-based; nested case-control study within the cohort started in 1948 with 5209 persons; of these, 205 excluded because alcohol data missing; in 1971, the children of the original cohort and their spouses were invited to join the Offspring Study; of the 5124 subjects in this cohort, 3 were excluded (missing alcohol data); mean age of 10 125 participants, 40.3 years (range, 5–70 years); 9821 subjects included; average follow-up, 27.3 years	Biennial examinations, asking about alcoholic beverage intake, smoking	133 confirmed incident cases of bladder cancer	<i>Total intake (g/day)</i>			Age/sex, cohort, smoking status, pack-years of smoking; beverage-specific data also controlled for the other two types	
				0	14	1.0		
				0.1–6.0	43	0.9 (0.5–1.8)		
				6.1–12.0	21	0.9 (0.4–1.9)		
				12.1–24.0	14	0.6 (0.3–1.3)		
				24.1–48.0	22	0.9 (0.5–1.9)		
				>48	8	0.5 (0.2–1.2)		
				<i>Beer (drinks/week)</i>				
				0	48	1.0		
				<1	20	0.6 (0.3–1.2)		
				1–4	23	0.7 (0.4–1.3)		
				>4	31	0.5 (0.1–0.8)		
				<i>Wine (drinks/week)</i>				
				0	49	1.0		
<1	42	0.9 (0.5–1.6)						
1–4	17	0.6 (0.3–1.2)						
>4	14	0.8 (0.4–1.7)						
<i>Spirits (drinks/week)</i>								
0	21	1.0						
<1	20	1.0 (0.5–2.0)						
1–4	28	1.4 (0.4–2.9)						
>4	53	1.6 (0.9–3.1)						

CI, confidence interval; ICD, International Classification of Diseases

Table 2.66 Case-control studies of alcoholic beverage consumption and cancer of the urinary bladder

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Mommsen <i>et al.</i> (1983), Denmark, 1977-79/80	212 (165 men, 47 women), mean age, 66.1 years (range, 42-85 years); newly diagnosed over 2 (men) or 3 years (women)	259 (165 men, 94 women) selected from the same area; matched with cases on sex, age, degree of urbanization, geographic area	Questionnaire and interview with physician on job history, use of alcohol, tobacco, coffee, sugar substitutes	Bladder	Alcohol drinking	193	2.3 (1.3-3.9)	Matching factors	
Thomas <i>et al.</i> (1983), USA, 1978-79	2982 newly diagnosed identified over a 1-year period from cancer registries in 10 areas in the USA; 100% histologically confirmed; participation rate, 73%	Population in same areas selected by random-digit dialling (2469; aged 21-64 years) and from files of Health Care Finance Administration (3313; aged 65-84 years); stratified on age, sex, geographic distribution; response rates, 84% (21-64 years) and 82% (65-84 years)	At-home interview with standardized questionnaire on job/residential history, use of sweeteners and coffee, tobacco products; number of alcoholic servings in a typical winter week 1 year before	Bladder	Servings per week <i>All alcohol</i>		<i>Men/women</i>	Age, sex, race, smoking status, hazardous occupational exposure	[No CIs provided]
					0	835/426	1.0 (1.0)		
					<3	216/92	0.94 (0.80)		
					4-6	228/75	0.86 (0.93)		
					7-13	335/62	0.98 (0.77)		
					14-27	359/59	0.88 (0.97)		
					28-41	139/9	1.13 (0.87)		
					≥42	114/2	0.99 (0.66)		
					<i>Beer</i>		<i>Men + women</i>	Age, race, smoking status, hazardous occupational exposure	
					0	1261	1.0		
					<3	275	0.89		
					4-6	223	0.98		
					7-13	154	0.92		
					14-27	161	1.01		
					28-41	43	1.16		
					≥42	46	0.93		

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Thomas <i>et al.</i> (1983) (contd)					<i>Wine</i>				[No CIs provided]
					0	1261	1.0		
					<3	370	0.94		
					4–6	175	0.86		
					7–13	128	0.81		
					14–27	89	1.00		
					≥28	15	0.60		
					<i>Spirits</i>				
					0	1261	1.0		
					<3	294	0.78		
					4–6	259	0.91		
					7–13	255	0.95		
					14–27	235	0.99		
					28–41	53	1.04		
				≥42	51	1.14			

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Claude <i>et al.</i> (1986), Germany, 1977–82	431 patients (340 men, 91 women) in three hospitals in Lower Saxony; mean age, 68.6 (men) and 69.7 years (women); refusal rate, 2%	Patients in the same hospitals; mean age, 69.7 (men) and 70.9 (women) years; matched 1:1 to cases by age (± 5 years), sex; due to a lack of suitable patients >65 years, 21% recruited from homes for the elderly; about 70% of the men had prostate adenoma and infections	Interviews with a questionnaire on smoking, use of alcohol, coffee, drugs, medical history, radiation, urination habits, use of hair dyes, job history and exposures	Lower urinary tract (90% bladder); 89% transitional-cell carcinoma	<i>Beer (L/day)</i>	NR	<i>Men</i>	Smoking	Beer drinkers consumed ≥ 1 glass of beer (0.3 L) per day for ≥ 5 years; odds ratio for all beer drinkers, 1.6; odds ratio for nonsmokers among them, 0.8; odds ratio for beer drinkers who smoke, 1.7; also seen for spirits, not for wine; information on histology available
					0.1–0.5		1.16		
					0.6–1.0		2.14 ($p < 0.05$)		
					>1		2.77 ($p < 0.05$)		
					<i>Wine (L/day)</i>	NR	0.97		
					0.1–0.3		0.82		
>0.30									
<i>Spirits (L/week)</i>	NR	1.46							
0.1–0.5		2.71 ($p < 0.05$)							
>0.5									
<i>Ever</i>	NR	<i>Women</i>							
Beer		1.42							
Wine		1.88							
Spirits		1.21							

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Kunze <i>et al.</i> (1986), Germany, 1977–82	340 patients from three hospitals in Lower Saxony; cancers of the bladder (309), pelvis (15), ureter (4), urethra (1) or multifocal tumours (11); 100% histologically confirmed; refusal rate, 2%	Patients in the same hospitals without any tumour primarily from urological departments; matched with cases on age, sex, hospital	Interviews at the hospital, about smoking, drinking, medical history, drug use, urinary habits, use of hair dyes.	Lower urinary tract (91% bladder, 4.4% pelvis, 1.2% ureter, 3.3% multifocal)	<i>Beer (L/day)</i>	NR	1.16	Smoking	[Numerical data identical to Claude <i>et al.</i> (1986)]
					0.6–1.0		2.14 ($p<0.05$)		
					>1		2.77 ($p<0.05$)		
					<i>Wine (L/day)</i>	NR	0.97		
					<0.3		0.82		
					>0.30				
					<i>Spirits (L/week)</i>	NR	1.46		
					<0.5		2.71 ($p<0.05$)		
					>0.5		1.6 ($p<0.05$)		
					<i>Beer drinkers</i>		1.7 ($p<0.05$)		
<i>Smoker</i>		0.8							
<i>Nonsmoker</i>									
Slattery <i>et al.</i> (1988), Utah, USA, 1977–82	419 patients identified via Utah Cancer Registry (all white); aged 20–84 years; 100% histologically confirmed carcinomas; completion rate, 76.3%	889 population-based selected by random-digit dialling (aged 21–64 years) or via Health Care Finance records (aged 65–84 years); matched 2:1 to cases by 5-year age group, sex; completion rate, 81.5%	Personal interviews on smoking, drinking, use of sweeteners, medical history, job history, demographics; intake of fluid noted for a typical winter week 1 year prior to interview	Bladder (ICD-0, 188)	<i>Alcohol (oz/week)</i>			<i>Never smokers</i>	Age, sex, diabetes, bladder infections
					0	110	1.0		
					1–30	14	1.2 (0.6–2.2)		
					≥31	7	2.1 (0.8–5.4)		
							<i>Ever smokers</i>		
					0	159	4.1 (2.5–6.7)		
					1–30	59	2.8 (2.1–3.9)		
					≥31	66	2.9 (2.0–4.4)		
					<i>Alcohol (oz/week)</i>		<i>Never smokers</i>		
					0	110	1.0		
0.1–3.64	11	1.0 (0.5–2.0)							
≥3.65	10	2.4 (1.1–5.4)							
		<i>Ever smokers</i>							
0	159	3.8 (2.4–6.2)							
0.1–3.64	51	2.8 (2.1–3.9)							
≥3.65	74	3.0 (2.0–4.4)							

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Nomura <i>et al.</i> (1989), Hawaii, USA, 1979–86	261 patients of Caucasian or Japanese ancestry in 7 large hospitals on Oahu, Hawaii; 261 participated (195 men, 66 women), aged 30–93 years; 100% histologically confirmed; overall reponse rate 73%; 31 cases diagnosed in 1977–79	522 population-based identified from lists of the Health Surveillance Program; matched 2:1 for age (± 5 years), sex, race, current residency on Oahu; 89% of those eligible	Interviews on smoking history, alcohol intake 1 year before the interview, job history, use of hair dyes	Lower urinary tract (90% bladder)	Alcohol intake				Cigarette smoking (pack-years)
					<i>Drinks/week</i>				
					<i>Men</i>				
					Non-drinker	46	1.0		
					Drinker	149	1.2 (0.8–1.9)		
					1–14	78	1.1 (0.7–1.8)		
					>15	71	1.3 (0.8–2.2)		
					<i>Women</i>				
Non-drinker	33	1.0							
Drinker	33	0.9 (0.5–1.6)							
1–7	22	0.7 (0.4–1.4)							
>8	11	1.5 (0.6–3.8)							

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Akdaş <i>et al.</i> (1990), Turkey, 1980–87	194 patients (168 men, 26 women) admitted to 2 hospitals, aged 24–80 years (mean age, 60 years); 100% histologically confirmed	194 patients in the same hospitals with no gross haematuria or cancer history; 91% had IVU done, showing a normal bladder; 57% had cystoscopy, showing absence of tumour; matched on age, sex	Interview on past and present residence, job history, socio-economic status, drinking habits (tea, alcohol, Turkish coffee), smoking habits, medical history, use of fertilizers or insecticides	Bladder	No drinking* Ever drinking Daily drinker <i>Drinking duration</i> 11–20 years >20 years >175 mL liquor/day		<i>Case control ratio</i> 0.67 1.67 $p < 0.001$ $p < 0.01$ $p < 0.001$ $p < 0.01$ $p < 0.05$	Unadjusted Smoking	Risk for bladder cancer increased with intensity and duration of alcohol drinking * read from graph

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Momas <i>et al.</i> (1994), France, 1987–89	219 men living in the Hérault district for >5 years diagnosed with primary bladder carcinoma, checked with the Hérault Cancer Registry; mean age, 67.8 years; papillomas and polyps excluded; 100% histologically confirmed; participation rate, 81% (53 died)	928 men living in Hérault region for >5 years, randomly selected from electoral rolls; aged >50 years; 558 of 692 in the telephone book agreed to be interviewed (80.6%); 236 of 329 not in phone book replied by mail (71.7%).	Interviews (direct or by phone) on past and present residence, level of education, jobs of >1 year, smoking/drinking habits, intake of spiced food, sweeteners	Bladder (188)	<i>Lifelong intake of pure alcohol (kg)</i> <15 15–600 >600–1200 >1200	7 47 57 50	1.0 2.2 (0.9–5.6) 1.7 (0.7–4.3) 3.1 (1.2–8.2)		Stepwise logistic regression, using the largest possible data set in the regression model, i.e. with the set of persons having no missing values for any of the model variables
Nakata <i>et al.</i> (1995), Gunma Prefecture, China	303 men; mean age, 70.1 years	303 men from the general population from 15 areas of the Gunma prefecture; mean age, 70.2 years; age-matched (± 1 year)	Not reported	Bladder	History of drinking (yes/no)	191 190	1.0 (0.7–1.5) 0.9 (0.7–1.4)	Age Smoking	

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Bruemmer <i>et al.</i> (1997), USA, 1987–90	427 Caucasian patients with invasive or non-invasive (in-situ or papillary) bladder cancer living in Washington State with no prior bladder cancer history; aged 45–65 years; 262 completed the interview; response rate, 62.4%	535 identified via random-digit dialling; matched to cases by sex, county of residence; 405 interviewed (79% of those eligible and selected)	Telephone interviews on demographics, history of cancer, smoking; fluid intake over a 10-year period before reference date (2 years before diagnosis)	Bladder (188)	<i>Alcoholic drinks (per day)</i>				
						0	33	1.0	<i>Men</i>
						≤0.5	49	1.4 (0.7–2.7)	
						>0.5–2.0	57	1.2 (0.6–2.2)	
						>2	63	1.1 (0.6–2.1)	
									<i>Women</i>
						0	19	1.0	
						≤0.5	22	0.4 (0.2–0.8)	
						>0.5–2.0	10	0.6 (0.2–1.6)	
						>2	9	0.5 (0.2–1.3)	

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments				
Donato <i>et al.</i> (1997), Brescia, Italy, 1990–92	172 patients (135 men, 37 women) diagnosed in a large hospital in Brescia; all but one histologically confirmed	578 patients (398 men, 180 women) in the same and two other hospitals with prostate adenoma, urolithiasis or obstructive uropathy; men age-matched (\pm 5 years) with cases; this could not be achieved for women	Questionnaire on education, history of smoking, coffee/alcohol drinking	Bladder (188)	<i>Alcohol drinking (g/day)</i>		<i>Men</i>	Age, place of residence, education, date of interview, smoking, coffee consumption	People who drank alcohol less than daily were considered non-drinkers				
										Non-drinker	10	1.0	
										Former drinker	16	1.0 (0.4–2.7)	
										Current drinker	109	2.1 (1.0–4.8)	
										1–20	18	1.7 (0.6–4.7)	
										21–40	33	1.6 (0.6–3.8)	
										41–60	36	4.3 (1.7–11.0)	
										>61	22	4.6 (1.6–13.4)	
										<i>Women</i>	Non-drinker	12	1.0
											Current drinker	25	3.4 (1.2–9.7)
											1–20	14	3.1 (1.0–9.3)
											\geq 21	11	3.9 (1.1–13.7)
Probert <i>et al.</i> (1998), United Kingdom	116 patients with transitional-cell carcinoma recruited from haematuria clinics in two Bristol hospitals; tumours staged and graded by a clinical pathologist; 100% histologically confirmed	91 patients from the same clinics with benign haematuria or no bladder disease	Personal interview by the same person on job history, smoking history and status, coffee and alcohol use, place of residence	Bladder (188)	<i>Alcohol consumption</i>	34%	Crude	No relative risks given					
									Wine		Cases/controls [odds ratio] [1.59]		
									Quantity/week		3.9/3.5 units		
									Started drinking		54.1/39.9 years		
									Beer	66%	[1.85]		
									Quantity/week		11.9/9.6 units		
									0	62			
1–20	37												
>20	15												
<i>p</i> for trend		<0.05											

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments		
Pohlabein <i>et al.</i> (1999), Hessen, Germany, 1989–92	300 patients (239 men, 61 women) newly diagnosed in 4 hospitals in Hessen; 89.6% bladder cancer; 100% histologically confirmed; 98.7% carcinomas; response rate, 92.6%	300 patients from the same hospitals with non-neoplastic diseases of the lower urinary tract; matched 1:1 on age (\pm 5 year), sex, area of residence; response rate, 98%	Questionnaire and interview on job history, active smoking history, dietary habits (foods/drinks) 10–15 years previously	Lower urinary tract	Alcohol intake				Adjusted for smoking categories: none, 1– \leq 20, 20– \leq 40, >40 pack–years, cigar, pipe	1 bottle of beer = 2 glasses of wine = 20 g alcohol	
					<i>Total intake</i>			<i>Men</i>			
					Not daily	102	1.0				
					1–20 g/day	74	1.10 (0.70–1.73)				
					21–40 g/day	35	0.83 (0.46–1.47)				
					>41 g/day	28	1.71 (0.78–3.73)				
					<i>Not daily</i>		52	1.0			
					<i>Daily</i>		9	2.84 (0.69–11.68)			
					<i>Beer</i>			<i>Men</i>			
					<i>Not daily</i>		119	1.0			
					1–2 bottles/day		96	1.05 (0.70–1.59)			
					\geq 3 bottles/day		24	1.82 (0.79–4.21)			
					<i>Not daily</i>		58	1.0			
\geq 1 bottle/day		3	4.53 (0.32–65.24)								
<i>Wine</i>			<i>Men</i>								
<i>Not daily</i>		211	1.0								
1–2 glasses/day		24	1.18 (0.60–2.33)								
\geq 3 glasses/day		4	2.48 (0.41–14.89)								
<i>Not daily</i>		55	1.0								
\geq 1 glass/day		6	2.29 (0.44–11.92)								

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
van Dijk <i>et al.</i> (2001), Netherlands, 1997–2000	120 patients (86% men) recruited at the Nijmegen University Medical Centre; 100% histologically confirmed; <i>ADH3</i> genotyping on 115 patients	133 patients (89% men) with benign prostatic hyperplasia and visitors to the urology ward; <i>ADH3</i> genotyping on 131 patients	Self-administered questionnaire on demographics, smoking/drinking/dietary habits, jobs, familiarity of cancer, disease history	Bladder	<i>Alcohol intake</i>	NR	1.0	Adjustment unclear; moderate drinkers taken as reference	Moderate = 1–14 glasses per week; high = >14 glasses per week
					High		1.2 (0.6–2.4)		
					<i>ADH3 genotype $\gamma_1\gamma_2$ and $\gamma_2\gamma_2$</i>		1.0		
					Moderate		2.0 (0.9–4.5)		
					<i>ADH3 genotype $\gamma_1\gamma_1$</i>		3.3 (1.3–8.8)		
					Moderate		2.2 (0.8–5.8)		
					High				

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Pelucchi <i>et al.</i> (2002a), Italy, 1985–92	727 patients with invasive transitional cell cancer (617 men, 110 women) in various hospitals in the Milan area and the Pordenone region; aged 27–79 years (median, 63 years); 100% histologically confirmed; refusal rate, 2.6%	1067 patients (769 men, 298 women) in the same hospitals, admitted for acute, non-neoplastic, non-urolological or genital tract diseases; aged 27–79 years (median, 60 years); refusal rate, 2.2%	Questionnaire on smoking habits, intake of coffee and tea, medical history, family history of urological cancer, alcohol use, relevant occupational exposures	Bladder (188)	<i>Total intake (drinks/day)</i>				Age, sex, study centre, education, smoking, tea or coffee consumption, green vegetable intake, occupation 'at risk'	
					Non-drinker	117	1.0			
					Ever drinker	607	0.8 (0.6–1.1)			
					<3	192	0.8 (0.6–1.1)			
					3–<6	193	0.8 (0.5–1.1)			
					≥6	222	0.8 (0.6–1.2)			
					<i>Wine (drinks/day)</i>					
					Non-drinker	126	1.0			
					Ever drinker	599	0.9 (0.6–1.1)			
					<3	207	0.9 (0.7–1.3)			
					3–<5	175	0.8 (0.6–1.1)			
					≥5	217	0.9 (0.6–1.2)			
					<i>Beer</i>					
					Never	608	1.0			
					Ever	118	0.7 (0.5–0.9)			
					<i>Spirits</i>					
					Never	538	1.0			
Ever	189	0.9 (0.7–0.9)								
<i>Years of drinking</i>										
Never drinker	117	1.0								
1–24	65	0.7 (0.5–1.1)								
25–39	199	0.7 (0.5–1.0)								
≥40	342	1.0 (0.7–1.4)								

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Band <i>et al.</i> (2005), British Columbia, Canada, 1983–90	25 726 male patients aged ≥ 20 years listed in the British Columbia Cancer Registry, detailed questionnaire returned by 15 463 (60.1%); of these, 1129 bladder cancer patients responded (64.7%); 1125 cases had at least one matching control	8492 patients with cancer at all other sites, except lung (2998) and 'unknown sites' (708); matched on age, year of diagnosis	Questionnaire on lifetime job history (usual occupation/industry, ever occupation), smoking/drinking habits.	Bladder (188)	<i>Alcohol intake</i> Never Ever Unknown	119 858 148	1.0 0.9 (0.7–1.1) 1.2 (0.9–1.5)		Focus on identifying occupational cancer risks; similar alcohol use between cases and controls

Table 2.66 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Lu <i>et al.</i> (2005), Taiwan, China, 1997–98	103 (66 men, 37 women) patients in Kaohsiung; upper tract metastases or recurrent urinary neoplasm not eligible; 100% histologically confirmed; all genotyped for <i>N</i> -acetyltransferase (<i>NAT2</i>); response rate, 100%	103 (68 men, 35 women) ophthalmic patients with non-neoplastic and non-urological diseases, and normal renal and liver function; all genotyped for <i>NAT2</i> ; response rate, 100%	Interview with questionnaire on demographics, socioeconomic, dietary factors, jobs, smoking, betel quid use, alcohol use,	Bladder	<i>Alcohol drinking</i>		<i>Odds ratio</i>		*Adjusted for blackfoot disease-endemic area, alcohol drinking
					No	98	1.0		
					Yes	5	2.7 (1.3–5.9)		
					<i>NAT2 genotype*</i>				
					Rapid		1.0		
					Slow		1.5 (0.8–2.8)		
Baena <i>et al.</i> (2006), Spain	74 men admitted to the Department of Urology of the University Hospital of Cordoba over 1 year; mean age, 67.1 years	89 male patients in the same department, with non-malignant urological disease; mean age, 58.7 years	Interview with questionnaire on smoking/drinking habits, diet and chronic diseases	Bladder	Alcohol drinking	60	[2.38]	Crude	In multivariate analysis, alcohol was not an independent risk factor for bladder cancer, but no point estimates were given; unclear whether current or ever drinker.
							(<i>p</i> =0.036 in univariate analysis)		

CI, confidence interval; ICD, International Classification of Diseases; IVU, intravenous urography; NR, not reported

Given the likelihood of residual confounding and the absence of an association in large studies, there is no clear pattern of association between total alcoholic beverage consumption or consumption of various types of alcoholic beverage and the risk for cancer of the urinary bladder.

2.12 Cancer of the endometrium

2.12.1 Cohort studies (Tables 2.67 and 2.68)

Since 1988, three prospective cohort studies have examined the association between alcoholic beverage intake and the risk for endometrial cancer in special populations, namely women hospitalized or being treated for alcohol dependence (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Weiderpass *et al.*, 2001a; Table 2.67) and three have studied the association in the general population (Gapstur *et al.*, 1993; Terry *et al.*, 1999; Jain *et al.*, 2000b; Folsom *et al.*, 2003; Table 2.68) (see the Tables for overlapping study populations).

These studies were conducted in North America (Gapstur *et al.*, 1993; Jain *et al.*, 2000b; Folsom *et al.*, 2003) and in Scandinavia (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Terry *et al.*, 1999; Weiderpass *et al.*, 2001a).

Three studies (Gapstur *et al.*, 1993; Terry *et al.*, 1999; Jain *et al.*, 2000b) presented risk estimates adjusted for multiple possible confounders (body size and reproductive factors), while only one (Jain *et al.*, 2000b) adjusted the analysis of alcoholic beverages for smoking (ever/never). Smoking showed a non-significant protective effect in all of these studies.

In one study among alcoholics (Weiderpass *et al.*, 2001a), there was an inverse association between alcoholic beverage consumption and endometrial cancer, but the analytical models did not include important covariates that may have confounded the association, such as cigarette smoking and body size. In the two other studies among alcohol-dependent populations, there was no evidence of an association. There was no evidence of an association between alcoholic beverage intake and the risk for endometrial cancer in the three cohort studies conducted in the general population (Gapstur *et al.*, 1993; Terry *et al.*, 1999; Jain *et al.*, 2000b).

2.12.2 Case-control studies (Table 2.69)

Case-control studies that have investigated the relationship between alcoholic beverage consumption and the risk for endometrial cancer were carried out in Japan, North America and Europe.

Seven of these were hospital-based, particularly studies from southern Europe (La Vecchia *et al.*, 1986; Shu *et al.*, 1991; Austin *et al.*, 1993; Levi *et al.*, 1993; Parazzini *et al.*, 1995a; Kalandidi *et al.*, 1996; Petridou *et al.*, 2002), two were based on cases and controls who were included in a cancer survey or registry database (Williams

Table 2.67 Cohort studies of alcoholic beverage consumption and endometrial cancer in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Adami <i>et al.</i> (1992a), Sweden, National Board of Health and Welfare/ Study of Alcoholics Women	9353 individuals (1013 women) with a diagnosis of alcoholism in 1965–83; follow-up for 19 years (mean, 7.7 years); all cancers in the first year of follow-up excluded	Registry-based	<i>Corpus uteri</i>	Women with diagnosis of alcoholism	3	SIR 1.4 (0.3–4.2)		
Tønnesen <i>et al.</i> (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 male and female alcohol abusers admitted to an outpatient clinic in Copenhagen during 1954–87; 3093 women observed for 9.4 years	Registry-based	<i>Corpus uteri</i>	Alcohol abusers	3	0.4 (0.1–1.3)		

Table 2.67 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Temperance Boards Study	Nested case–control study; records of 15 508 alcoholic women born between 1870 and 1961 obtained from Temperance Boards; controls matched for region and day of birth; incidence data from Swedish Cancer Registry	Registry-based	<i>Corpus uteri</i> (ICD-7, 172)	Alcohol abusers	30	0.7 (0.4–1.1)		

Table 2.67 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Weiderpass <i>et al.</i> (2001a), Sweden, National Board of Health and Welfare/ Study of Alcoholic Women	36 856 women (mean age, 42.7 years) hospitalized for alcoholism between 1965 and 1994 based on data from Inpatients Register; linkages to nationwide Registers of Causes of Death and Emigration and national Register of Cancer; average follow-up time, 9.6 years; the first year of follow-up was excluded from all analysis	Registry -based; linkages	Endometrium	Women with diagnosis of alcoholism	69	SIR 0.76 (0.59–0.96)	Age, calendar period	Enlarged population with longer follow-up than Adami <i>et al.</i> (1992a)

CI, confidence interval; ICD, International Classification of Diseases; SIR, standardized incidence ratio

Table 2.68 Cohort studies of alcoholic beverage consumption and endometrial cancer in general populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Gapstur <i>et al.</i> (1993), USA, Iowa Women's Health Study	25 170 women, aged 55–69 years, randomly selected from Iowa's 1985 drivers' licence list; cohort at risk, 24 848 women; questionnaire mailed in 1986; exclusions: prevalent cancer other than skin, prior hysterectomy, menstruation during the last year; 167 incident endometrial cancers	Mailed, self-administered questionnaire	Endometrium; <i>corpus uteri</i> (182.0) and <i>isthmus uteri</i> (182.1)	<i>Ethanol</i> (g/day) 0 <4.0 ≥4.0	101 27 32	1.0 (reference) 0.7 (0.5–1.1) 1.0 (0.7–1.6)	Age, body mass index, number of live births, age at menopause, non-contraceptive estrogen use	The same population as Folsom <i>et al.</i> (2003); Cox proportional hazard regression

Table 2.68 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Terry <i>et al.</i> (1999), Sweden, Swedish Twin Registry and Swedish Cancer and Death Registry	11 659 women born 1886–1925; follow-up through to 1992; record linkages to Swedish Cancer and Death Registries; 133 incident cases detected	Questionnaire concerning lifestyle factors, diet, physical activity, 1967	Endometrium	<i>Drinks/week</i>			Age, physical activity, weight at enrolment, parity	
				0	78	1.0 (reference)		
				<2	22	1.7 (1.0–2.8)		
				2–4	10	1.2 (0.6–2.4)		
Jain <i>et al.</i> (2000b), Canada, National Breast Screening Study, 1980–85	56 837 women, aged 40–59 years, enrolled between 1980 and 1985; subcohort of 10% of randomly selected women from the main study in the dietary cohort; follow-up to 31 December 1993; 221 women diagnosed with incident adenocarcinoma	Self-administered questionnaire	Endometrium	<i>Alcohol consumption</i>			Age, total energy intake, body mass index, ever smoked, oral contraceptive use, hormone-replacement therapy use, university education, live births, age at menarche	
				1 (low)	65	1.00 (reference)		
				2	62	1.01 (0.69–1.46)		
				3	41	0.78 (0.52–1.18)		
				4 (high)	53	1.00 (0.67–1.50)		

Table 2.68 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Folsom <i>et al.</i> (2003), USA, Iowa Women's Health Study	23 335 women, aged 55–69 years, randomly selected from Iowa's 1985 drivers' licence list; follow-up from 1986 through 2000; 415 incident endometrial cancers detected	Baseline questionnaire	Endometrium	<i>Alcohol consumption</i> Yes No	260 155	1.00 (reference) 0.73 (0.59–0.89)	Age	$p < 0.05$; p for difference from reference category
Beral <i>et al.</i> (2005), United Kingdom, Million Women Study	716 738 post-menopausal women in the UK without previous cancer or hysterectomy recruited into the Million Women Study in 1996–2001	Questionnaire	Endometrium	<i>Alcohol consumption</i> ≤10 g/week >10 g/week	69 17	1.77 (1.39–2.18) 1.81 (1.08–3.05)	Time since menopause, parity, oral contraceptive use, body mass index, region of residence, economic status	

CI, confidence interval; ICD, International Classification of Diseases

Table 2.69 Case-control studies of alcoholic beverage consumption and endometrial cancer

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horn (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967-71	7518 patients (all sites, men and women) interviewed; 57% selected randomly	Randomly selected patients with cancer of other, non-related sites	Interview	<i>Corpus uteri</i>	<i>Wine level</i>	Relative odds	Age, race,	Consumers of alcohol were divided in categories 1 and 2 with 51 drink x years as level of division (years of alcohol consumption \geq once per week)
					1	0.77		
					2	0.60		
					<i>Beer level</i>			
					1	0.23		
					2	0.42		
					<i>Hard liquor level</i>			
					1	0.91		
					2	0.79		
					<i>Total alcohol oz-years level</i>			
					1	0.72		
					2	0.65		
					<i>Wine level</i>			
					1	0.78		
					2	0.49		
					<i>Beer level</i>			
1	0.23							
2	0.31							
<i>Hard liquor level</i>								
1	0.95							
2	0.77							
<i>Total alcohol oz-years level</i>								
1	0.69							
2	0.63							

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
La Vecchia <i>et al.</i> (1986), Milan, Italy, Jan. 1983– Jun. 1984	206 women, aged 75 years and less, admitted to the Obstetrics and Gynecology Clinics of the University, The National Cancer Institute and oncology, gynecology wards of the Ospedale Maggiore, Milan	206 women matched by 5-year range to the same hospital network for acute conditions; women who undergone hysterectomy excluded	Structured questionnaire	Endometrium	<i>Alcohol consumption</i> (drinks/day) 0 <2 ≥2 and <3 ≥3 and <4 ≥4	1.00 (reference) 1.59 (0.80–3.18) 1.57 (0.77–3.21) 3.44 (1.03–11.51) 4.33 (1.02–18.43) χ^2 trend=5.73 $p=0.02$	Various dietary items, interviewer, age, marital status, years of education, body mass index, parity, history of diabetes, hypertension, age at menarche, age at menopause, of oral contraceptives, hormone-replacement therapy use	
Cusimano <i>et al.</i> (1989b), Ragusa, Italy, 1 Jan. 1983–30 Jun. 1985	57 women from Ragusa and province (Italy/Sicily) diagnosed between 1 Jan. 1983 and 30. Jun 1985; aged 37–79 years; 100% histologically confirmed; participation rate; 95%	228 women from the same geographical region; aged 36–79. matched to cases by age (2.5-year range), type of health service consulted; women who had undergone hysterectomy excluded	Structured questionnaire; interview	Endometrium	<i>Alcohol consumption</i> No Yes	1.00 (reference) 1.31 (0.73–2.34)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Kato <i>et al.</i> (1989), Japan, 1980–86	417 women registered at Aichi Cancer Registry, diagnosed between 1980 and 1986; aged ≥20 years	8920 cancers at other sites excluding cancers known to be alcohol-related	Records from Aichi Cancer Registry with available data on alcohol drinking habits	<i>Corpus uteri</i>	<i>Alcohol drinking</i>		Age	Possible bias due to control selection from cancer patients and the effect of alcohol consumption diminished; however, status of the controls' illness may have changed their alcohol drinking habit before diagnosis; lack of information on important risk factors.
					Current versus none	0.67 (0.41–1.09)		
					Daily versus less	0.46 (0.15–1.41)		
					Occasional versus none	0.74 (0.44–1.26)		
					Daily versus none	0.44 (0.15–1.38)		
					Daily versus less	0.53 (0.16–1.70)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Webster <i>et al.</i> (1989), USA, multicentre: Atlanta, Detroit, San Francisco, Seattle, states of Connecticut, Iowa, 1980–82	351 women newly diagnosed with primary epithelial endometrial cancer (from 1 December 1980 to 31 December 1982); aged 20–54 years; 100% histologically confirmed	2247 women selected by random-digit dialling, from same geographical areas as cases, during the same period; aged 20–54 years; frequency-matched by 5-year age groups	Structured questionnaire; interview at participants' home.	Endometrium	<i>Alcohol consumption (g/week)</i> Non-drinker 1–49 50–149 ≥150	1.83 (1.11–3.10) 1.61 (1.04–2.49) 1.11 (0.68–1.81) 1.00	Age, race, parity, oral contraceptive use, smoking	27% women unable to be interviewed
Shu <i>et al.</i> (1991), Shanghai, China, 1988–90	268 Shanghai residents diagnosed between 1 April 1988 and 30 January 1990; aged 18–74 years; data obtained from cancer registry in Shanghai; 98.5% histopathologically confirmed; participation rate, 91.2%	268; matched to cases by age (2-year range) randomly; participation rate, 96.4%	In-person interview at participants' home; questionnaire	Endometrium	<i>Drinking</i> No Yes	1.0 1.2 (0.6–2.6)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Austin <i>et al.</i> (1993), Alabama, USA, 1985–88	168 women identified through University Hospital and private gynaecological–oncological practice in Birmingham between June 1985 and December 1988, aged 40–82 years; 100% histologically confirmed; participation rate, 93%	334 women attending the University optometry clinic, aged 40–82 years; intact uterus; frequency-matched by age, race; participation rate, 77%	Standardized and food-frequency questionnaires	Endometrium	<i>Alcohol category</i> Any type	<i>Relative rate</i> 0.64 (0.32–1.28) $p=0.20$	Age, race, education, body mass, index of central obesity, cigarette habit, use of replacement estrogens, number of pregnancies	
Levi <i>et al.</i> (1993), northern Italy and Switzerland, 1988–9	274 patients from local cancer registry, aged 31–75 years; 100% histologically confirmed	572 women admitted to the same hospitals for acute, non-gynaecological, non-hormone-related, metabolic or neoplastic disorders, aged 30–75 years	Structured questionnaire/interview at hospital	Endometrium	Frequency of alcohol consumption <i>Wine</i> Low Intermediate High <i>Beer</i> Low Intermediate High <i>Liquor</i> Low Intermediate High	<i>Odds ratios</i> 1.0 1.03 1.70 $\chi^2=5.67$ $p<0.05$ 1.0 0.99 2.43 $\chi^2=0.27$ 1.0 1.46 5.24 $\chi^2=4.39$ $p<0.05$	Study centre, age	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Swanson <i>et al.</i> (1993), USA, 1987–90	400 women newly diagnosed in June 1987 to May 1990 from seven hospitals in Chicago, Hershey, Irwine and Long Beach, Minneapolis, Winston-Salem, aged 20–74 years; inclusion criteria: no previous treatment for the cancer and intact uterus; 100% pathologically confirmed; participation rate, 87.1%	297 women selected by random-digit dialling or Health Care Financing Administration; matched by age (5-year range), race, residence; participation rate, 65.6%	Short telephone interview	Endometrium	<i>Alcohol intake in adulthood (drinks per week)</i> None Any <1 1–4 >4	1.00 0.82 (0.53–1.26) 0.75 (0.47–1.19) 1.04 (0.61–1.76) 0.72 (0.39–1.35)	Age, education, smoking status, age at menarche, use of oral contraceptives, Quetelet index, body fat distribution	13% of eligible cases and 35% of eligible controls not interviewed; bias if non-response associated with alcohol use; possible recall bias among cases due to their condition

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Parazzini <i>et al.</i> (1995a), Milan, Italy, 1979–93 [population partially overlapping with La Vecchia <i>et al.</i> (1986)]	726 patients admitted to six greatest hospitals and clinics in Milan until 1 year before interview, aged 28–74 years; 100% histologically confirmed	2123 women admitted to the same network of hospitals for acute, non-malignant, non-gynaecological conditions, unrelated to hormonal diseases, aged 25–74 years; exclusion: women with hysterectomy	Standard questionnaire, by trained interviewers	Endometrium	<i>Total alcoholic beverages (drinks/day)</i> 0 >0–≤1 >1–≤2 >2	1.0 (reference) 1.1 (0.9–1.4) 1.4 (1.1–1.8) 1.6 (1.2–2.2) χ^2 trend=11.33 $p<0.001$	Age, education, Quetelet index, parity, menopausal status, smoking, oral contraceptive and estrogen replacement therapy use, diabetes, hypertension, alcohol	Data on alcohol consumption may not represent a lifelong pattern; common weaknesses for hospital-based case-control study.
Kalandidi <i>et al.</i> (1996), Greater Athens, Greece, 1992–94	145 women diagnosed between 1992 and 1994, operated in two specialized cancer hospitals in Greater Athens; 100% histologically confirmed; participation rate, 83%	298 women, residents of Greater Athens, admitted at the same time to the greater hospitals in Athens for bone fractures or other orthopaedic conditions	Structured questionnaire; hospital interview	Endometrium	<i>Alcohol intake</i> No Yes	1.0 (reference) 0.72 (0.44–1.37) $p=0.67$	Age, education, body mass index, occupation, age at menarche, menopausal status, oral contraceptive use, smoking, menopausal estrogens, coffee	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Goodman <i>et al.</i> (1997b), Oahu, Hawaii, USA, 1985–93	332 women diagnosed between 1 January 1985 and 1 June 1993, residents of Oahu and of Japanese, Caucasian, native Hawaiian, Filipino, Chinese origin, obtained from Hawaii Tumor Registry, aged 18–84 years; 100% histologically confirmed; participation rate, 66%	511 women selected randomly from lists of Oahu residents; matched to cases on ethnicity, age (range, 2.5 years); intact uteri; exclusions: hysterectomized women, mental incompetence; participation rate, 73%	Interviewer-administered standardized questionnaire	Endometrium	<i>Alcohol use</i>	1.00 (reference)	Pregnancy history, oral contraceptive use, unopposed estrogen use, diabetes, body mass index	
					No	0.90 (0.6–1.4)		
					<i>Alcohol type (g ethanol equivalent)</i>	1	Carbohydrate or fat calories, pregnancy history, oral contraceptive use, unopposed estrogen use, diabetes, body mass index	
					Reference	0.8		
					0	0.8		
					0.2	0.8		
					17.8	0.8		
						<i>p</i> for trend=0.44		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Newcomb <i>et al.</i> (1997), Wisconsin, USA, 1991–94	739 female residents of Wisconsin, diagnosed between 1991 and 1994, aged 40–79 years; identified by a state-wide mandatory cancer registry; limited to cases with listed telephone numbers and drivers' licences; 98% histologically confirmed; participation rate, 87%	2313 women selected randomly from lists of licensed drivers; matched by age distribution; criteria: listed telephone number, no previous diagnosis of uterine cancer; participation rate, 85.2%	Structured telephone interview	Endometrium	<i>Recent consumption (drinks/week)</i> None Any <1 1–2 3–6 7–13 ≥14 <i>Continuous</i>	1.00 1.07 (0.86–1.33) 1.22 (0.96–1.56) 0.86 (0.65–1.14) 1.11 (0.83–1.50) 0.81 (0.55–1.19) 1.27 (0.78–2.07) 1.00 (0.98–1.02) <i>p</i> =0.82	Age, smoking status, education, relative weight, hormone replacement therapy use, parity	Any possible information and recall bias unlikely to have an important effect on the results

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Jain <i>et al.</i> (2000c), Ontario, Canada, 1994–98	552 women diagnosed in August 1994–June 1998 (adenocarcinoma, carcinoma, cystadenocarcinoma or mixed Mullerian carcinoma), aged 30–79 years; data from Ontario Cancer Registry (four areas: Toronto, Peel, Halton, York); 100% histologically confirmed; response rate, 70%	562 randomly selected women from property assessment lists; frequency-matched by age group, geographical areas (Toronto, Peel, Halton, York); selection criteria: intact uterus, no history of hysterectomy and listed with telephone number	Home interview, standardized questionnaire	Endometrium	<i>Intake (g absolute alcohol)</i> 0 <1.2 <8.3	<i>Odds ratio</i> 1.0 (reference) 0.85 (0.63–1.18) 0.72 (0.52–0.99) <i>p</i> ≤0.05 <i>p</i> trend=0.04	Total energy, age, body weight, ever smoked, diabetes, oral contraceptive use, hormone replacement therapy use, university education, live births, age at menarche	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
McCann <i>et al.</i> (2000), western New York, USA, 1986–91	232 women, aged 40–85 years; exclusions: women with more than one primary carcinoma and non-adenomatous carcinoma of the endometrium; 100% histologically confirmed; response rate, 51%	639 women randomly selected from the drivers' lists (<65 years) and from Health Care Finance administration (≥65 years); exclusions: hysterectomy and early menopause, before age 37 years; frequency-matched for age, county of residence	Interview: self-reported food-frequency questionnaire (2 years before) and additional telephone interview of controls	Endometrium	<i>Alcohol intake (g)</i> Q1 ≤0.5 Q2 0.6–2.1 Q3 2.2–9.0 Q4 >9.0	1.0 (reference) 1.0 (0.6–1.6) 0.8 (0.5–1.3) 1.0 (0.5–1.8) <i>p</i> =0.58	Age, education, body mass index, diabetes, hypertension, smoking pack-years, age at menarche, parity, oral contraceptive use, menopausal status, post-menopausal estrogen use, total energy	Limitations due to low response rate among cases and controls

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Weiderpass & Baron (2001), Sweden, 1994–95	709 born in Sweden and residing Sweden in 1 January 1994–31 December 1995 identified through six regional cancer registries, aged 50–74 years; intact uterus and no previous diagnosis of endometrial or breast cancer; 100% histologically confirmed by one pathologist (blinded); participation rate, 75%	3368 randomly selected from population register at the same time as cases; participation rate, 79.9%	Mailed questionnaire, or/and telephone interview	Endometrium	<i>Alcoholic beverage consumption (g/day)</i> Non-drinkers Drinkers >0–<1.59 1.6–3.99 ≥4	1.00 (reference) 1.00 (0.83–1.21) 1.16 (0.90–1.49) 0.92 (0.70–1.20) 0.92 (0.70–1.20) <i>p</i> =0.44	Smoking, age, body mass index, parity, age at menopause, age at last birth, hormone replacement therapy use, oral contraceptive use, diabetes mellitus (self-reported)	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Petridou <i>et al.</i> (2002), Greater Athens area, Greece, 1999	84 women with no history of malignancy, resident in Greater Athens area, speaking Greek	84 women admitted at the same time as cases to the same hospital and department for small gynaecological operations; matched to cases for age; no history of malignancy, resident in Greater Athens, speaking Greek	Standardized questionnaire, interview	Endometrium	<i>Alcohol drinking</i> No Yes ≥ 2 glasses/week	1.00 (reference) 0.57 (0.23–1.42) $p=0.23$	Age, education, height, body mass index, age at menarche, ever pregnant, age at first pregnancy, number of children, abortions, menopausal status, alcohol, coffee, current smoking, appendectomy, cholecystectomy, thyroidectomy	Possible information and selection bias did not influence the validity of the results

CI, confidence interval; ICD, International Classification of Diseases

& Horm, 1977; Kato *et al.*, 1989) and eight were population-based (Cusimano *et al.*, 1989b; Webster *et al.*, 1989; Swanson *et al.*, 1993; Goodman *et al.*, 1997b; Newcomb *et al.*, 1997; Jain *et al.*, 2000c; McCann *et al.*, 2000; Weiderpass & Baron, 2001).

Ten studies (Cusimano *et al.*, 1989b; Kato *et al.*, 1989; Webster *et al.*, 1989; Austin *et al.*, 1993; Swanson *et al.*, 1993; Parazzini *et al.*, 1995a; Kalandidi *et al.*, 1996; Newcomb *et al.*, 1997; Weiderpass & Baron, 2001; Petridou *et al.*, 2002) were designed to examine the association between alcoholic beverage intake, other lifestyle factors such as cigarette smoking, use of hormone-replacement therapy and other risk factors in the etiology of endometrial cancer. Six studies (La Vecchia *et al.*, 1986; Shu *et al.*, 1991; Levi *et al.*, 1993; Goodman *et al.*, 1997b; Jain *et al.*, 2000c; McCann *et al.*, 2000) were designed to evaluate nutritional factors in relation to the risk for endometrial cancer.

Confounding factors were considered in all of the above studies except for one (Cusimano *et al.*, 1989b), although adjustment may have been incomplete in three studies (Williams & Horm, 1977 [age, race and smoking]; Shu *et al.*, 1991 [pregnancies and weight]; Levi *et al.*, 1993 [only adjusted for age and centre]). Interviews were conducted with or questionnaires were completed by the subjects in all studies.

The results of case-control studies were not consistent. Ten reported little or no association between alcoholic beverage consumption and the risk for endometrial cancer (Kato *et al.*, 1989; Webster *et al.*, 1989; Austin *et al.*, 1993; Swanson *et al.*, 1993; Kalandidi *et al.*, 1996; Goodman *et al.*, 1997b; Newcomb *et al.*, 1997; McCann *et al.*, 2000; Weiderpass & Baron, 2001; Petridou *et al.*, 2002). Two found an inverse association (Williams & Horm, 1977; Jain *et al.*, 2000c), which was significant in the latter study. Four studies reported an increased risk for endometrial cancer with higher alcoholic beverage consumption (La Vecchia *et al.*, 1986; Cusimano *et al.*, 1989b; Shu *et al.*, 1991; Levi *et al.*, 1993; Parazzini *et al.*, 1995a); in two of these, the association was non-significant (Cusimano *et al.*, 1989b; Shu *et al.*, 1991), in one it was significant with a positive trend analysis (Parazzini *et al.*, 1995a) and one (Levi *et al.*, 1993) found a positive association relative to wine and liquor, but not to beer.

2.12.3 Evidence of a dose-response

There was no evidence of a trend of increasing risk for endometrial cancer with increasing alcoholic beverage consumption in the cohort studies.

In the case-control studies, there was no dose-response association between alcoholic beverage consumption and the risk for endometrial cancer in most studies. One study (Jain *et al.*, 2000c) presented a negative dose-response association and one report showed a clear dose-response trend (Parazzini *et al.*, 1995a). In another study, there was an indication of a dose-response in the association but no formal test for trend was presented (Webster *et al.*, 1989).

2.12.4 *Types of alcoholic beverage*

Only one cohort study investigated the effect of specific types of alcoholic beverage (beer, wine, spirits) on the risk for endometrial cancer (Gapstur *et al.*, 1993) and found no evidence of any association.

Seven case–control studies evaluated different alcoholic beverages in relation to risk for endometrial cancer (Williams & Horm, 1977; Austin *et al.*, 1993; Levi *et al.*, 1993; Swanson *et al.*, 1993; Parazzini *et al.*, 1995a; Goodman *et al.*, 1997b; Weiderpass & Baron, 2001). The studies by Levi *et al.* (1993) and Parazzini *et al.* (1995a) showed an increased risk for endometrial cancer with increasing consumption of wine and hard liquor, but not beer. Overall, there were no consistent patterns of association between any specific type of alcoholic beverage and risk for endometrial cancer.

2.12.5 *Interactions*

Few studies presented information on possible interactions between alcoholic beverage intake and other variables. One cohort study investigated alcohol as an interacting factor with hormone-replacement therapy (Beral *et al.*, 2005). A positive association was found for Tibolone and an inverse association for continuous combined hormone-replacement therapy among women who consumed less than one drink daily.

Among the case–control studies, there was no consistent evidence of an interaction between alcoholic beverage consumption and different variables known or suspected to be associated with endometrial cancer, such as use of hormone-replacement therapy, body size, age, tobacco smoking, parity, education, physical activity, calory intake and other dietary aspects, oral contraceptive use or menopausal status.

2.13 Cancer of the ovary

2.13.1 *Cohort studies (Tables 2.70 and 2.71)*

Since 1988, four prospective cohort studies have examined the association between alcoholic beverage intake and the risk for ovarian cancer in special populations, namely women hospitalized or being treated for alcohol dependence (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Lagiou *et al.*, 2001; Table 2.70) and four have examined the association in the general population (Kushi *et al.*, 1999; Kelemen *et al.*, 2004; Schouten *et al.*, 2004; Chang *et al.*, 2007; Table 2.71). The studies were conducted in Europe (Denmark, the Netherlands and Sweden) and the USA. The studies in special populations presented results adjusted for age and calendar period only, whereas the population-based cohort studies presented results adjusted for a large variety of factors.

There was no evidence of an overall association between alcoholic beverage intake and the risk for ovarian cancer in these cohort studies.

Table 2.70 Cohort studies of ovarian cancer and alcoholic beverage consumption in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Comments
Adami <i>et al.</i> (1992a) Sweden, Cohort of people with a discharge diagnosis of alcoholism	Cohort of 9353 individuals (1013 women) with a discharge diagnosis of alcoholism in 1965–83; follow-up for 19 years (mean, 7.7 years); exclusion of cancer in the first year of follow-up	Registry-based	Women with diagnosis of alcoholism	4	SIR 1.9 (0.5–4.9)	
Tønnesen <i>et al.</i> (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 male and female alcohol abusers who entered an outpatient clinic in Copenhagen during 1954–1987; 3093 women observed for 9.4 years	Registry-based	Alcohol abusers	6	0.9 (0.3–1.8)	
Sigvardsson <i>et al.</i> (1996), Sweden, Alcoholic women from the records of the Temperance Boards	Ovarian and fallopian tube cancer detected among 65 women	Registry-based	Alcohol abusers	65	1.2 (0.9–1.8)	
Lagiou <i>et al.</i> (2001), Sweden, Cohort of alcoholic women	Cohort of 36 856 women diagnosed with alcoholism between 1965 and 1994; mean duration of follow-up, 9.6 years, 317 518 person–years; first year of follow-up excluded from all analysis.	Registry-based	All women	76	SIR 0.86 (0.68–1.08) <i>p</i> =0.19	Expanded population and follow-up of the cohort reported by Adami <i>et al.</i> (1992a)

CI, confidence interval; SIR, standardized incidence ratio

Table 2.71 Cohort studies of ovarian cancer and alcoholic beverage consumption in the general population

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kushi <i>et al.</i> (1999), Iowa, USA, Iowa Women's Health Study	29 083 women, aged 55–69 years (postmenopausal); follow-up 1986–95 (10 years); 139 incident cases of epithelial ovarian carcinoma; exclusions: cancer history other than skin, bilateral oophorectomy, incomplete questionnaire, energy intake implausibly high or low	Mailed self-administrated questionnaire (in 1986) and follow-up questionnaires (1987, 1989, 1992)	Ovary	<i>Alcohol consumption (g/day)</i> 0 0.9–3.9 4.0–10 >10	78 43 8 10	1.00 (reference) 1.37 (0.93–2.04) 0.61 (0.28–1.34) 0.49 (0.24–1.01) <i>p</i> trend=0.01	Age, total energy intake, number of live births, age at menopause, family history of ovarian cancer in a first degree relative, hysterectomy/unilateral oophorectomy status, waist-to-hip ratio, level of physical activity, cigarette smoking, educational level	

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kelemen <i>et al.</i> (2004), Iowa, USA, Iowa Women's Health Study	27 205 women, aged 55–69 years (postmenopausal); follow-up, 1986–2000 (15 years); 147 incident epithelial ovarian cancers detected; association between ovarian cancer and alcohol in the context of folate consumption examined	Self-administered questionnaires	Ovary	<i>Alcohol consumption (g/day)</i>			Age, folate, age at menopause, physical activity, postmenopausal hormone use, oral contraceptive use, family history of breast cancer, family history of ovarian cancer, known diabetes at baseline, smoking, carotene, vitamin C and vitamin E	
				<0.01	48	1.00 (reference)		
				0.01–3.9	75	0.78 (0.54–1.13)		
				4.00–9.9	12	0.75 (0.39–1.42)		
				≥10	12	0.58 (0.30–1.11)		
						<i>p</i> trend=0.08		

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schouten <i>et al.</i> (2004), Netherlands, The Netherlands Cohort Study	62 573 Dutch postmenopausal women, aged 55–69 years; started September 1986; follow up of sub-cohort of 2211 members; exclusion criteria: any cancer diagnosis other than skin, women who had undergone oophorectomy; follow-up biennially by mail to December 1995 (9.3 years); 235 cases of epithelial ovarian cancer detected; analysis based on 214 cases	Self-administered questionnaire	Ovary	<i>Alcohol consumption (categorical mean)</i>			Age, use of oral contraceptives, parity, height, body mass index, energy intake, current cigarette smoking	Possible limitation: misclassification of alcohol consumption (if any, expected to be non-differential); former-drinkers not separated from abstainers (small proportion)
				No (0) g/day	57	1.00 (reference)		
				0.1–4 (1.9) g/day	74	1.13 (0.79–1.63)		
				5–14 (9.3) g/day	28	0.85 (0.53–1.37)		
				≥15 (26.3) g/day	21	0.92 (0.55–1.54)		
Total increment per 10 g alcohol		1.01 (0.84–1.21)	<i>p</i> trend=0.54					

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chang <i>et al.</i> (2007), USA, California Teachers Study	90 371 teachers; baseline assessment 1995–96; follow-up to end of 2003; excluded: women >85 years of age, with previous history of ovarian cancer, bilateral oophorectomy before baseline, when information not provided or invalid; 253 women diagnosed with epithelial ovarian cancer (227 invasive, 26 borderline)	Mailed questionnaire	Ovary (invasive and borderline)	Year before baseline			Race, total energy intake, parity, oral contraceptive use, strenuous exercise, menopausal status/hormone replacement therapy, stratified by age at baseline; other alcohol types, race, total energy intake, parity, oral contraceptive/hormone-replacement therapy use, strenuous exercise, menopausal status, stratified by age at baseline;	
				<i>Total alcohol intake (g/day)</i>				
				None	77	1.00 (reference)		
				<10	81	1.04 (0.76–1.42)		
				10–20	72	1.47 (1.06–2.03)		
				≥20	23	1.15 (0.71–1.84)		
						<i>p</i> trend=0.19		
				<i>Alcohol from wine (g/day)</i>				
None	91	1.00 (reference)						
<11.1	99	1.09 (0.80–1.50)						
≥11.1	63	1.57 (1.11–2.22)						
			<i>p</i> trend=0.01					

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chang <i>et al.</i> (2007) (contd)				Interactions			(contd) race, total energy intake, parity, oral contraceptive use, strenuous exercise, menopausal status/hormone replacement therapy, stratified by age at baseline	
				Wine intake (g/day)				
				<i>Socioeconomic status:</i>				
				<i>upper</i>				
				25%				
				≥11.1	39	1.96 (1.19–3.24) <i>p</i> trend=0.004		
				<i>Lifetime strenuous physical activity ≤1.4 h</i>				
				None	61	1.00 (reference)		
				<11.1	58	1.07 (0.72–1.59)		
				≥11.1	40	1.68 (1.09–2.59) <i>p</i> trend=0.01		
				<i>Parity: parous</i>				
				None	71	1.00 (reference)		
				<11.1	73	1.05 (0.73–1.50)		
				≥11.1	48	1.57 (1.06–2.34) <i>p</i> trend=0.02		
				<i>Median age >50 years</i>				
				None	68	1.00 (reference)		
<11.1	72	1.10 (0.76–1.57)						
≥11.1	51	1.62 (1.09–2.39) <i>p</i> trend=0.01						
<i>Menopausal status:</i>								
<i>Peri/postmenopausal</i>								
None	66	1.00 (reference)						
<11.1	72	1.16 (0.80–1.66)						
≥11.1	51	1.72 (1.16–2.55) <i>p</i> trend=0.01						

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Chang <i>et al.</i> (2007) (contd)				Alcohol intake					
				≥11.1 g/day					
				<i>Oral contraceptive use</i>					
				Never	29	1.70 (1.02–2.82)		<i>p</i> trend=0.03	
				Ever	14	1.78 (0.85–3.72)		<i>p</i> trend=0.09	
				<i>Hormone therapy use</i>					
				None	9	1.20 (0.51–2.78)		<i>p</i> trend=0.73	
				Estrogen+progestin	16	1.17 (0.58–2.34)		<i>p</i> trend=0.45	
				Estrogen only	15	2.03 (0.95–4.35)		<i>p</i> trend=0.06	
				<i>Cigarette smoking</i>					
				Ever	27	1.42 (0.80–2.50)		<i>p</i> trend=0.24	
				Never	36	1.77 (1.13–2.78)		<i>p</i> trend=0.01	
				<i>Total folate intake</i>					
≤473 µg/day	25	1.34 (0.78–2.30)		<i>p</i> trend=0.27					
>473 µg/day	37	2.07 (1.29–3.35)		<i>p</i> trend=0.002					

CI, confidence interval; ICD, International Classification of Diseases

2.13.2 *Case-control studies (Table 2.72)*

Twenty-three case-control studies investigated the relationship between alcoholic beverage consumption and the risk for ovarian cancer in Australia, India, Japan, North America, Scandinavia and western Europe.

Twelve of these were hospital-based (West, 1966; Williams & Horm, 1977; Byers *et al.*, 1983; Tzonou *et al.*, 1984; Mori *et al.*, 1988; Whittemore *et al.*, 1988; Hartge *et al.*, 1989; La Vecchia *et al.*, 1992; Nandakumar *et al.*, 1995; Tavani *et al.*, 2001a; Yen *et al.*, 2003; Pelucchi *et al.*, 2005), one was based on cases and controls who were included in a cancer registry database (Kato *et al.*, 1989) and 10 were population-based (Gwinn *et al.*, 1986; Polychronopoulou *et al.*, 1993; Kuper *et al.*, 2000b; Goodman & Tung, 2003; McCann *et al.*, 2003; Modugno *et al.*, 2003; Riman *et al.*, 2004; Webb *et al.*, 2004; Peterson *et al.*, 2006).

Confounding factors were considered in all studies, although adjustment was less extensive in studies published during the 1980s. Overall, the results of case-control studies do not suggest any association between alcoholic beverage consumption and the risk for ovarian cancer, although a few studies indicated either positive or negative associations.

2.13.3 *Evidence for a dose-response*

There was no consistent evidence of a trend of increasing risk for ovarian cancer with increasing alcoholic beverage consumption based on the cohort or case-control studies.

2.13.4 *Types of alcoholic beverage*

In two population-based cohort studies the association between types of alcoholic beverage was investigated (Schouten *et al.*, 2004; Chang *et al.*, 2007). Intake of wine during the year before baseline was associated with an increased risk for ovarian cancer in one study (Chang *et al.*, 2007), but was not confirmed in the other (Schouten *et al.*, 2004).

Seven case-control studies evaluated different alcoholic beverages in relation to the risk for ovarian cancer (Gwinn *et al.*, 1986; La Vecchia *et al.*, 1992; Tavani *et al.*, 2001a; Goodman & Tung, 2003; Modugno *et al.*, 2003; Webb *et al.*, 2004; Peterson *et al.*, 2006). Overall, there were no consistent patterns of association between any specific type of alcoholic beverage (beer, wine, spirits) and risk for ovarian cancer.

2.13.5 *Interactions*

Three of the cohort studies (Kelemen *et al.*, 2004; Schouten *et al.*, 2004; Chang *et al.*, 2007) investigated possible interactions between alcoholic beverage intake and

Table 2.72 Case–control studies of ovarian cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
West (1966), Massachusetts, USA, 1959–60 (controlled case–history study)	92 (of 97) patients with primary ovarian malignancy, resident within a 50-mile radius of Boston, MA; aged 25–74 years; from 50 hospitals in Boston and greater Boston area, operated from 1 January 1959 until 31 March, 1960 (date of incidence = date of surgery); exclusions: women aged >75 years, women with co-existent malignancy of another organ, not metastatic from ovary	92 (of 97) hospital patients with benign ovarian tumour; matched for age, residence, day of surgery.	Interview based on the same protocol for cases and controls	Ovary	Use of alcohol	Data not shown $p=0.28$		No significant difference between alcohol users and non-users

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967–71	7518 cancer patients (all sites, men and women) interviewed; 57% selected randomly	Randomly selected patients with cancer of other, non-related sites	Interview	Ovary	<i>Wine level</i>	<i>Relative odds</i>	Age, race,	
					1	0.62		
					2	1.00		
					<i>Beer level</i>			
					1	0.54		
					2	0.88		
					<i>Hard liquor level</i>			
					1	0.61		
					2	0.93		
					<i>Total alcohol oz–years level</i>			
					1	0.88		
					2	0.87		
					<i>Wine level</i>			
					1	0.49		
					2	0.85		
					<i>Beer level</i>			
					1	0.51		
					2	0.81		
					<i>Hard liquor level</i>			
					1	0.52		
2	0.94							
<i>Total alcohol oz–years level</i>								
1	0.74							
2	0.85							

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Byers <i>et al.</i> (1983), USA, 1957–65	274 white women patients, diagnosed within 2 years of interview, admitted to Roswell Park Memorial Institute, aged 30–79 years	1034 hospitalized white women admitted to same institute at the same time for non-malignant conditions, not related to the reproductive system or gastrointestinal system, or diagnosed with <i>diabetes mellitus</i> or thyroid disease, aged 30–79 years	Mailed questionnaire before admission to hospital, individual interview on the day of admission and second interview at admission by trained interviewer	Ovary	Drinks per week		Age	Possible selection bias does not account for the observed risks; possible recall bias; nearly all patients of advanced stage; analysis by stage not possible.
					<i>At age 30–49 years</i>			
					0	1.0 (reference)		
					<8	0.84		
					≥9	0.56		
					<i>At age 50–79 years</i>			
					0	1.00 (reference)		
					<8	0.98		
					≥9	1.09		
					<i>At age 30–79 years</i>			
0	1.00 (reference)							
<8	0.92							
≥9	0.83							
Tzonou <i>et al.</i> (1984), Athens, Greece, 1980–81	150 women with common and primary epithelial ovarian cancer, operated in any of 10 large hospitals of the Greater Athens area; 100% histologically confirmed; participation rate, 82.4%	250 women hospitalized at the same time in the Athens hospitals for first-time orthopaedic disorders, randomly chosen; participation rate, 100%	Standard questionnaire at interview by the same physician	Ovary	Non-drinkers Drinkers <i>Duration (years)</i> ≤9 10–19 20–29	(reference) 1.5 (0.9–2.5) 0.7 (0.2–2.2) 1.9 (0.7–4.8) 2.9 (1.1–7.6)	Age, parity, age at menopause, use of exogenous estrogens	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Gwinn <i>et al.</i> (1986), Atlanta, Detroit, San Francisco, Seattle, the states of Connecticut, Iowa and New Mexico and the four urban counties of Utah, USA, December 1980–December 1982	433 women diagnosed between December 1980 and December 1982, lived in one of the study areas at the time of diagnosis, aged 20–54 years; 100% histologically confirmed; participation rate, 71%	2915 women identified by randomly selecting telephone numbers of households in the geographic areas where the cases lived, aged 20–54 years; matched by age (5-year intervals); no history of bilateral oophorectomy; response rate, 83.4%	Standard questionnaire in participants' homes by trained interviewers; questions about alcohol consumption habits in the last 5 years added to the questionnaire in August 1981	Ovary	<i>Average weekly consumption</i> Never drank Ever drank <50 g/week 50–149 g/week 150–249 g/week ≥250 g/week	1.0 (reference) 0.9 (0.7–1.2) 1.0 (0.7–1.4) 0.8 (0.5–1.1) 1.0 (0.6–1.6) 0.5 (0.2–0.9)	Age, geographic region, religion, education, smoking, oral contraceptive use, parity, infertility, family history of ovarian cancer	Lack of information on drinking status for 13 cases and 50 controls (one drink=12.6 g alcohol)

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Mori <i>et al.</i> (1988), Hokkaido, Japan, 1980–81 and 1985–86	110 women with primary epithelial ovarian cancer, hospitalized in any hospital in Hokkaido; participation rate, 100%	220; two series: 110 patients from wards in hospitals in Hokkaido with diseases other than ovarian cancer; 110 identified from outpatients without any malignant gynaecological diseases; matched to cases by year of birth, year of the survey; participation rate, 100%	In-person interview	Ovary	<i>Consumption of alcoholic beverages</i> Less than once a week At least once a week	1 (reference) 1.0 (0.6–1.9)	Unclear (none?)	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Whittemore <i>et al.</i> (1988), San Francisco Bay area, USA, 1983–85	188 women from northern California diagnosed between January 1983 and December 1985 in one of the seven hospitals in Santa Clara County or at University of California San Francisco, Medical Center, aged 18–74 years	539; 280 hospitalized in one of the hospitals where cases were admitted, without overt cancer; 259 chosen from the general population by random-digit dialling; matched to cases by age (within 5-year intervals), race (white, black, oriental)	Structured home interviews by trained interviewers	Ovary	<i>Previous alcohol consumption</i> Non-drinker Drinker Non-drinker Heavy drinker (>20 drinks/week)	1 0.74 <i>p</i> =0.14 1 0.66 <i>p</i> =0.34	Observations not altered by adjustment for cigarette smoking or coffee consumption	No evidence of a trend in risk with increasing duration or amount of alcohol consumption; absence of data on diet may preclude examination of potential confounders.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Hartge <i>et al.</i> (1989), Washington DC, USA, August 1978–June 1981	296 women with primary epithelial ovarian cancer, residents of metropolitan area of Washington DC, aged 20–79 years; diagnosis microscopically confirmed after operation; participation rate, 74%	343 women hospitalized at the same time and the same hospitals as cases, identified from hospital discharge lists; matched to cases by hospital, age, race; exclusion criteria: patients with psychiatric diagnosis and with diagnosis related to the major exposures of interest; patients with bilateral oophorectomy; participation rate, 78%	Standardized questionnaire by trained interviewers at participants' home shortly after diagnosis	Ovary	<i>Average weekly consumption</i> 0 Occasional drink 1–6 drinks 7–13 drinks ≥14 drinks	1.0 (reference) 1.1 (0.7–1.9) 1.4 (0.8–2.3) 1.2 (0.7–2.2) 1.5 (0.8–2.8) <i>p</i> =0.14	Age, race	
Kato <i>et al.</i> (1989), Japan, 1980–86	417 women registered at Aichi Cancer Registry, diagnosed between 1980 and 1986, aged ≥20 years	8920 cases of cancer of other sites excluding cancers known to be alcohol-related	Records from Aichi Cancer Registry with available data on alcohol drinking habits	Ovary	<i>Alcohol drinking</i> Daily versus less	0.38 (0.15–0.95) <i>p</i> <0.05	Age	Possible bias due to control selection from cancer patients; no information on important risk factors

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
La Vecchia <i>et al.</i> (1992), Milan, Italy, January 1983–May 1990 (overlaps with La Vecchia <i>et al.</i> , 1986)	801 women with incident ovarian cancer, aged 22–74 years; 100% histologically confirmed	2114 women admitted to a network of teaching or general hospitals in the greater Milan area for acute, non-neoplastic, gynaecological or hormone-related conditions diagnosed within the year before the interview, and not undergone bilateral oophorectomy, aged 24–74 years	In-person interview based on a standardized questionnaire during hospital admission	Ovary	<i>Alcohol consumption (drinks/day)</i> 0 <1 1<2 2<3 ≥3	1.0 1.0 (0.7–1.4) 1.1 (0.9–1.4) 1.2 (1.0–1.5) 1.3 (0.9–1.8) $p \leq 0.05$ $\chi^2 = 4.29$	Age, education, smoking, menstrual and reproductive factors, oral contraceptive use, indicators of fat and green vegetable consumption	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Polychronopoulou <i>et al.</i> (1993), Greater Athens, Greece, June 1989–March 1991	189 women residents of Greater Athens, operated for epithelial ovarian cancer in two hospitals, aged ≤75 years	200 residents of Greater Athens, visitors of patients hospitalized in the same wards as the cancer patients at the same time, aged <75 years; exclusion criteria: previous cancer diagnosis or at least one ovary removed; not matched by age	In-person interview questionnaire by resident doctor at each of the hospitals	Ovary	<i>Consumption of alcoholic beverages (glasses/day)</i> Never ≥1 1 1–2 >2	1.00 0.85 (0.52–1.39) 1.06 (0.82–1.36) 0.94 (0.49–1.79) 1.62 (0.66–3.96) <i>p</i> =0.67	Age (10-year group) Age, years of education, age at menarche, weight before the onset, menopausal status, age at menopause, parity, age at first birth, smoking, coffee drinking	
Nandakumar <i>et al.</i> (1995), Bangalore, India, 1982–85	97 ever-married women obtained from the cancer registry in Bangalore; mean age, 48.3 years	194 women from the same area, attending a referral hospital for cancer or suspected cancer, with the diagnosis of no evidence of cancer; no hysterectomy; matched by age, material status, calendar time	Interview	Ovary	<i>History of alcohol consumption</i> No Yes	1.00 (reference) 1.3 (0.2–8.0)	Age, marital status, calendar time, area of residence	Statistical analysis accounted for the matched design of the study

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Kuper <i>et al.</i> (2000b), eastern Massachusetts/New Hampshire, USA, May 1992–March 1997	549 women born and resident in New Hampshire or Massachusetts, without any previous ovarian malignancy or bilateral oophorectomy, aged 50–74 years; reported to the regional Cancer Registries; specimens reviewed by one of authors; histological classification based on original histology of local pathologists; participation rate, 79%	516 identified by combination of random-digit dialling and selection from community lists; matched to cases by community of residence, age within 4 years	In-person interview self-administered food-frequency questionnaire	Ovary	<i>Drinks/day</i> 0 0–1 >1–2 >2–3 >3	1.00 0.91 (0.67–1.23) 1.33 (0.88–2.01) 0.92 (0.50–1.69) 1.35 (0.80–2.26) <i>p</i> =0.20	Age, centre, material status, parity, body mass index, oral contraceptive use, family history of breast, ovarian and prostate cancer, tubal ligation, education, alcohol consumption, pack-years of smoking	Low participation rate for cases and controls, possible selection bias; heavy alcohol drinkers could be under-represented, especially among controls.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Tavani <i>et al.</i> (2001a), Milan, Pordenone, Pauda, Gorizia, Latina, Naples, Italy, January 1992–September 1999	1031 women with incidental invasive epithelial ovarian cancer, aged 18–79 years; 100% histologically confirmed	2411 women admitted to the hospital for acute, non-neoplastic, non-hormone-related diseases and unrelated to known and potential risk factors for ovarian cancer, aged 17–79 years	Structured questionnaire, in-person interview at hospitals	Ovary	<i>Total alcohol (g/day)</i> Never drinker <12 12–<24 24–<36 ≥36	1.00 (reference) 1.02 (0.80–1.30) 1.29 (1.00–1.67) 1.04 (0.80–1.36) 1.09 (0.76–1.57) χ^2 for trend=0.68 $p=0.409$	Study centre, year of interview, age, education, parity, age at menopause, oral contraceptive use, family history of ovarian or breast cancer, body mass index, energy intake	Limitations common to other hospital-based case-control studies

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Goodman & Tung (2003), Hawaii, Los Angeles, CA, USA, 1993–99	558 women resident in Hawaii or Los Angeles County for at least 1 year, no history of ovarian cancer before, identified through the rapid reporting systems of Hawaii Tumor Registry and Los Angeles County Cancer Surveillance Program, aged ≥ 18 years; 100% histologically confirmed; response rate, 62%;	607 women with no prior history of ovarian cancer and at least one intact ovary; from lists of female Oahu residents/Hawaii; if ≥ 65 years, supplemented by participants of Health Care Financing Administration in Oahu; in Los Angeles, >95% selected based on a neighbourhood walk procedure; frequency-matched to patients based on ethnicity, 5-year age group, study site; participation rate, 67%	Structured in-person interviews; reference date for cases, year before diagnosis; for controls, interview date	Ovary	<i>Total alcohol</i> Never drinker Ever drinker Former drinker Current drinker	1.00 0.88 (0.67–1.16) 1.16 (0.82–1.64) 0.69 (0.50–0.96)	Age, ethnicity, education, study site, oral contraceptive use, parity, tubal ligation	Possibility of recall bias; participation rates not optimal and may have affected the validity of the findings.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
McCann <i>et al.</i> (2003), western New York, USA, 1986–91	124 women with primary ovarian cancer, aged 40–85 years; 100% histologically confirmed	696; randomly selected from driver's licence lists for women <65 years and from Health Care Financing Administration for women ≥65 years of age; frequency-matched to cases on age (±5 years), county of residence	In-person interview	Ovary	<i>Alcohol intake (g/day)</i> <0.2 0.2–1.1 1.1–3.7 3.7–12.9 >12.9	1.00 0.55 (0.30–1.02) 0.67 (0.36–1.25) 0.97 (0.54–1.73) 0.62 (0.34–1.12) <i>p</i> <0.05	Age, education, total months menstruating, difficulty becoming pregnant, oral contraceptive use, menopausal status, total energy	Small number of cases, possible recall and information bias, short time between diagnosis and interview
Modugno <i>et al.</i> (2003), Delaware Valley, USA, May 1994–July 1998	761 women from 39 hospitals around Delaware Valley diagnosed within 9 months before interview, aged 20–69 years, 100% confirmed by pathology; response rate, 88%	1352 women ascertained by random-digit dialling (aged ≤ 65 years) or through Health Care Financing Administration lists (aged 65–69 years); frequency-matched to cases by 5-year age groups, three-digit telephone exchanges	Standardized, in-person interview	Ovary	Ethanol consumption <i>Non-mucinous cancers</i> Never Ever Current Former <i>Mucinous cancers</i> Never Ever Current Former	1.0 (reference) 1.03 (0.84–1.26) 0.96 (0.75–1.23) 1.12 (0.86–1.46) 1.0 (reference) 0.92 (0.61–1.40) 0.97 (0.60–1.57) 0.87 (0.51–1.49)	Age, parity, use of oral contraceptive, education, race, tubal ligation, smoking, family history of ovarian cancer	Possibility of error in the histological classification; possibility for selection bias among controls and under representation of heavy drinkers in the control group

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Yen <i>et al.</i> (2003), Taipei, Taiwan, China, 1993–98	86 women with primary epithelial ovarian cancer resident in Taiwan for at least 20 years, aged 20–75 years; hospital pathological records; exclusions: major gynaecological operation, hysterectomy, oophorectomy	369 women hospitalized for non-malignant, non-gynaecological conditions, unrelated to hormones or digestive tract or to long-term modification of diet; matched by age (5-year range), hospital, admission date	In-person interviews at the hospitals	Ovary	<i>Alcohol consumption</i> No Yes	1.0 (reference) 0.71 (0.20–2.51)	Age, income during marriage, education	Limitation on power of the test due to small sample involved; possible selection bias
Riman <i>et al.</i> (2004), Sweden, 1 October 1993–31 December 1995	655 women born and resident in Sweden, with primary, newly diagnosed epithelial ovarian cancer, aged 50–74 years; 100% histologically confirmed; participation rate, 79%	3899 women randomly selected from a national population registry and sampled simultaneously with cases; frequency-matched to the expected age distributions; exclusion: women with previous bilateral oophorectomy	Mailed, self-administered questionnaires and additional telephone interview with cases who failed to respond	Ovary	Alcohol consumption (g/day) Non-users <5 ≥5	1.0 (reference) 0.94 (0.77–1.14) 0.99 (0.75–1.29) <i>p</i> =0.80	Age, parity, body mass index, age at menopause, duration of oral contraceptive use, ever use of hormone replacement therapy; <i>p</i> -value for the likelihood ratio test of heterogeneity	Possible recall bias

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Webb <i>et al.</i> (2004), Australia (New South Wales, Victoria and Queensland), August 1990–December 1993	696 Australian women treated in the major treatment centres in New South Wales, Victoria and Queensland, aged 18–79 years; 100% histologically confirmed; participation rate, 89%	786 cancer-free women selected at random from the electoral roll; frequency-matched to the cases for age (within 10-year bands), urban/rural district of residence; women with reported history of ovarian cancer or bilateral oophorectomy excluded	Face-to-face interview and food-frequency questionnaire	Ovary	None 1/week 1–6/week 1–1.9/day ≥2/day	<i>Invasive cancers</i> 1.0 0.84 (0.62–1.14) 0.73 (0.53–1.02) 0.85 (0.53–1.36) 0.46 (0.27–0.79) $p=0.009$ $p=0.05$ (excluding non-drinkers)	Age (in years), age squared, education, body mass index, smoking (newer, past, current), duration of oral contraceptive use, parity, caffeine intake	
Pelucchi <i>et al.</i> (2005), Italy (four areas), 1992–99	1031 women admitted to the major teaching and general hospitals; 100% histologically confirmed	2411 women admitted to the same network of hospitals for acute, non-malignant and non-gynaecological conditions, unrelated to hormonal diseases or to long-term modifications of diet	Standard questionnaire during hospital stay by centrally trained interviewers; food-frequency questionnaire	Ovary	Non-drinkers/light alcohol drinkers (<1.8 g/day) Moderate/heavy alcohol drinkers (≥1.8 g/day)	0.93 (0.76–1.14) $\chi^2=0.97$ $p=0.32$ 1.02 (0.86–1.23) $\chi^2=0.10$ $p=0.75$	Age, study centre, year of interview, education, parity, body mass index, alcohol consumption, oral contraceptive use, physical activity, non-alcohol energy intake	Ovarian cancer risk for folate intake in alcohol strata (null results in brief)

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Peterson <i>et al.</i> (2006), Massachusetts (excluding Boston) and Wisconsin, USA, 1993–95 and 1998–2001	762 English-speaking women from two case–control studies (new diagnosis reported to the respective state cancer registries with listed telephone numbers and drivers' licences) verified by self report if less than 65 years of age or Medicare beneficiaries if 65 years or older, aged 40–79 (1993–95) or 20–75 years (1998–2001); 63 cases excluded due to unclear pathological diagnosis and 7 due to missing data on alcohol consumption; participation rate, 66%	6271 randomly selected from lists of licensed drivers if less than 65 years and from rosters of Medicare beneficiaries compiled by the Health Care Financing Administration if 65 years or older; all women had publicly available telephone number; frequency-matched to the age distribution of ovarian cancer and breast cancer cases enrolled in a breast cancer study; participation rate, 80.6%	Structured telephone interview with interviewers blinded to case/control status of the subjects	Ovary	<i>Recent past</i> None Ever drank <1 drink/week 1–6 drinks/week ≥1 drink/day	1.00 1.06 (0.87–1.29) 1.05 (0.84–1.32) 1.15 (0.92–1.42) 0.89 (0.70–1.20) <i>p</i> =0.77	Age, state of residence	Possible bias related to control selection and recall bias

CI, confidence interval; ICD, International Classification of Diseases

other variables. Some weak interactions were found by Chang *et al.* (2007) for women who drank more than one glass of wine daily and were over 50 years of age, post-menopausal, used estrogen only hormone therapy, belonged to a higher social class, were never smokers and had higher total folate intake. Among the case–control studies, there was no consistent evidence of interaction between alcoholic beverage consumption and different variables known or suspected to be associated with ovarian cancer, such as reproductive history, education, body size or diet.

2.14 Cancer of the uterine cervix

2.14.1 Cohort studies (Table 2.73)

A total of six prospective cohort studies have examined the association between alcoholic beverage intake and risk for cervical cancer, all of which were carried out in special populations, namely women who were treated for alcohol abuse or alcoholism (Prior, 1988; Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Weiderpass *et al.*, 2001b) or worked as waitresses (Kjaerheim & Andersen, 1994).

These studies were conducted in Scandinavia (Adami *et al.*, 1992a; Kjaerheim & Andersen, 1994; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Weiderpass *et al.*, 2001b) and in the United Kingdom (Prior, 1988), and were all based on record linkages between existing databases, such as registries for hospitalizations and clinical care for alcoholism, and data from trade-union files. The cancer outcome was obtained by the respective cancer registries in each country/region. The comparison of incidence rates of cervical cancer was made between the special populations selected for the studies and women from the general population who were the same age as the study participants, during the same time periods.

All five studies conducted among women who were treated for alcohol abuse or alcoholism presented elevated risk estimates for invasive cervical cancer. However, none of them were able to adjust for known risk factors for cervical cancer, namely human papillomavirus (HPV) infections, number of sexual partners and tobacco smoking, or attendance of cervical cancer-screening programmes. It is possible that women who abuse alcohol have other behavioural patterns that may affect the risk for cervical cancer, such as non-compliance with screening, tobacco smoking and having a higher prevalence of HPV than the general populations in their respective countries.

2.14.2 Case–control studies (Table 2.74)

The association between alcoholic beverage intake and cervical cancer was evaluated in 12 case–control studies, seven of which were hospital-based (two from Italy, two from Thailand, one from Uganda and studies from United Kingdom and the USA), three were register- or cohort- based (from the USA and Zimbabwe), one was population-based (from Lesotho) and one was a large multicentre study from Latin America

Table 2.73 Cohort studies of alcoholic beverage consumption and cervical cancer in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Prior (1988), Birmingham, United Kingdom, Study of hospitalized patients for alcohol-related diseases	1110 patients (234 women) hospitalized in the Birmingham Region between 1948 and 1971 for alcohol-related conditions; follow-up to 1981; compared with the West Midlands Region	Hospital discharge record	<i>Cervix uteri</i> (ICD-8/180)	Cancer morbidity among women hospitalized for alcohol-related conditions	<i>Obs/Exp</i> 3	3.7 ($p < 0.05$)		
Adami <i>et al.</i> (1992a) Sweden, Cohort of people with a discharge diagnosis of alcoholism	9353 individuals (1013 women) with a discharge diagnosis of alcoholism in 1965–83; follow up for 19 years (mean, 7.7 years); exclusion of cancer in the first year of follow-up	Registry based	<i>Cervix uteri</i>	Alcohol abusers	6	SIR 4.2 (1.5–9.1)		

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Kjaerheim & Andersen (1994), Norway, Norwegian Cohort of Waitresses	5314 waitresses organized in the Restaurant Workers Union between 1932 and 1978; follow-up 1959–91	Employers lists from Restaurant Workers Union	<i>Cervix uteri</i> (ICD-7/171)	Waitresses versus women in Norway except Oslo	51	SIR 1.7 (1.3–2.3)			
				<i>Type of restaurant</i>					
				Alcohol serving	28	1.8 (1.3–2.5)			
				Non-alcohol serving	13	1.6 (0.8–2.7)			
				<i>Years since first employment</i>					
				0–9	20	1.5			
10–19	22	1.8							
≥20	9	1.8							
Tønnesen <i>et al.</i> (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 alcohol abusers (men and women) who entered an outpatient clinic in Copenhagen during 1954–198?; 3093 women observed for 9.4 years	Registry based	<i>Cervix uteri</i>	Alcohol abusers	22	2.00 (1.2–3.0) ($p \leq 0.01$)			

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Temperance Boards Study	Nested case–control study; records of 15 508 alcoholic women born between 1870 and 1961 obtained from Temperance Boards; control matched for region and day of birth; incidence data from Swedish Cancer Registry	Registry based	<i>Cervix uteri</i> (ICD-7/171)	Alcohol abusers	187	3.9 (2.8–5.4)		

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Weiderpass <i>et al.</i> (2001b), Sweden, National Board of Health and Welfare/ Study of Alcoholic Women	36 856 women (mean age, 42.7 years) registered and hospitalized with alcoholism between 1965 and 1994; data from Inpatients Register; linkages to nationwide Registers of Causes of Death and Emigration and national Register of Cancer; average follow-up time, 9.4 years	Registry based; linkages	<i>Cervix uteri in situ</i>	Total <i>Age at cancer diagnosis (years)</i>	502	SIR 1.7 (1.6–1.9)		
				<35	180	1.5 (1.3–1.8)		
				35–49	246	1.8 (1.6–2.0)		
				50–59	55	2.4 (1.8–3.1)		
				≥60	21	2.7 (1.7–4.2)		
				Total <i>Age at cancer diagnosis (years)</i>	129	2.9 (2.4–3.1)		
			<i>Cervix uteri</i>	Invasive	16	3.2 (1.8–5.2)		
			(ICD-7/171)	<35	40	2.4 (1.7–3.2)		
				35–49	35	3.7 (2.6–5.2)		
				50–59	38	2.9 (2.1–4.0)		
				≥60				

CI, confidence interval; ICD, International Classification of Diseases; Obs/Exp, observed/expected; SIR, standardized incidence ratio

Table 2.74 Case-control studies of invasive cervical cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967-71	57% randomly selected and interviewed from 7518 cancer patients from the Third National Cancer Survey (all sites)	Randomly selected patients with cancer of other, non-related sites	Interview	Cervix		Relative odds		Age, race
					Wine level			
					1	0.61		
					2	1.44		
					Beer level			
					1	1.29		
					2	1.29		
					Hard liquor level			
					1	0.61		
					2	0.79		
					Total alcohol oz-years level			
					1	0.88		
					2	0.81		
					Wine level			
					1	0.62	Age, race, smoking	
					2	1.53		
					Beer level			
					1	1.22		
					2	1.20		
					Hard liquor level			
1	0.54							
2	0.76							
Total alcohol oz-years level								
1	0.82							
2	0.73							

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Harris <i>et al.</i> (1980), Oxford United Kingdom, 1974–79	237 women with abnormal cervical smears and who had undergone cervical punch biopsy or surgical conisation at two hospitals in Oxford (John Radcliffe and Churchill Hospital) between October 1974 and June 1979; 65 cases of carcinoma <i>in situ</i>	422 women who attended gynaecological clinics at the John Radcliffe Hospital or who received inpatient or outpatient gynaecological care at the Churchill Hospital during the same time period; small numbers of controls were patients receiving initial cervical smear at the Abington Health Centre; exclusions: women who had hysterectomy, history of cancer or a mental illness	Interview at the hospital prior to histological diagnosis	Cervix, cervical carcinoma <i>in situ</i>	Alcohol consumption Carcinoma <i>in situ</i> Never Monthly Weekly Daily	1.0 0.83 0.87 1.23	Age (<30, 30–40, ≥40)	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Marshall <i>et al.</i> (1983), Buffalo, NY, USA	513 white women, patients admitted to the Roswell Park Memorial Institute between 1957 and 1965, diagnosed with cervical cancer during admission; diagnoses were histologically confirmed	490 white women matched to the cases by age (5-year group); ascertained from patient lists; diagnosed mainly with non-neoplastic diseases of sites other than genitourinary and gastrointestinal tract; for 234 of these patients, no diagnosis was established at discharge	Mailed pre-admission questionnaire; interview at admission; both were completed before diagnosis	Cervix	Alcohol consumption <i>Types of alcohol</i> None Beer Wine Distilled liquor Beer and wine Beer and distilled liquor Wine and distilled liquor All types of alcohol <i>Monthly consumption (drinks)</i> 0 1–10 11–20 21–30 ≥31	1.0 (reference) 1.8 (1.2–2.7) 0.8 (0.3–1.6) 0.7 (0.4–1.1) 1.5 (1.2–2.0) 1.3 (0.8–2.0) 0.6 (0.3–1.2) 0.8 (0.5–1.3) 1.0 (reference) 1.0 (0.7–1.3) 1.1 (0.7–1.7) 1.3 (0.7–2.5) 1.2 (0.8–1.9)		

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Martin & Hill (1984), Lesotho, 1950–74	257 hospital patients from 14 geographical areas diagnosed between 1950 and 1969, aged 23–86 years (average, 47.9 years); followed in 1970–74; diagnosis based on histological examination, cervical smear or very strong clinical evidence (invasive cervical cancer)	257 women free of cancer from the same or adjacent geographical areas (provided they were of the same character), aged 22–89 years	Questionnaire	<i>Cervix uteri</i>	<i>Indigenous alcohol consumption</i>	2.4 $\chi^2=9.47$ $p<0.01$	Tobacco, European alcohol consumption Tobacco, indigenous alcohol consumption	The mycotoxin zearalenone in indigenous alcohols suggested to be correlated with cervical cancer; limitations: lack of quantities of alcohol consumption; cervical cancer patents represent a lower educational and social status than the rest of society in Lesotho.
					<i>European alcohols</i>	Drinker versus non-drinker		

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Cusimano <i>et al.</i> (1989b), Italy, Ragusa, 1 Jan. 1983–30 Jun. 1985	39 women from Ragusa and province (Italy/Sicily) diagnosed with cervical cancer between 1 Jan. 1983 and 30. Jun 1985, aged 35–79 years; 100% histologically confirmed (invasive); participation rate, 83%	156 women from the same geographical region, aged 30–76 years; matched to cases by age (2.5-year range), type of health service consulted; women who had undergone hysterectomy excluded	Structured questionnaire; interview	<i>Cervix uteri</i>	<i>Alcohol consumption</i> No Yes	1.0 (reference) 0.72 (0.35–1.50)	‘Adjusted for confounding variables’ (unclear which ones: parity, number of spontaneous miscarriages, use of oral contraceptives, young age of proband’s mother at birth)	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Herrero <i>et al.</i> (1989), Latin America: Colombia, Costa Rica, Mexico, Panama, Jan. 1986–June 1987	667 patients living in the study area for at least 6 months prior to diagnosis; diagnosed with incidental invasive squamous-cell carcinoma between January 1986 and June 1987 in hospitals in Bogota (Colombia)-the Ministry of Health cancer referral center, three Social Security hospitals in San Jose, Costa Rica, the Social Security's Oncology Hospital in Mexico City, Mexico, and The National Oncology Institute in Panama, aged <70 years; 100% histologically confirmed	1430 (1064 hospital, 366 community) randomly selected from the hospital patients in Bogota and Mexico City and both from referral hospitals and community in Costa Rica and Panama; matched by age (5-year range); women with history of hysterectomy or cancer, endocrine, nutritional, psychiatric, gynaecological, smoking-related diseases excluded	Interview	<i>Cervix uteri</i>	<i>Ethanol (g/week)</i> Non-drinker Occasional ≤48.6 >48.6	<i>Risk ratios</i> 1.0 (reference) 2.1 1.6 1.1	Smoking, number of sexual partners, other covariates	Study of smoking and cervical cancer where alcohol drinking was a confounder

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Licciardone <i>et al.</i> (1989), Missouri, USA, 1984–86	331 white women identified by Missouri Cancer Registry between July 1984 and June 1986 (invasive cervical cancer)	993 white women randomly selected from Missouri Cancer Registry, reported at the same time (1984–86) for malignancies unrelated to smoking or alcohol; frequency matched to cases by age	Hospital records	<i>Cervix uteri</i> (ICD180)	<i>Alcohol consumption</i> Never drank Former drinker Light drinker (<2 drinks/day) Heavy drinker (≥2 drinks/day) Drinker (quantity unknown) Unknown	<i>Odds ratio</i> 1.00 (reference) 0.7 (0.2–2.9) 0.8 (0.5–1.2) 0.8 (0.4–1.6) 1.0 (0.5–1.8) 1.0 (0.6–1.7)	Age, smoking, alcohol consumption, stage at diagnosis	
Parkin <i>et al.</i> (1994), Bulawayo, Zimbabwe, 1963–77	1263 data records from cancer registry of Bulawayo (covering provinces Matabeleland North and South, Masvingo and Midlands); 86% squamous-cell carcinoma, 3.4% adenocarcinoma	2347 women with cancer at sites other than breast, <i>corpus uteri</i> , uterus unspecified	Standard questionnaire; interview of cases or relatives	<i>Cervix uteri</i>	<i>Alcohol intake</i> Never Occasional Frequent	1.0 (reference) 1.4 (1.1–1.8) <i>p</i> <0.05 1.6 (1.3–1.9) <i>p</i> <0.001 <i>p</i> trend<0.001	Age group, time period, province, education, age at first intercourse, number of full-term pregnancies	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Thomas <i>et al.</i> (2001a), Bangkok, Thailand, 1991–93	232 women admitted to public wards of Sirairaj Hospital, Bangkok, with diagnosis of cervical carcinoma between 1 September 1991 and 1 September 1993; born in 1930 or later and who lived in Thailand at least the past year; 100% histologically confirmed; squamous (190) and adenomatous (42) carcinoma; gave DNA specimen for study	Collected from the same hospital, up to 24 h after the case had been admitted; matched by age (5-year range); resident of the same region of the country as case; exclusion: women who were treated for diseases associated with use of steroid contraceptives	All cases and controls were interviewed at hospital; women gave a blood specimen	<i>Cervix uteri</i>	<i>Ever drank alcoholic beverages</i> No Yes	Odds ratio <i>HPV</i> <i>16-positive</i> 1.0 (ref) 1.1 (0.7–1.6) <i>HPV</i> <i>18-positive</i> 1.0 (ref) 1.5 (0.8–2.9)	Age	Study of risk factors for invasive cervical carcinoma with HPV types 16 and 18; controls in this analysis were women HPV-positive for types 16 and 18, respectively.

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Thomas <i>et al.</i> (2001b), Bangkok, Thailand, 1991–93	190 women with invasive cervical cancer compared with 65 women with in-situ disease, admitted to public wards of Sirairaj Hospital in Bangkok between 1 September 1991–1 September 1993; born in 1930 or later and lived in Thailand at least the past year; 100% histologically confirmed	291 for invasive cancers and 124 for <i>in situ</i> ; collected from the same hospital, up to 24 h after the case had been admitted; matched by age (5-year range), resident of the same region of the country as case; exclusion: women who were treated for diseases associated with use of steroid contraceptives	All cases and controls were interviewed at hospital	<i>Cervix uteri</i>	<i>Ever drank alcoholic beverages</i> No Yes	Odds ratio <i>Invasive</i> 1.0 (reference) 1.0 (0.7–1.5)	Age, HPV type or other/unknown HPV type, or no HPV infection	Control group presented: women without in-situ lesions

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Chiaffarino <i>et al.</i> (2002), northern Italy, 1981–93	791 women admitted to university and general hospitals, aged 17–79 years; diagnosis of incident invasive cervical cancer; exclusion: alcoholic women; 100% histologically confirmed; participation rate, >95%	916 women admitted to the same hospitals for acute conditions; exclusion: alcoholic women; participation rate, >95%	Structurized questionnaire; interview	Cervix uteri	<i>Total alcohol</i> Non-drinker Drinker Occasional Regular	1.00 (reference) 1.23 (0.99–1.53) 1.21 (0.88–1.65) 1.24 (0.98–1.56) χ^2 trend=3.24 $p=0.072$	Age, year of interview, education, cervical screening history, smoking habit, menopausal status, number of partners, parity, oral contraceptive use, hormone replacement therapy use	Data from two case–control studies of Parazzini <i>et al.</i> (1992, 1997); residual confounding could not be excluded for modest association.
Newton <i>et al.</i> (2007), Kampala, Uganda, 1994–1998	343 HIV-seronegative women, 15 years old and older, with a provisional diagnosis of cervical cancer from all wards and outpatient clinics of the four main hospitals in Kampala, Uganda	359 controls diagnosed with other cancer at sites or type (except for cancer of the breast, ovary or the female genital tract) and benign tumours derived from wards and outpatients clinics of the main hospitals in Kampala, Uganda	Interview by trained counsellors; questions about social and demographic factors, sexual and reproductive history	<i>Cervix uteri</i>	<i>Alcohol consumption</i> Never Once/week 2–4/week Most days χ^2 trend=0.2 $p=0.7$	1.0 (reference) 1.6 (1.1–2.5) 1.6 (0.9–2.7) 0.4 (0.2–0.9)	Age group	

CI, confidence interval; HIV, human immunodeficiency virus; HPV, human papillomavirus; ICD, International Classification of Diseases

that included both hospital and population controls. Seven studies did not show any or any significant relative risk among alcoholic beverage drinkers (Harris *et al.*, 1980; Marshall *et al.*, 1983; Cusimano *et al.*, 1989b; Licciardone *et al.*, 1989; Thomas *et al.*, 2001a; Chiaffarino *et al.*, 2002). Significantly elevated relative risks emerged from two case–control studies from Africa, in which adjustment for confounding was incomplete (Martin & Hill, 1984; Parkin *et al.*, 1994). In the study from Latin America, in which adjustment for possible confounders was adequate, there was an elevated risk for cervical cancer among occasional drinkers (confidence intervals not given) but no association with heavy drinking (Herrero *et al.*, 1989). No consistent results with a higher risk among moderate drinkers were found in a study from Uganda (Newton *et al.*, 2007).

2.14.3 *Evidence of a dose–response*

The cohort studies did not present convincing evidence of a dose–response between risk for cervical cancer and duration of alcoholic beverage consumption, which was roughly estimated as years since cohort enrolment (first hospitalization/clinical treatment for alcoholism).

Two case–control studies from the USA and Latin America (Herrero *et al.*, 1989; Licciardone *et al.*, 1989), in which at least smoking habits and number of sexual partners were adjusted for, showed no dose–response effect. In four other case–control studies in which there was some indication of a possible dose–response association (Harris *et al.*, 1980; Marshall *et al.*, 1983; Martin & Hill, 1984; Parkin *et al.*, 1994), the adjustment for possible confounders was incomplete. In one study, such a trend was observed only among consumers of wine and other alcoholic beverages combined (Chiaffarino *et al.*, 2002).

2.14.4 *Types of alcoholic beverage*

The cohort studies did not investigate the effect of specific types of alcoholic beverages (beer, wine, spirits) on risk for cervical cancer.

Almost all case–control studies that tried to evaluate specific types of alcoholic beverage (Marshall *et al.*, 1983; Martin & Hill, 1984; Chiaffarino *et al.*, 2002) did not find consistent differences in risk for cervical cancer. Only Williams and Horm (1977) found an elevated risk for cancer of the cervix among beer drinkers.

2.14.5 *Interactions*

None of the cohort or case–control studies presented information on possible interactions between alcoholic beverage intake and other variables in the causation of cervical cancer. Information for histological subtypes was not given.

2.15 Cancer of the prostate

2.15.1 Cohort studies

(a) Special populations (Table 2.75)

Only one of the eight studies of special populations showed an association between alcoholic beverage consumption and cancer of the prostate. In a Danish study of alcohol abusers, higher numbers of prostate cancers were observed compared with those expected from the general population (Tønnesen *et al.*, 1994).

(b) General population (Table 2.76)

Studies of prostate cancer that were conducted more recently generated concern when no attempt was made to distinguish between cases that were detected by screening, with a possibility that many might not have presented clinically during the lifetime of the individual in the absence of screening, and those that presented clinically and were more likely to be progressive. Among the 17 cohort studies, two specifically identified more advanced cases (Platz *et al.*, 2004; Baglietto *et al.*, 2006) but neither suggested any association between alcoholic beverage consumption and such cases of prostate cancer. A few of the other cohort studies that did not make this distinction suggested an increased risk for prostate cancer at elevated levels of alcoholic beverage consumption (Hirayama, 1992; Schuurman *et al.*, 1999; Putnam *et al.*, 2000; Sesso *et al.*, 2001), but there was no consistent dose–response relationship and many other cohort studies showed no association.

2.15.2 Case–control studies (Table 2.77)

Five of the 33 case–control studies considered type of disease. Slattery and West (1993) considered ‘aggressive’ tumours, Hodge *et al.* (2004) studied ‘clinically important’ disease, Hayes *et al.* (1996) conducted stratified analyses by tumour grade and stage, Chang *et al.* (2005) considered localized and advanced disease and Schoonen *et al.* (2005) classified cases as less and more aggressive cancers. The remainder did not appear to make any distinction, although, in the study of Walker *et al.* (1992), 90% of the cases were advanced at presentation. The majority of the studies showed no association between alcoholic beverage consumption and prostate cancer. Of those that suggested a positive association, one (De Stefani *et al.*, 1995) showed a borderline elevation of risk for high levels of consumption of beer, but the risk at high levels of total alcoholic beverage consumption was not significant; one (Hayes *et al.*, 1996) showed significant elevations in risk for ‘heavy’ and ‘very heavy’ consumers of alcoholic beverages, with higher risks among those with poorly or undifferentiated tumours, or with regional or distant metastases; and another (Sharpe & Siemiatycki, 2001) reported an elevation in risk for those with long duration of drinking, and the greatest elevation in risk for those who started drinking at age <15 years.

Table 2.75 Cohort studies of alcoholic beverage consumption and cancer of the prostate^a in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sundby (1967), Oslo, Norway	1722 men treated for alcoholism in 1925–39; follow-up to 1963; 29 lost to follow-up, 1061 died before the end of study; 632 alive at the end of study	Not reported	Not reported	16	Not reported	Not reported	Expected number based on Oslo urban mortality data
Hakulinen <i>et al.</i> (1974), Finland	Male ‘chronic alcoholics’, >30 years of age, registered in 1967–70 when under custody of alcohol-misuse supervision, or when sent to a labour institute because of the vagrant law; mean annual number in registry=4370	Alcohol misusers registry; Finnish Cancer Registry; Social Welfare Board of Helsinki	Not reported	1	Not reported	Not reported	Two categories of drinkers examined: alcohol misusers and chronic alcoholics; quantity of drinking not reported

Table 2.75 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Adelstein & White (1976), England and Wales, 1953–64, UK Alcoholics Study	629 men discharged from four mental hospitals in 1953–57; 966 men diagnosed with alcoholism and admitted to hospital in 1964; of the total of 1595, 605 had died by July 1974	Patient discharge	Deaths from prostate cancer	3	Not reported	Not reported	
Jensen (1979), Denmark, Danish Brewery Workers	14 313 male Union members employed >6 months in a brewery in 1939–63; follow-up, 1943–73	Not reported	Brewery workers were allowed 2.1 L of free beer/day (77.7 g pure alcohol/day)	80	SIR 1.0 (0.8–1.2)	Age, sex, area, time trends	Cancer morbidity and mortality compared with those in the general population

Table 2.75 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schmidt & Popham (1981), Ontario, Canada	9889 men admitted to clinical service for alcoholics in 1951–70; 7719 still alive after 1971	Not reported	Average daily intake of a sample from this group: 25.4 cL pure alcohol	11	SMR 1.09 (NS) CI not reported	Not reported	SMR based on age-standardized death rates in Ontario population; compared with US Veterans, SMR for prostate cancer was 1.24 (NS); 96% of a representative sample of the clinical population drank >15 cL per day; ICD-7 177
Carstensen <i>et al.</i> (1990), Sweden, Swedish brewery workers	6230 men employed in the brewery industry in 1960; follow-up by linkage to Swedish Cancer Registry, 1961–79		Workers receive 3 bottles of beer/day (1 L) free	112	1.06 (0.87–1.27)	Not reported	No information available on when a worker ceased working in the industry; ICD-7 177

Table 2.75 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Adami <i>et al.</i> (1992a), Sweden, Cohort of people with a discharge diagnosis of alcoholism	9353 individuals (8340 men) with a discharge diagnosis of alcoholism in 1965–83; mean age at entry, 49.8 years; at diagnosis, 68.1 years; follow-up through to 1984 (maximum, 19 years; mean, 7.7 years); first year of follow-up excluded	Registry based	No data on individual alcohol or tobacco use	68	SIR 1.0 (0.8–1.3)		Risk did not vary by length of follow-up
Tønnesen <i>et al.</i> (1994), Denmark, Alcoholic men and women	15 214 male alcoholics who entered an outpatient clinic in Copenhagen during 1954–87; average follow-up, 12.9 years	History of alcohol intake obtained by an experienced social worker and psychiatrist	Most subjects consumed about 200 g alcohol daily; consumption in Denmark was 26 g/day in 1987 (per person >14 years)	91	1.4 (1.2–1.8) $p \leq 0.01$	Not reported	Subjects consumed more alcohol than previous cohort studies examining alcohol intake and prostate cancer; lack of consistency with previous studies may be due to higher intake.

CI, confidence interval; ICD, International Classification of Diseases; NS, not significant; Obs, observed; SIR, standardized incidence ratio; SMR, standardized mortality ratio

^a Unless otherwise noted in the 'Comments', the ICD code for prostate cancer is 185

Table 2.76 Cohort studies of alcoholic beverage consumption and cancer of the prostate^a in general populations

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Whittemore <i>et al.</i> (1985), USA, Harvard and University of Pennsylvania Alumni Study	33 915 male students who entered Harvard in 1916–50 and 13 356 male and 4076 female students examined at the University of Pennsylvania in 1931–40; followed for cancer mortality through to July 1978	College physical examination, questionnaires	Not reported	243	Not reported	Not reported	Data on collegiate alcohol consumption limited; prostate cancer not associated with collegiate alcohol use; ICD-7 177

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Mills <i>et al.</i> (1989), USA, Seventh-day Adventists study	60 000 Seventh-day Adventists in California identified by census questionnaire in 1974, aged >25 years; cancer incidence monitored among 35 000 non-Hispanic white Adventists for up to 6 years; response rate among non-Hispanic whites, 75% (much lower for others)	Lifestyle questionnaire in 1976; annual mailings enquiring about hospitalization, medical records, diagnosis; follow-up 99% complete	<i>Alcohol intake (any)</i> No Yes	142 5	1.0 0.7 (0.3–1.74)	Age	

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Stemmermann <i>et al.</i> (1990), Hawaii, USA, Americans of Japanese Ancestry	7572 Japanese men on Oahu island; examination and interview 1965–68; follow-up through to 1988	Questionnaire on diet, alcohol and tobacco use, socioeconomic factors, demographic variables	<i>Alcohol intake (oz/month)</i> 0 <5 5–14 15–39 >40	227 total cases; no. of cases by level of intake not reported	SIR 1.0 0.9 (0.6–1.3) 0.9 (0.6–1.3) 1.0 (0.7–1.5) 0.9 (0.6–1.5)	Age at exam 1, current smoker status, age started smoking (current smokers), number of cigarettes smoked per day (current smokers), ex-smoker status, maximum number of cigarettes smoked per day (ex-smokers), years of smoking with maximum number per day (ex-smokers)	Mean alcohol intake fell from 14.6 to 11.6 oz/month for age groups 45–49 years to >65 years, respectively; incidence rates, adjusted for age and smoking, showed no relation with the amount of alcohol consumed; update of Pollack <i>et al</i> (1984) and Severson <i>et al</i> (1989).

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Hsing <i>et al.</i> (1990), USA, Lutheran Brotherhood Cohort Study	17 633 male white policy holders, aged ≥ 35 years, of the Lutheran Brotherhood Insurance Society	Response to a questionnaire (mailed) in 1966; followed-up until 1986	<i>Beer</i>	149 total deaths;	1.7 (1.0–2.9)	Smoking	Users defined as those who drank beer or liquor ≥ 6 times a year; information on dietary habits and alcohol/tobacco use was only obtained once, in 1966.
			Former drinker	no. of	1.2 (0.8–1.7)		
			Current drinker	cases/deaths by drinking level not reported	0.7 (0.3–1.5)		
			<i>Liquor</i>		1.0 (0.7–1.4)		
Hirayama (1992), Japan	265 118 adults (122 261 men), aged ≥ 40 years, representing 94.8% of the 1965 census population	Interview (1965) on diet, tobacco/ alcohol use, occupation and reproductive history; 17-year follow-up (1966–82)	Non-daily drinker/ nonsmoker	Not reported	1.0	Age, smoking	Update of Hirayama (1989)
			Daily drinker/ nonsmoker		2.65		
			Non-daily drinker/smoker		1.07		
			Daily drinker/ daily smoker		2.46		
			[no details reported]		CI not reported		

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Hiatt <i>et al.</i> (1994), California, USA, Health Plan Cohort	43 432 members of a prepaid health plan; received a health check-up in 1979–85	Questionnaire: current and past consumption of alcohol, number of drinks/day, type of beverage	Non-drinker	25	1.0	Age, smoking, race, education	No significant association between alcohol consumption and prostate cancer
			Former drinker	17	1.4 (0.7–2.7)		
			Occasional drinker	37	1.4 (0.8–2.3)		
			<1 drink/day	73	1.3 (0.8–2.2)		
			1–2 drinks/day	59	1.2 (0.7–2.1)		
			3–5 drinks/day	22	1.1 (0.6–2.0)		
>6 drinks/day	5	1.0 (0.4–2.8)					
Le Marchand <i>et al.</i> (1994), Hawaii, USA	Random 2% household surveys of the Hawaiian State Department of Health held since 1968 to collect demographic and health-related data; linked with Hawaiian Tumour Registry; final population, 41 400 persons (20 316 men); participation rate, 95%	Lifestyle questionnaire added to the survey during 1975–80 and addressed to all aged >18 years on height, weight, diet, alcohol use, smoking	<i>Alcohol intake (g/week)</i>	198 cases of invasive prostate cancer recorded through to 1989, all >45 years old at interview; no. of cases by alcohol intake not reported	1.0	Age, ethnicity, income	Data recorded on current drinking status, age when drinking started, amount and frequency of intake of beer, wine, saké, and hard liquor.
			0–52	53–104	104–156		
			<i>Lifetime intake (g)</i>				
			0–1750		1.0		
			1751–3500		1.0 (0.6–1.5)		
			3501–5261		1.1 (0.7–1.7)		
					<i>p</i> -trend=0.72		

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Cerhan <i>et al.</i> (1997), USA, 1982–93, Iowa 65+ Rural Health Study	3673 residents (1420 men), aged >65 years, from two rural counties in Iowa; 80% of the population (>65 years) were enrolled in 1982; data on prostate cancer obtained from 1050 men (mean age, 73.5 years) without registered cancer during 1972–82 and with no self-reported prior prostate cancer; cancer data obtained by linking with the Iowa State Health Registry	Interview on demographics, health and social characteristics, current alcohol use (beer, wine, liquor); annual follow-up by telephone or in-person interview	<i>Alcohol consumption</i>			Age	Number of prostate cancer cases through to 1993: 71 (histologically confirmed); mean age at diagnosis, 79.2 years
			Never	22	1.0		
			Former	6	0.6 (0.3–1.6)		
			Current	39	1.0 (0.6–1.8)		

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Breslow <i>et al.</i> (1999), USA, NHANES I Epidemiological Follow-up Study	<i>Cohort I</i> (1971–75): 5766 men, aged 25–74 years; followed-up through to 1992; median follow-up, 17 years	Baseline (1972–74): questionnaire to assess ‘usual consumption’ (over the previous year); follow-up (1982–84): food-frequency questionnaire to assess current and ‘distant past’ alcohol intake at 25, 35, 45 and 55 years of age	<i>Alcohol intake (drinks/week)</i> >0–1 2–7 8–14 15–21 >22	96	<i>Cohort I</i> 1.0 1.0 (0.7–1.4) 0.9 (0.6–1.2) 1.0 (0.6–1.5) 0.9 (1.4–1.8) 1.4 (0.8–2.4)	Race, design variables (age <65 versus ≥65 years, poverty census enumeration district, family income)	No association between alcohol consumption and prostate found; ICD 185, 233.4.
				41			
				65			
				25			
				8			
	<i>Cohort II</i> (1982–84): 3868 men from Cohort I free of prostate cancer in 1982–84; followed-up through to 1992; median follow-up, 9 years; response rate in 1982–84 interview, 88%	food-frequency questionnaire to assess current and ‘distant past’ alcohol intake at 25, 35, 45 and 55 years of age	>0–1 2–7 8–14 15–21 >22	59	<i>Cohort II</i> 1.0 0.7 (0.4–1.3) 1.1 (0.7–1.8) 1.1 (0.6–1.9) 1.1 (0.6–2.3) 0.2 (0.06–0.95)		
				19			
				29			
				16			
				9			
2							

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments		
Schuurman <i>et al.</i> (1999), Netherlands, Netherlands Cohort Study	58 279 men in 1986 followed up for prostate cancer incidence by computerized record linkage with all nine Dutch cancer registries and with the Dutch national database of pathology reports; follow-up, $\geq 96\%$ complete; person-years at risk estimated using a random sample (subcohort) of 1688 men	Questionnaire completed in 1986 to assess consumption of food and drinks during the year prior to the start of the study	<i>Total alcohol (g)</i>				Age; multivariate-adjusted relative risks (age, socioeconomic status, family history of prostate cancer, total alcohol intake) not substantially different	Consumption of beer, red wine, white wine, sherry and other fortified wines, liquor (Dutch gin, brandy, whiskey) and liqueurs evaluated; alcohol content (in g/100 g): beer, 4; wine, 10; fortified wines, 14; liqueurs, 17; liquor, 29; relative risks for alcohol from beer, liquor, red wine and liqueur not different from unity; alcohol intake showed stronger association with localized than with advanced prostate tumours	
			Non-drinkers	109	1.0				
			0.1–4	143	1.1 (0.8–1.5)				
			5–14	161	0.9 (0.7–1.3)				
			15–29	161	1.1 (0.8–1.4)				
			≥ 30	101	1.1 (0.8–1.6)				
			<i>Alcohol from wine (g)</i>						<i>p</i> -trend=0.74
			No wine	219	1.1 (0.8–1.5)				
			0.1–4	198	1.1 (0.8–1.4)				
			5–14	90	0.9 (0.6–1.4)				
			15–29	39	1.1 (0.7–1.8)				
			≥ 30	20	2.3 (1.0–5.3)				
			<i>White wine (g)</i>						<i>p</i> -trend=0.67
			0	359	1.1 (0.8–1.4)				
			0.1–4	180	1.0 (0.7–1.4)				
5–14	19	1.2 (0.6–2.2)							
≥ 15	8	3.3 (1.2–9.2)							
<i>Fortified wines (g)</i>				<i>p</i> -trend=0.54					
0	408	1.1 (0.8–1.5)							
0.1–4	108	0.9 (0.6–1.3)							
5–14	26	0.7 (0.4–1.1)							
≥ 15 –29	24	2.3 (1.2–4.7)							
				<i>p</i> -trend=0.77					

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Dennis (2000) Meta-analysis	Meta-analysis of six cohort studies of the association between prostate cancer and men	Articles published between January 1976 and July 1978	Ever versus never		1.0 (0.89–1.13)		
Ellison (2000), Canada, Nutrition Canada Survey Cohort	Population survey (1970–72) among 12 795 respondents (47%) and 3295 unsolicited volunteers, aged 50–84 years at interview or entering this age range during the follow-up period through to 1993; data from 3400 men used	Interviews on diet, 24-h food recall and 1-month food frequency	<i>Total intake (mL/day)</i> 0 >0–9.9 10.0–24.9 ≥25 Any	38 54 22 25 101	1.0 1.0 (0.6–1.5) 0.9 (0.5–1.5) 0.9 (0.6–1.6) 0.9 (0.6–1.4)	Tea and coffee consumption, serum level of vitamin A, 5-year age group	Alcohol content: beer, 5%; wine, 13.5%; spirits, 40%; consumption of wine (<10 g alcohol per day) versus none: relative risk, 1.5 (95% CI, 1.1–2.1) [no details given]

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Putnam <i>et al.</i> (2000), USA, 1986–95, Iowa Cohort	1601 (81%) men of 1989 from controls in a population-based case-control study of six cancer sites conducted 1986–89 in Iowa; data reported for 1572 men (mean age, 68.1 years; 99% white; 24% smokers; 57% drinkers); follow-up through to 1995.	Questionnaire (mailed) and interview by telephone on demographics, education, usual occupation, weight, height, family history of cancer, usual adult diet (55-item food list), usual intake of beer, wine, spirits, use of tobacco	<i>Any alcohol</i>				
			No		1.0	Age (40–64, 65–69, 70–74, 75–79, >80 years)	
			Yes		1.7 (1.1–2.6)		
			<i>Wine (8-oz glasses/week)</i>				
			None	30	1.0		
			<0.2	6	1.2 (0.5–3.0)		
			0.2–0.9	54	1.5 (0.9–2.4)		
			>0.9	11	1.9 (0.9–3.7)		
					<i>Liquor (1-oz shots/week)</i>		
			None	30	1.0		
<0.5	12	1.6 (0.8–3.2)					
0.5–2.5	41	1.5 (0.9–2.4)					
>2.5	18	1.7 (0.9–3.0)					
					<i>p</i> -trend=0.02		
							<i>p</i> -trend=0.05

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments		
Putnam <i>et al.</i> (2000) (contd)			<i>Beer (12-oz cans/week)</i>				Additional adjustment for body mass index, total energy, linoleic acid, lycopene, carbohydrates, retinal, red meat, history of prostate cancer		
			None	30	1.0				
			<1	22	2.4 (1.4–4.3)				
			1–3	15	1.3 (0.7–2.5)				
			>3	19	1.7 (0.9–3.0)				
						<i>Total alcohol intake (g/week)</i>			
			None	30	1.0				
			<22	17	1.1 (0.6–2.1)				
			22–92	27	2.6 (1.4–4.6)				
			>92	18	3.1 (1.5–6.3)				
					<i>p</i> -trend=0.001				

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lund Nilssen <i>et al.</i> (2000), Norway, 1984–95, Norwegian Cohort Study	77 310 residents (≥ 20 years of age by 31/12/1983) of the Norwegian county Nord-Trøndelag invited to participate in a health survey: in 1984–861 among these, 22 895 men (≥ 40 years) with no history of any cancer included; incident cases of prostate cancer identified through linkage with the Norwegian Cancer Registry; response rate, 90.8%	Questionnaire on tobacco and alcohol use, physical activity education level, occupation	<i>Alcohol consumption the past 2 weeks</i>			Age	
			None (not teetotaler)	281	1.0		
			1–4 times	148	1.2 (0.94–1.41)		
			>4 times	40	0.9 (0.64–1.25) <i>p</i> -trend=0.862		
			<i>Teetotaler</i>				
No	469	1.0					
Yes	80	1.22 (0.96–1.55)					

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Sesso <i>et al.</i> (2001), USA, Harvard Alumni Health Study	7612 male Harvard alumni (mean age, 66.6 years) followed prospectively during 1988–93	Questionnaire in 1988 on alcohol use, smoking, use of 23 food items, parental cancer history, weight, height; response from 6686 alumni to a questionnaire sent in 1977 also available	Servings		Multivariate-adjusted	Age, body-mass index, smoking (never/former/current), physical activity, parental history of cancer	Mean total alcohol intake, 123.1 (SD, 136.3) g/week; 28.6% from wine, 15.8% from beer and 55.6% from liquor (e.g. whiskey); significant increase in relative risk not seen for beer or wine; men who reduced alcohol intake in the period 1977–88 still at elevated risk compared with the ‘almost never’ group.	
			<i>Total alcohol</i>	Almost never	38			1.0
			1/month–3/week	54	1.3 (0.9–2.0)			
			3/week–1/day	76	1.7 (1.1–2.4)			
			1–3/day	151	1.9 (1.3–2.6)			
			≥3/day	47	1.3 (0.9–2.1)			
								<i>p</i> -trend=0.35
			<i>Liquor</i>	Almost never	93			1.0
1/month–3/week	82	1.2 (0.9–1.6)						
3/week–1/day	68	1.7 (1.2–2.3)						
1–3/day	108	1.6 (1.2–2.1)						
≥3/day	15	1.1 (0.6–1.9)						
			<i>p</i> -trend=0.10					

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Albertsen & Grønbaek (2002), Copenhagen, Denmark, three pooled studies	26 496 men, aged 20–98 years; data from 12 989 men used in the study (1976–94); follow-up time, 4.5–22.9 years (average, 12.3 years); mean participation rate, 80%	Multiple-choice questions on intake of wine, beer, spirits, tobacco, age, education, physical activity, body mass index	Drinks/week				Age, education, physical activity body mass index, smoking status, study of origin	Standard drink of wine, beer and spirits in Denmark considered to contain 12 g alcohol; ICD-7 177, ICD-10 DC619
			<i>Total intake</i>	<1	42	1.0		
			1–6	59	0.9 (0.6–1.3)			
			7–13	54	0.9 (0.6–1.3)			
			14–20	36	0.9 (0.6–1.4)			
			21–41	35	0.9 (0.6–1.5)			
			>41	7	0.7 (0.3–1.5)			
			<i>Beer</i>			<i>p</i> -trend=0.48		
			0	53	1.0			
			1–13	141	1.0 (0.7–1.5)			
			>13	39	1.0 (0.6–1.5)			
						<i>p</i> -trend=0.85		
			<i>Wine</i>					
			0	106	1.0			
			1–13	120	1.2 (0.9–1.6)			
>13	7	0.9 (0.4–2.0)						
			<i>p</i> -trend=0.96					
<i>Spirits</i>								
0	101	1.0						
1–13	122	1.0 (0.7–1.3)						
>13	10	1.0 (0.5–2.0)						
			<i>p</i> -trend=0.90					

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Platz <i>et al.</i> (2004), USA, 1986–98, Health Professionals Follow-up Study	51 529 men, aged 40–75 years at enrolment in 1986; excluded: men diagnosed with cancer (except non-melanoma skin cancer) or returned incomplete questionnaire in 1986 (3.1%); 47 843 men, of whom 76.4% in 1986 reported drinking alcohol (2.9% consumed > 50 g/day); verification of cases via medical records and pathology reports; overall follow-up response, 94% at the end of 1998	Questionnaire, mailed and returned every 2 years, on diet, medical history, lifestyle factors; updated via the questionnaires mailed and returned in 1990 and 1994; deaths recorded via the National Death Index	<i>Intake (g/day)</i>		Hazard ratios	Current age, body mass index at 21 years, height, smoking (pack-years in past decade), family history of prostate cancer, major ancestry, vasectomy, high physical activity, diabetes, intake of: total energy, calcium, tomato sauce, fructose, red meat, fish, vitamin E, α -linolenic acid	Consumption over past year of beer, red wine, white wine and liquor (assumed to contain, resp., 12.8, 11.0, 11.0 and 14 g alcohol per serving); analysis of drinking pattern: for men who took ≥ 105 g alcohol on only 1 or 2 days of the week, hazard ratio was 1.64 (95% CI, 1.13–2.38); this group represented 1% of the cases in the cohort; advanced cases were Stage C or D or fatal.
			0	576	<i>All cases</i>		
			0.1–4.9	537	1.0		
			5.0–14.9	694	1.0 (0.9–1.1)		
			15.0–29.9	336	1.1 (0.9–1.2)		
			30.0–49.9	266	1.1 (1.0–1.3)		
			≥ 50	70	1.1 (1.0–1.3)		
					1.0 (0.7–1.3)		
					<i>p</i> -trend=0.20		
					<i>Advanced cases</i>		
0	154	1.0					
0.1–4.9	118	0.8 (0.7–1.1)					
5.0–14.9	175	1.0 (0.8–1.3)					
15.0–29.9	80	1.0 (0.8–1.4)					
30.0–49.9	81	1.0 (0.7–1.3)					
		<i>p</i> -trend=0.70					

Table 2.76 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Baglietto <i>et al.</i> (2006), Australia, Melbourne Collaborative Cohort Study	528 people (17 049 men), aged 27–75 years, recruited 1990–94 in the Melbourne metropolitan area via electoral rolls, advertisements and community announcements; data from 16 872 men, aged 27–70 years, used; follow-up through to 31 December 2003	Interview to collect data on age, country of birth, education, tobacco use, drinking habits, medical history; cases ascertained through the Victoria Cancer Registry	Lifetime abstainer	Not reported	Hazard ratios <i>All cases</i> 1.0	Co-variate: country of birth; adjustments for education, body mass index, smoking, total energy intake or medical history did not change risk ratios.	Lifetime abstainers never drank ≥ 12 drinks/year; former drinkers did not drink alcohol at start of study; no difference in risk according to the type of alcohol consumed; ‘aggressive’ cancers defined as Gleason score >7 or advanced stage (T4 or N+ or M+)
			Former drinker 1–19 g alcohol/day		1.2 (0.8–1.6)		
			20–39 g alcohol/day		1.0 (0.8–1.2)		
			40–59 g alcohol/day		1.0 (0.7–1.3)		
			≥ 60 g alcohol/day		0.9 (0.7–1.3) <i>p</i> -trend=0.62		
			Lifetime abstainer	Not reported	<i>Aggressive cases</i> 1.0		
			Former drinker 1–19 g alcohol/day		0.7 (0.3–1.7)		
			20–39 g alcohol/day		0.7 (0.4–1.1)		
40–59 g alcohol/day		0.7 (0.4–1.2)					
≥ 60 g alcohol/day		0.7 (0.3–1.3)					
					0.8 (0.4–1.5) <i>p</i> -trend=0.58		

CI, confidence interval; ICD, International Classification of Diseases; NHANES, National Health and Nutrition Examination Survey; SD, standard deviation; SIR, standardized incidence ratio ^a Unless otherwise noted in the comments, the ICD code for prostate cancer is 185

Table 2.77 Case-control studies of alcoholic beverage consumption and cancer of the prostate^a

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schwartz <i>et al.</i> (1962), France, 1954–58	139 patients	139 age-matched non-cancer patients (accident victims)	Subjects interviewed in the hospital about alcohol drinking	Prostate cancer cases, average consumption of 11.0 cL pure alcohol per day; controls, same average daily alcohol intake	139	NR		Consumption according to age varied from 9.6 to 14.0 cL pure alcohol/day; ICD 177
Wynder <i>et al.</i> (1971), New York, USA, 1965–67	217 patients (167 alcohol drinkers)	200 patients (163 drinkers)	Epidemiological questionnaire	<i>Alcohol consumed (units per day)</i> 1–2 3–6 >7 Binge	106 36 22 3	NR		Unit/day = 1 oz spirits, 4 oz wine, 8 oz beer; a second study included 83 prostate cancer patients and 200 control patients
Williams & Horm (1977), USA, Third National Cancer Survey, 1969–71	465 patients	1323 patients with other cancers, not tobacco-related	Interview to collect data on the amount and the duration of alcohol and tobacco use	<50 oz-years >50 oz-years	62 127	Odds ratio 0.78 0.87	Age, race, smoking	Alcohol use expressed as ‘oz-years’ (units/week × years drinking)

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schuman <i>et al.</i> (1977), USA, Study period not reported	200 white patients from major hospitals in the Minneapolis-St Paul area	Patients in same hospital with non-genitourinary conditions; matched by age, race, date of admission; age- and race-matched neighbourhood controls (same street of residence)	Personal interview on history of residence, jobs, medication, hospitalization, smoking/drinking habits, drugs, marital history	<i>Alcohol use</i> Yes No	39 1	NR		Preliminary report
Nijjima & Koiso (1980), Japan, 1963–78	187 patients diagnosed and treated at the Department of Urology, University of Tokyo; mean age, 68.7 years	200 patients without known prostatic disease: 106 cancers of the kidney, ureter, bladder or other organs; 94 diseases other than cancer	Not specified	About 56% of patients and 55% of controls were alcohol drinkers		NR	NR	NR
Jackson <i>et al.</i> (1981), USA, 1973–78	231 black patients with prostate carcinoma at Howard University and DC General Hospitals; data from 205 patients used; 100% histologically confirmed	205 age-matched patients free of neoplastic, urological and endocrine conditions	Interview using a pre-tested epidemiological questionnaire			NR	NR	A higher proportion of controls than of patients had a history of heavy alcohol use (beer, wine or liquor) in the 10 years before diagnosis [no data].

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Mishina <i>et al.</i> (1981), USA	100 prostatic cancer patients	100 matched for age (± 1 year) and residence in the same prefecture	Questionnaire and interview on education, job history, income, religion, diet, marriage, sexual activity, physical condition	Rare No alcohol	61 39	1.73 CI not reported		
Talamini <i>et al.</i> (1986), northern Italy, 1980–83	166 patients recently diagnosed at the General Hospital of Pordenone (Friuli Venezia-Giulia), aged 48–79 years (median age, 66 years); 100% histologically confirmed; refusal rate, <2%	202 patients in the General Hospital of Pordenone admitted for acute conditions (no malignant, hormonal or urogenital disease) <1 year before interview, aged 50–79 years (median age, 63 years); refusal rate, <2%	Interview with questionnaire on general lifestyle habits, socio-demographic aspects, height, weight, frequency of food intake	Not specified		NR	NR	Risk for prostate cancer not related to wine drinking [data not shown]

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Ross <i>et al.</i> (1987), USA, 1977–80	316 black residents of Los Angeles County with prostate cancer (diag-nosed between January 1977 and August 1980), aged 60–75 years; a total of 179 were interviewed, 19 refused to participate; 190 white incident prostate cancer patients of a Los Angeles area retirement community (diagnosed 1972 through 1982), aged, 65–79 years; 142 patients interviewed, 48 refused to participate	142 neighbourhood controls; age-matched (± 5 years) with cases 142 controls individually matched to cases on age (± 1 year), length of residence in the community (± 1 year)	Interview	Any alcohol use Any alcohol use	NR	<i>Blacks</i> 0.9 <i>Whites</i> 0.9	NR	No confidence intervals reported

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Yu <i>et al.</i> (1988), USA, 1969–84	1162 patients (14% blacks) in 20 hospitals across the USA, recently diagnosed and identified in the American Health Foundation registry; mean age, 62.9 years; verified through medical records and pathology reports	3124 patients (54% cancers, excluding cancers at ‘alcohol-related’ sites; 13% benign neoplasms, 33% non-neoplastic diseases; ~10% blacks) from the same hospitals; mean age, 62.2 years; 3:1 frequency-matched to cases by age at diagnosis (± 2 years), race, year of interview, hospital	Interviews at time of admission or diagnosis on race, education, marital status, years of education, height, weight, religion, occupation, smoking, alcohol use	<i>Intake</i>		<i>Whites</i>	Age at diagnosis	Consumption of alcohol expressed as whiskey equivalent, (beer amount/8) + (wine amount/4) + whiskey amount in oz/day
				0	436	1.0		
				1 oz/day	321	1.0 (0.6–1.7)		
				3 oz/day	211	1.2 (0.9–1.5)		
				0	74	1.0		
				1 oz/day	46	1.4 (0.8–2.3)		
3 oz/day	37	1.3 (0.7–2.3)						
Mettlin <i>et al.</i> (1989), Roswell Park Memorial Institute, USA, 1957–65	371 patients, 55–85 years of age (mean age, 68.3 years); 2.2% non-white; 100% histologically confirmed	371 patients (4.0% non-white) without diagnosis or history of cancer (12.1% benign prostatic hyperplasia), aged 55–85 years (mean age, 68.1 years)	Questionnaire with 45-item food-frequency check-list; weekly frequency of consumption of beer, wine or liquor			NR		No significant increase or reduction in risk was found for beer, wine or liquor [no details were reported].

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Fincham <i>et al.</i> (1990), Canada, 1981–83	382 identified via the Alberta Cancer Registry (April 1981–September 1983), aged ≥ 45 years	625 age group-matched to cases, chosen from the roster of the Alberta Health Care Insurance Plan	Interview with questionnaire on ethnicity, marital status, job history personal/family medical history, tobacco/alcohol use, puberty age, physical status; diet history over 2-month periods with 6-month interval	NR				Cases consumed somewhat more alcohol (mean, 127 oz/month) than controls (mean, 120 oz/month)
Walker <i>et al.</i> (1992), South Africa	166 black hospitalized patients (90% advanced-stage D), residents of Soweto; mean age, 69.2 years (range, 48–84 years); 100% histologically confirmed	166 black age-matched selected from immediate neighbours of patients; mean age, 69.6 years (range, 52–85 years)	Patients questioned as to their diet before they became ill	Non-drinker Occasional drinker Regular drinker	20 35 45	No data		Differences between patients and controls not significant
Nakata <i>et al.</i> (1993), Japan	294 patients	294 general population controls chosen from 13 areas in Gunma Prefecture; age-matched (± 2 years)	Questionnaire or interview	History of drinking: yes/no		<i>Odds ratio</i> 0.93 (0.62–1.39)	Age	Prostate cancer risk not statistically different between cases and controls

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Slattery & West (1993), Utah, USA, 1983–86	362 white men living in 4 counties in Utah, diagnosed between 1 January 1984 and 15 November 1985 with first-primary prostate cancer, aged 45–74 years; 100% histologically confirmed; completion rate, 77.4%	685 matched to cases by 5-year age group, selected by random-digit dialling (<65 years) or from Social Security records (≥65 years); completion rate, 76.9%	Quantitative food-frequency questionnaire to assess use of alcohol, coffee, tea	<i>Total alcohol</i>			Crude odds ratio values given; adjustment for dietary intake, body size, age within strata, demographic features did not change the results.	Data are shown for all prostate tumour types, and for cases/controls ≤67 years; results for 'aggressive tumours' or for subjects >67 years did not change the outcome.
				None	90	1.0		
				Any	89	1.2 (0.9–1.6)		
				<i>Beer</i>				
				None	114	1.0		
				Any	65	1.2 (0.9–1.7)		
van der Gulden <i>et al.</i> (1994), Netherlands 1988–90	345 prostate cancer cases from the Comprehensive Cancer Centre IKO diagnosed January 1988 until April 1990; mean age, 72 years; 100% histologically confirmed; response rate, 84%	1346 patients treated in the IKOregion for prostate hyperplasia, but without histological signs of malignancy; mean age, 69 years	Questionnaire (mailed) on smoking/drinking habits, work history, socio-economic status; response rate, 78%	<i>Alcohol use</i>			Age	Age at which drinking began or duration of drinking not related to risk for prostate cancer
				Never	21	1.0		
				<1 day/week	324	1.2 (0.7–2.0)		
				1–4 days/week	90	1.4 (0.8–2.3)		
				5–7 days/week	176	1.4 (0.8–2.5)		
				All drinkers	58	1.4 (0.8–2.2)		

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Tavani <i>et al.</i> (1994b), northern Italy, 1985–92	Histologically confirmed, incident prostate cancer cases ($n=281$; median age, 67 years; range 25–79 years) diagnosed during the year before interview, admitted to cancer institutes and major hospitals	Patients ($n=599$; median age, 63 years; range 27–79 years) admitted to the same network of hospitals as the cases for acute, non-neoplastic conditions	Interviews with questionnaire on age, education, height, weight, marital status, smoking and drinking habits, intake of several indicator foods	<i>Total alcohol intake (drinks/day)</i>			Age, study centre; estimates from multiple logistic regression with age, centre, education, marital status, body mass index and smoking status gave comparable results.	Average number of drinks/day (a drink defined as 150 mL wine, 330 mL beer, or 30 mL spirits, each with 12–15 g ethanol); separate analyses for wine (0, <5, ≥ 5 per day), beer (no/yes), spirits (no/yes) or duration of use (0, <40, ≥ 40 years) did not substantially change the results.
				0	22	1		
				<3	63	1.3 (0.7–2.4)		
				3–<5	55	1.9 (0.5–1.6)		
				5–<8	63	1.2 (0.6–2.3)		
				≥ 8	78	1.1 (0.6–2.1)		
				<i>Wine (drinks/day)</i>				
				0	26	1		
				<5	152	1.2 (0.7–2.0)		
				≥ 5	103	0.9 (0.5–1.7)		
				<i>Beer (drinks/day)</i>				
				No	197	1		
Yes	84	1.1 (0.8–1.6)						
<i>Spirits (drinks/day)</i>								
No	184	1						
Yes	97	0.8 (0.5–1.1)						
<i>Duration of use/years</i>								
0	22	1						
>0–<40	92	1.1 (0.6–2.1)						
≥ 40	167	1.3 (0.7–2.3)						
Wei <i>et al.</i> (1994), China	27 admitted to the hospital of West-China University of Medical Sciences	27 patients with malignant, non-urolological tumours, 27 with urolological (non-malignant) disease	Questionnaire to assess lifestyle, diet, marital status, history of prostate disease	Not specified		1.0 (0.4–2.5)	Age, sex, race, day of admission	Ten drinkers among cases and 21 drinkers among controls

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments		
De Stefani <i>et al.</i> (1995), Uruguay, 1988–94	156 adenocarcinoma of the prostate admitted (1988 through 1994) at the Instituto Nacional de Oncologia; 100% histologically confirmed; no refusals recorded	302 patients admitted to the same institute, with diagnoses not related to alcohol, tobacco or diet, aged 40–89 years	Interview by 3 social workers; routine questionnaire given to all patients admitted.	Odds ratios*						
				<i>Beer</i>						
				Non-drinkers	134					
				1–9 mL/day	5	0.7 (0.2–2.1)	Age, residence, level of education, cigarette smoking, dietary items (meat, milk, fruits)	* Odds ratio versus lifelong abstainers; daily alcohol intake expressed as mL pure ethanol, using 60, 120 and 460 mL/L for beer, wine and hard liquor, respectively; odds ratios for beer drinkers versus lifelong abstainers (intake in mL pure ethanol/day): 1–30, 1.2 (0.5–2.8); ≥31, 3.2 (1.2–8.1)		
				10–60 mL/day	9	1.7 (0.7–4.3)				
				≥61 mL/day	8	3.2 (1.0–9.6)				
						<i>p</i> =0.04				
				<i>Wine</i>						
				Non-drinkers	67					
				1–30 mL/day	42	1.3 (0.7–2.1)				
				31–60 mL/day	17	0.8 (1.4–1.5)				
				≥61 mL/day	30	1.4 (0.8–2.6)				
						<i>p</i> =0.35				
<i>Liquor</i>										
Non-drinkers	103									
1–45 mL/day	37	0.7 (0.3–1.3)								
46–69 mL/day	29	1.1 (0.6–2.1)								
≥70 mL/day	38	1.2 (0.6–2.3)								
		<i>p</i> =0.62								
<i>Total alcohol</i>										
Non-drinkers	52									
1–45 mL/day	37	1.4 (0.8–2.4)								
46–120 mL/day	29	0.9 (0.5–1.7)								
≥121 mL/day	38	1.8 (0.9–3.1)								
		<i>p</i> =0.18								
Andersson <i>et al.</i> (1996), Sweden, 1989–91	256 eligible prostate cancer patients (aged <80 years) from Orebro county, January 1989–September 1991; response rate, 74.6%	252 age-matched screened for prostate cancer with negative results; response rate, 76.6%	Interviewer-administered standardized food-frequency questionnaire; clinical data	Non-drinker <24.4 g/week 24.4–48.5 g/week 48.6–96 g/week >96 g/week	106 18 23 29 31	1.0 0.9 (0.4–1.7) 1.1 (0.6–2.1) 1.4 (0.8–2.6) 1.5 (0.8–2.8) <i>p</i> for trend=0.11	Age	Adjustment for smoking reduced alcohol estimates modestly [data not given]		

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Ewings & Bowie, (1996), United Kingdom, 1989–91	159 newly diagnosed prostatic cancer patients in three hospitals; patients interviewed between May 1989 and October 1991; 100% histologically confirmed	2 controls for each case; frequency-matched (5-year age groups), selected from the same hospital: one with benign prostate enlargement, one with non-urological condition (avoiding alcohol- and diet-related disorders)	Questionnaires completed	<i>Ever use of alcohol</i>	134	Odds ratio 0.6 (0.4–1.2)	NR	
Grönberg <i>et al.</i> (1996), Sweden 1959–89	Link between Swedish Twin Registry and Swedish Cancer Registry yielded 406 cases of prostate cancer; mean age at diagnosis, 72.6 years (range, 47–91 years).	1218 3:1 age-matched, unrelated	Questionnaire mailed in 1967 to all same-sex, male twin pairs born in 1886–1925 on food intake and use of beer, wine spirits; 19 (4.7%) cases diagnosed	Non-users Former versus non-user Current versus non-user	64 25 275	Odds ratio 1 0.8 (0.5–1.4) 0.9 (0.6–1.3) <i>p</i> -trend=0.54	Age	Non-users, former users (did not drink during the last year), current users; beer, wine or spirits: non-users, <1 time/week, 1–2 times per week, almost daily; no increased risk found for total alcohol consumption, nor for beer, wine or spirits

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Hayes <i>et al.</i> (1996), USA, 1986–89	479 black, 502 white patients diagnosed 1 August 1986–30 April 1989, aged 40–79 years; 100% pathologically confirmed; response rate, 76%	594 black, 721 white residents of Atlanta, Detroit and 10 counties in New Jersey, covered by three cancer registries; response rate, 71%	In-person interviews (1986–89) on alcohol intake, duration of use, age when started, age when stopped	<i>Drinks per week</i>			Age, ethnicity, study site	Drinkers: >1 drink per month for at least 6 months; increased risk with higher consumption apparent for beer and liquor, not for wine; elevated risks also reported for those with poorly or undifferentiated tumours
				Never used	94	1		
				Any	385	1.2 (1.0–1.5)		
				≤7	96	1.1 (0.9–1.4)		
				8–21	113	1.1 (0.9–1.4)		
				22–56	119	1.4 (1.0–1.8)		
				≥57	54	1.9 (1.3–2.7)		
						<i>p</i> -trend<0.001		
				<i>Recent drinker</i>				
				Never used	94	1		
				≤7	57	1.1 (0.8–1.5)		
				8–21	64	1.1 (0.8–1.5)		
				22–56	67	1.2 (0.9–1.7)		
				≥57	28	1.7 (1.1–2.6)		
				<i>Former drinker</i>				
				Never used	94	1		
				≤7	36	1.2 (0.8–1.8)		
				8–21	45	1.3 (0.9–1.9)		
				22–56	48	1.6 (1.1–2.4)		
≥57	24	2.0 (1.2–3.4)						
<i>Regional/distant</i>								
None	56	1						
≤7	65	1.0 (0.7–1.5)						
8–21	84	1.1 (0.8–1.7)						
22–56	63	1.3 (0.9–1.9)						
≥57	36	2.1 (1.3–3.5)						

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Guess <i>et al.</i> (1997), USA, nested case-control study 1964-71	106 incident cases selected from >125 000 members of the Kaiser Permanente Medical Care Program with health examination data and serum samples available (1964-71); diagnosis between September 1970 and November 1987	106 pair-matched to each case on age, date of serum sampling, location of clinic.	Multi-phasic health examination; bioassay	Non-drinker ≤2 drinks/day ≥3 drinks/day	17 46 28	NR		Alcohol consumption was examined as a confounder.

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Jain <i>et al.</i> (1998), Canada	Ontario: 187 patients listed in Ontario Cancer Registry between April 1990 and April 1992 and living in or around Toronto; refusal rate for interview, 20.2% Quebec: 229 patients admitted to five Montreal hospitals between 1989 and 1993; refusal rate, 15.5% British Columbia: 201 patients (random sample from 6183) in the British Columbia Cancer Registry, in the years 1989–1991; refusal rate, 7%; all histologically confirmed prostate adenocarcinoma	Ontario: 207 chosen at random from lists of the Ministry of Finance; matched with cases by geographic area, 5-year age group; refusal rate, 37% Quebec: 230 chosen via a modified random-digit dialling method, with the same first three phone digits as the cases British Columbia: 199 selected at random from Medical Services Plan rosters; refusal rate, 15%	Questionnaires; weight, physical activity, personal and medical history (e.g. rectal examinations), smoking habits, frequency of use of medical system and demographic data, amount and frequency of food intake in the year before the diagnosis (cases) or before the date of the interview (controls)	<i>Total alcohol intake</i>		Odds ratio	Age (continuous), total energy intake	Percentage alcohol in beer, 3.6%; wines and sherry, 11.5%; liquor/spirits, 37.9%; amount of alcohol in 350mL beer, 12.6 g; in 120mL wine, 13.8 g; in 45mL whiskey, 17.1 g; odds ratios for combined data for all 3 centres; odds ratios for individual centres and for different types of beverage not significantly different from unity; additional adjustment for smoking (ever versus never), educational level, family history of prostate cancer, history of benign prostate hypertrophy, Quetelet index, energy intake and retinol intake had little impact on the results.
				0	175	1.0		
				>0–<10 g/day	168	0.8 (0.6–1.1)		
				10–<20 g/day	82	0.8 (0.6–1.2)		
				20–<30 g/day	57	0.8 (0.5–1.1)		
				≥30 g/day	135	0.9 (0.6–1.3) <i>p</i> for trend=0.51		
				<i>Beer</i>				
				0	333	1.0		
				>0–9 g/day	189	0.8 (0.6–1.1)		
				≥10 g/day	95	0.7 (0.5–0.9) <i>p</i> for trend=0.01		
				<i>Wine</i>				
				0	323	1		
>0–9 g/day	193	0.8 (0.6–1.0)						
≥10 g/day	101	1.12 (0.8–1.55) <i>p</i> for trend=0.8						
<i>Liquor</i>								
0	331	1						
>0–15 g/day	190	0.9 (0.7–1.2)						
≥16 g/day	96	0.9 (0.6–1.2)						

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lumey <i>et al.</i> (1998), USA, 1977–91	699 identified in computerized registry of the American Health Foundation (1977–1991) in 20 US hospitals; mean age, 62.6 years; 100% histologically confirmed; response rate, 94%	2041 hospital patients without tobacco- or alcohol-related disease and without benign prostatic hypertrophy; mean age, 61.1 years; 3:1 matched with cases by age at diagnosis (within 5 years), year of diagnosis, hospital, race; response rate, 94%	Interview at the time of admission to the hospital, with a structured questionnaire on demographic, socioeconomic and behavioural aspects, smoking, drinking	<i>Drinks/week</i> Never Any ≤7 8–21 22–56 ≥57	106 593 235 160 123 62	Odds ratios 1.0 1.2 (0.9–1.5) 1.2 (0.9–1.6) 1.1 (0.8–1.5) 1.3 (1.0–1.8) 1.1 (0.7–1.5)	Age at diagnosis, study site	Odds ratios for current and former drinkers similar; adjustment for marital status, occupation, religion, education, smoking habits did not change the results; separate analyses for beer, wine and liquor, or for different age groups (≤64 or ≥65 years) did not influence the results; one drink defined as a glass of whisky, a glass of wine or a glass of beer.
Hsieh <i>et al.</i> (1999), Greece, 1994–97	320 patients (95% aged >60 years) with prostate carcinoma from six hospitals in the Greater Athens area between 1994 and 1997; 100% histologically confirmed	246 (90% aged >60 years) non-cancer patients in the same hospitals as the cases	Interviews from February 1994 to January 1997 at the hospital, with questions about demographic, socioeconomic, reproductive, biomedical, dietary variables	<i>Alcohol drinking (glasses/day)</i> None <1 1–<2 2–<3 3–<4 ≥4	101 43 38 32 29 61	NR	Age, body mass index, height, years of schooling	

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Dennis (2000)	Meta-analysis of 27 case-control studies examining the association between alcohol use and prostate cancer		Articles published between January 1976 and July 1978	Ever versus never		1.1 (0.98–1.13)		
Sharpe & Siemiatycki (2001), Montreal, Canada, 1979–85	Interview data obtained from 449 of 557 (80.6%) eligible incident cases, histologically confirmed, in Montreal; reliable alcohol consumption data obtained from 399 cases	541 chosen from electoral lists 1979–82 and 1984–85, 199 by random digit dialling; 533 responded (rate, 72%), of whom 512 were interviewed; data from 476 were used	Interviews on use of beer, wine and spirits, frequency of use, time when drinking started; data expressed as 'drink-years'	Never drank daily	69	1.0	Age, ethnicity, respondent status, family income, body mass index, cigarette smoking	A drink of beer, wine or spirits was estimated to contain 13.6 g alcohol; the study was primarily designed to study occupational causes of cancer;
				Drank weekly, never daily	133	1.6 (1.1–2.4)		
				Drank daily				
				<i>Age at starting daily drinking (years)</i>				
				<15	17	3.8 (1.6–9.3)		
				15–19	51	1.4 (0.8–2.4)		
				20–24	49	1.6 (0.9–2.7)		
≥25	68	1.2 (0.8–2.0)						
						<i>p</i> -trend=0.009		
				<i>Duration of drinking (years)</i>				
				<20	32	1.3 (0.7–2.4)		
				20–39	64	1.1 (0.7–1.8)		
				>39	88	2.0 (1.2–3.1)		
								<i>p</i> -trend=0.01

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sharpe & Siemiatycki (2001) (contd)				<i>Cumulative consumption (daily drinkers)</i>				647 cancer controls selected from other, not alcohol-related cancer cases (response rates, 78–85%) also included; findings similar when using cancer controls
				<58 drink-years	54	1.4 (0.9–2.3)		
				58–125 drink-years	44	1.1 (0.7–1.9)		
				>125 drink-years	99	2.1 (1.3–3.3)		
							<i>p</i> -trend=0.003	
				<i>Combined use</i>				
				Beer only	57	1.6 (0.9–2.5)		
				Wine only	16	1.4 (0.7–2.9)		
				Spirits only	12	1.9 (0.4–1.9)		
				Beer and wine	17	1.2 (0.6–2.4)		
Beer and spirits	78	1.9 (1.2–3.1)						
Wine and spirits	20	1.1 (0.6–2.2)						
Beer, wine and spirits	130	1.8 (1.2–2.7)						

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Crispo <i>et al.</i> (2004), Italy 1991–2002	1294 patients with prostate carcinoma; median age, 66 years (range, 46–74 years); 100% histologically confirmed; refusal rate, <5%; 1369 patients with benign prostatic hyperplasia; median age, 65 years (range, 46–74 years); refusal rate, <5%	1451 patients admitted to the same hospitals for non-neoplastic disorders; median age, 63 years (range, 46–74 years); refusal rate, <5%	Personal interviews with questionnaire on alcohol drinking: number of drinks per week, number of drinks per week, duration (up to 1 year prior to diagnosis or admission)			<i>Prostate cancer patients</i>	Age, study centre, education, body mass index, physical activity, history of prostate cancer in first-degree relatives	Abstainers never consumed alcohol; former drinkers had abstained ≥ 1 year; one drink: 125 mL wine, 330 mL beer, 30 mL hard liquor (12–15 g alcohol); analysis by different types of beverage (beer, wine, spirits) did not show any significant association with risk for prostate cancer; some evidence for an inverse relationship with the risk for benign prostatic hyperplasia.
				<i>Abstainer</i>	71	1.0		
				<i>Former drinker</i>	93	0.8 (0.5–1.3)		
				<i>Current drinkers</i>	1130	0.9 (0.6–1.3)		
				<3 drinks/week	496	0.9 (0.6–1.3)		
				3–4 drinks/week	355	0.9 (0.6–1.3)		
5–6 drinks/week	177	1.1 (0.7–1.7)						
7–8 drinks/week	107	1.0 (0.6–1.5)						
≥ 9 drinks/week	88	0.9 (0.5–1.4)						
Hodge <i>et al.</i> (2004), Melbourne, Perth, Sidney, Australia, 1994–97	858 patients diagnosed 1994–97 with ‘clinically important’ prostate cancer (Gleason score ≥ 5), aged <70 years; registered to vote; 100% histologically confirmed; response rate, 65%	905 randomly selected from State Electoral Rolls; age-matched; response rate, 50%	Personal interviews, dietary habit questions and a 121-item food frequency questionnaire; men with energy intake from food >3 SD above the mean not included; alcohol intakes from beer, wine, spirits and total use recorded	<i>Total alcohol intake (g/day)</i> <20 20–39 40–59 ≥ 60	NR	1.0 1.0 (0.8–1.3) 1.0 (0.7–1.3) 1.0 (0.7–1.4)	State, age group, year, country of birth, socio-economic group, family history of prostate cancer	Analysis by different types of beverage (beer, wine, spirits) did not show any association with prostate cancer risk.

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Chang <i>et al.</i> (2005), Sweden, 2001–02	1499 incident prostate cancers identified from Swedish regional cancer registries; mean age, 66.4 years; histologically confirmed as adenocarcinoma; response rate, 79%	1130 identified from the Swedish Population Registry database; mean age, 67.3 years; response rate, 67%	Self-administered questionnaire to assess known and potential risk factors for prostate cancer	Non-drinker	122	1.0	Age (5-year categories), smoking history (ever, never), current body mass index, family history of prostate cancer, intake of other alcohol types, dairy products, red meat, fruit, vegetables	Light, medium and strong beers (33 cL) contain 6, 9.1 and 14.6 g ethanol; light and strong wines (15 cL) contain 14.2 and 20.7 g ethanol; a shot of liquor (4 cL) contains 12.6 g ethanol; light beers were not counted in number of drinks per week; non-drinkers included consumers of only light beer; former drinkers were those who stopped ≥ 18 months before; current drinkers included those who stopped < 18 months before.	
				Former drinker	112	2.1 (1.4–3.3)			
				Current drinker	1259	1.6 (1.2–2.1)			
				<i>Ethanol (g/week)</i>					
				0.0	218	1.0			
				0.1–45	379	1.1 (0.8–1.4)			
				45.1–90.0	311	1.2 (0.9–1.5)			
				90.1–135.0	202	1.3 (0.9–1.7)			
				>135.1	359	1.3 (1.0–1.7)			
						<i>p</i> -trend=0.06			
				<i>Localised disease</i>					
				0.0	NR	1.0			
				0.1–45		1.5 (1.1–2.1)			
45.1–90.0		1.4 (1.0–2.0)							
90.1–135.0		1.4 (1.0–2.1)							
>135.1		1.4 (1.0–2.0)							
		<i>p</i> -trend=0.27							
<i>Advanced disease</i>									
0.0	NR	1.0							
0.1–45		0.8 (0.6–1.0)							
45.1–90.0		0.9 (0.7–1.2)							
90.1–135.0		1.1 (0.8–1.5)							
>135.1		0.9 (0.7–1.2)							
		<i>p</i> -trend=0.50							

Table 2.77 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Schoonen <i>et al.</i> (2005), USA, 1993–96	753 Caucasian and African-American men living in King County (Washington State, USA), newly diagnosed with prostate cancer in 1993–96, aged, 40–64 years; 100% histologically confirmed; participation rate, 82.1%; participant refusal, 12.5%	941 identified using random-digit dialling; frequency-matched to cases by 5-year age group; 703 interviewed; participation rate, 75%; participant refusal, 24%.	Histological and clinical details on case subjects from the Seattle-SEER cancer registry; interview with food-frequency questionnaire and data on medical history, prostate-cancer screening history, family history of cancer, demographics, height, weight, lifetime alcohol use, smoking habits, marital and sexual history, lifestyle and occupational factors	Ever use	681	Odds ratio 1.1 (0.7–1.5)	Age, use of prostate screening, lifetime number of female sexual partners, smoking status Odds ratio values for red wine also adjusted for intake of other types of alcohol	One bottle of beer (12 oz), one glass of wine (4 oz), one shot of liquor (1.5 oz) contain 13, 11 and 14 g ethanol, respectively; analyses by age at first alcohol use, lifetime duration of use, or by heavy drinking period (yes/no) did not affect the outcome; associations were similar for less and more aggressive cancers; subjects consuming <1 drink/week were included in the reference group; non-drinkers had ≤12 drinks during life.	
				<i>Lifetime alcohol (g)</i>	0	72			1.0
				>0–6000	186	1.1 (0.8–1.7)			
				>6000–12 000	122	0.9 (0.6–1.4)			
				>12 000–24 000	138	1.0 (1.6–1.5)			
				>24 000	235	1.3 (0.8–2.0) <i>p</i> -trend=0.33			
				<i>Drinks per week</i>	None or <1	126			1.0
				1–7	266	0.9 (0.7–1.3)			
				8–14	166	1.0 (0.7–1.5)			
				≥15	195	1.1 (0.7–1.6) <i>p</i> -trend=0.32			
				<i>Red wine (drinks/week)</i>	Non-drinker	134			1.0
				1–3	121	0.8 (0.5–1.3)			
				4–7	66	0.5 (0.3–0.9)			
≥8	27	0.5 (0.2–0.9) <i>p</i> -trend=0.02							

CI, confidence interval; ICD, International Classification of Diseases; NR, not reported; SD, standard deviation; SEER, Surveillance, Epidemiology, and End Result

^a Unless otherwise noted in the comments, the ICD code for prostate cancer is 185

2.15.3 *Meta-analysis*

A meta-analysis that included six cohort and 27 case-control studies that were reported before July 1998 resulted in an estimate of 1.05 (95% CI, 0.98–1.11) for ever consumption of alcoholic beverages (Dennis, 2000). There was a suggestion of a weak dose-response relationship for increasing levels of alcoholic beverage consumption (relative risk, 1.21; 95% CI, 1.05–1.39 for four drinks/day) when data from 15 of the studies were used. [Results for the six cohort studies and the 27 case-control studies are presented in Tables 2.76 and 2.77, respectively.]

2.16 **Cancer of the kidney**

Twenty cohort studies that assessed the relationship between alcoholic beverage intake and kidney cancer were identified; six of these were in special populations of heavy alcoholic beverage consumers whose rates of kidney cancer were compared with those of other populations, one was a mortality follow-up of a Japanese population, one was a study among cirrhotic patients and twelve were part of a pooled analysis. Twenty-one case-control studies that included information on alcoholic beverages and kidney cancer were identified.

2.16.1 *Cohort studies (Tables 2.78 and 2.79)*

Several of the five follow-up studies of heavy alcoholic beverage consumers (Pell & D'Alonzo, 1973; Jensen, 1979; Robinette *et al.*, 1979; Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Table 2.78) were seriously limited by very small numbers of renal-cell cancer and an inability to control for confounding by smoking. Two of these had approximately 40 cases (Jensen, 1979; Tønnesen *et al.*, 1994); the SIRs were 1.0 and 1.4, respectively.

Recently, a pooled analysis that was part of the Pooling Project of Prospective Studies of Diet and Cancer (Lee *et al.*, 2007; Table 2.79) included 12 cohorts that found at least 25 incident cases of renal-cell carcinoma and consisted of 530 469 women and 229 575 men, with a maximum follow-up time of 7–20 years. Only four of these studies (Nicodemus *et al.* 2004; Mahabir *et al.*, 2005; Rashidkhani *et al.*, 2005; Lee *et al.*, 2006) had previously published findings, which tended to show inverse or null associations between alcoholic beverage intake and the incidence of renal-cell cancer. In most of the other cohorts, the numbers of renal-cell cancers were relatively small and the results may have not been published. A total of 1430 incident cases of renal-cell cancer were identified. Alcoholic beverage consumption was inversely related to risk; compared with non-drinkers, the relative risk was 0.72 (95% CI, 0.60–0.86) for consumption of ≥ 15 g alcohol per day (p for trend < 0.001). Although there was significant heterogeneity among studies, the inverse trends were similar and statistically significant in both men and women.

Table 2.78 Cohort studies of alcoholic beverage consumption and cancer of the kidney in special populations

Reference, location, name of study	Cohort description	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Follow-up studies of heavy drinkers							
Pell & D'Alonzo (1973), USA	Employees of a chemical company: 899 alcoholics identified through company physicians, 921 controls; matched for age, sex, payroll class, geographical location; follow-up, 1965–69; 88.1% of alcoholics and 96.3% of controls still alive in 1969	Kidney (189)	Alcoholics Controls	26 deaths (2 renal) 7 deaths (1 renal)			

Table 2.78 (continued)

Reference, location, name of study	Cohort description	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Jensen (1979), Denmark, Danish Brewery Cohort	14 313 Danish brewery workers employed at least 6 months in 1939–63; followed for cancer incidence and mortality in 1943–73; age not given; workers allowed 2.1 L of free beer/day (77.7 g pure alcohol).	Kidney (189); cases and deaths identified through Cancer Registry, classified with 4-digit code of ICD-7	All cancers Kidney cancer	1303 38	SIR 1.1 (1.0–1.2) 1.0 (0.7–1.4)	Age, sex, area, time trends	Cancer morbidity and mortality compared with those of the general population
Robinette <i>et al.</i> (1979), USA, World War II Veterans Study	4401 US Army service men, hospitalized for chronic alcoholism 1944–45; 4401 service men treated for nasopharyngitis matched to alcoholic subjects by age; follow-up through to 1974	Deaths; kidney (ICD-8, 189)	In 1974 <i>Alcoholics</i> All causes All cancers Cancer of kidney, ureter and other	Deaths 1438 166 1	Mortality rate ratio 1.78 (1.74–2.00) 1.08 (0.96–1.38) ^a 0.27 (0.01–2.09) ^b		^a Based on age- and time-specific US death rates in the USA ^b Ratio of observed/ person–years for alcoholism over nasopharyngitis

Table 2.78 (continued)

Reference, location, name of study	Cohort description	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Adami <i>et al.</i> (1992a), Sweden	9353 individuals (8340 men) with a discharge diagnosis of alcoholism in 1965–83; mean age at entry, 49.4 years; at diagnosis, 60.0–68.1 years; follow-up for through to 1984 (maximum, 19 years; mean, 7.7 years); first year of follow-up excluded	Ascertained through National Swedish Cancer Registry; 94% microscopically confirmed; cases occurring in the first year after entry into the cohort excluded	All cancers	491 deaths	SIR 1.4 (1.3–1.6)		No data on individual alcohol or tobacco use
			Kidney cancer				
			Men	20	1.3 (0.8–2.1)		
			Women	2	2.0 (0.2–7.1)		
Tønnesen <i>et al.</i> (1994), Denmark	15 214 male and 3093 female alcohol abusers who entered an outpatient clinic in Copenhagen during 1954–87; average follow-up, 12.9 years for men and 9.4 years for women	Cases identified by record linkage with the Danish Cancer Registry (95% complete)	All cancers	1623 deaths	1.6 (1.5–1.7)		Most subjects consumed about 200 g alcohol daily; cancer morbidity compared with total Danish population
			Kidney cancer				
			Men	42	1.4 (1.0–1.9)		
			Women	4	1.7 (0.5–4.4)		
			Total		1.4 (1.0–1.9)		

Table 2.78 (continued)

Reference, location, name of study	Cohort description	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Cohort of Alcoholic Women	15 508 alcoholic women identified from the Temperance Board records; comparison group of 15 508 women individually matched on day of birth, region; follow-up, [1947–77]; case ascertainment, Swedish Cancer Registry	Identified through Cancer Registry (ICD-7)	Alcoholics	20	1.2 (0.6–2.3)	Age, region	Estimates not adjusted for smoking

Table 2.78 (continued)

Reference, location, name of study	Cohort description	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sørensen <i>et al.</i> (1998), Denmark, Cohort of 1-year Survivors of Cirrhosis	11 605 1-year survivors of cirrhosis identified from Danish National Registry of patients that covered all hospital admissions in Denmark; follow-up, 1977–93; 7165 alcoholic cirrhosis (5079 men, 2086 men); case ascertainment, Danish Cancer Registry (100%)	Identified by linkage with Danish Cancer Registry (almost complete average of country); reports from pathology department and autopsy	Alcoholic cirrhosis	Total 45 Men 27 Women 18	SIR 2.2 (1.6–3.0) 2.1 ($p>0.05$) 2.5 ($p>0.05$)	Age, sex, calendar period	Estimate not adjusted for smoking; reference, national incidence rates

CI, confidence interval; ICD, International Classification of Diseases; SIR, standardized incidence ratio

2.16.2 Case-control studies (Table 2.80)

The 21 case-control studies generally showed no or inverse associations (some of which were statistically significant), and no significantly positive associations. Four relatively recent, large case-control studies of renal-cell cancer are particularly informative. A multicentre case-control study conducted in Australia, Denmark, Sweden and the USA is notable because of the large number of cases (1185 of renal-cell cancer) and the detailed data collected on potentially confounding factors (Wolk *et al.*, 1996). The relative risk in men for consumption of ≥ 15 drinks per week was 1.0 (95% CI, 0.70–1.4) and that in women for consumption of ≥ 10 drinks per week was 0.5 (95% CI, 0.3–0.8). In a large Italian case-control study of 348 cases, the relative risk was 0.8 (95% CI, 0.5–1.3) for six or more drinks per day (Pelucchi *et al.*, 2002b) and, in a large case-control study from Canada conducted by mailed questionnaire (1279 cases), the relative risks for 18 or more servings of alcoholic beverage per week were 0.7 (95% CI, 0.5–0.9) for men and 0.6 (95% CI, 0.4–1.1) for women with significant inverse trends in both sexes (Hu *et al.*, 2003). A multicentre hospital-based case-control study in eastern Europe (1065 cases) calculated average lifetime alcoholic beverage consumption (Hsu *et al.*, 2007); the relative risk for those who drank more than 137.5 g alcohol per week was 0.83 (95% CI, 0.61–1.12) and that for the top decile of intake was 0.39 (95% CI, 0.24–0.66).

All the large case-control studies and the pooled analysis of cohort studies were limited to renal-cell carcinomas. No studies of alcoholic beverage consumption in relation to cancer of the renal pelvis were identified.

2.16.3 Evidence of a dose-response

The best available evidence on dose-response comes from the pooled analysis of cohort studies (Lee *et al.*, 2007). Relative risks were 0.97 (95% CI, 0.85–1.11) for 0.1–4.9 g/day, 0.82 (95% CI, 0.69–0.96) for 5.0–14.9 g/day and 0.72 (95% CI, 0.60–0.86) for 15 or more g/day (p for trend < 0.001). A non-parametric regression curve was fit to the continuous data from these studies, and significant departure from linearity was suggested ($P=0.02$) with flattening of the curve above approximately 30 g/day.

The participating cohort studies had validated data for alcoholic beverage consumption; therefore, regression calibration was used to correct the observed associations for measurement error in alcoholic beverage intake, and limited this correction to the range of 0–30 g/day (94% of the data) because the relation appeared to be close to linear within this range. The uncorrected relative risk was 0.79 (95% CI, 0.70–0.89) for a 10-g/day increment within this range; after correction for measurement error, the relative risk was 0.81 (95% CI, 0.74–0.90).

The large case-control studies all found relative risks of 1.0 or below for the highest category of alcoholic beverage consumption and were generally consistent with

Table 2.79 Cohort studies of alcoholic beverage consumption and cancer of the kidney in the general population

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Nicodemus <i>et al.</i> (2004), USA, Iowa Women's Health Study Cohort [included in Lee <i>et al.</i> (2007)]	99 826 randomly selected women, aged 55–69 years, from Iowa driver's licence list, sent a questionnaire in January 1986; 41 836 (42%) women responded, 34 637 (98% white) included; follow-up, 15 years	Questionnaire on lifestyle, medical history, reproductive history, food intake, drinking habits, physical activity	Incident primary renal-cell carcinoma ascertained via the State Health Registry of Iowa; all cases histologically confirmed (ICD-9, 189.0)	<i>Alcohol intake (g/day)</i>	117 cases		Age, physical activity, high blood pressure, diuretic use, insulin use, hormone replacement therapy, regularity of menstrual cycles, parity	
				0	79	1.0		
				0.1–2.9	31	1.0 (0.7–1.6)		
				≥3	14	0.4 (0.2–0.8)		
				<i>Beer use</i>				
				No	110	1.0		
				Yes	14	0.6 (0.4–1.1)		
				<i>Red wine</i>				
				No	110	1.0		
				Yes	14	0.5 (0.3–0.8)		
				<i>White wine</i>				
				No	106	1.0		
				Yes	18	0.6 (0.4–1.0)		

Table 2.79 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Mahabir <i>et al.</i> (2005), Finland, 1985–99, Finnish Smokers Cohort Study [included in Lee <i>et al.</i> (2007)]	27 111 men in the α -Tocopherol, β -Carotene Cancer Prevention Study cohort for whom data on alcohol consumption and diet were available	Questionnaire: height, weight, blood pressure, medical history, food frequency during past year, alcohol intake	Incident cases identified via the Finnish Cancer Registry and confirmed with hospital records and reports from pathology; response rate, 93%	<i>Total alcohol (g/day) [median]</i>	195	<i>Multivariate-adjusted</i>	Age, body mass index, supplement group, calories (excluding alcohol sources), blood pressure, years of regular smoking, total number of cigarettes smoked per day, smoking inhalation, and fruits and vegetables	Alcohol use given in quartile groups, with 6774–6782 subjects per group
				0–2.5 [0.4]	56	1.0		
				2.6–11.0 [6.2]	52	0.91 (0.6–1.3)		
				11.1–24.0 [17.3]	53	0.94 (0.6–1.4)		
				24.1–278.5 [39.1]	34	0.53 (0.3–0.8)		
						<i>p</i> -trend=0.005		
				<i>Spirits (g alcohol/day) [median]</i>				
				0–0.4 [0]	62	1.0		
				0.5–5.3 [1.7]	42	0.9 (0.6–1.4)		
				5.4–15.9	56	0.8 (1.6–1.2)		
16.0–160 [22.8]	35	0.6 (0.4–0.9)						
		<i>p</i> -trend=0.02						
<i>Beer (g alcohol/day) [median]</i>								
0 [0]	65	1.0						
0.01–1.9 [1.2]	53	1.2 (0.9–1.8)						
2.0–7.4 [4.0]	45	0.8 (0.6–1.2)						
7.5–242.6 [14.8]	32	0.6 (0.4–0.9)						
		<i>p</i> -trend=0.002						

Table 2.79 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Rashidkhani <i>et al.</i> (2005), Sweden, Swedish Mammography Cohort [included in Lee <i>et al.</i> (2007)]	66 561 Swedish women, aged 40–76 years, living in the counties of Västmanland and Uppsala, who responded to a questionnaire in 1987–90 (participation rate, 74%), with follow-up questions in 1997 (rate of response, 70%); average follow-up, 14.2 years	Questionnaire in 1997 on diet (67 food items) during past 6 months, alcohol and tobacco use, education, weight, height, history of hypertension, diabetes	Incident cases of renal-cell carcinoma (ICD-9, 189.0); recorded by matching with Regional Cancer Register, between the return of the questionnaire (1987–90) and 30/06/2004	<i>Alcohol intake (g/day)</i>	132 cases	Rate ratio <i>All women</i>	Age, body mass index	* Includes strong (4.5%) and medium-strong (2.8%) but not light beer	
				<2.5 (median 1.1)	94	1.0			
				2.5–4.3 (median 3.3)	19	0.66 (0.40–1.09)			
				>4.3 (median 6.0)	19	0.7 (0.42–1.19)			
				<i>All alcoholic beverages (servings/week)</i>					
				<1	94	1.0			
				≥1	38	0.6 (0.4–0.9)			
				<i>Wine (servings/week)</i>					
				<1	120	1.0			
				≥1	12	0.6 (0.3–1.1)			
<i>Beer* (servings/month)</i>									
<1	116	1.0							
≥1	16	0.7 (0.4–1.2)							
<i>Hard liquor (servings/week)</i>									
<1	107	1.0							
≥1	25	0.8 (0.5–1.3)							

Table 2.79 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Rashidkhani et al. (2005) (contd)				<i>Alcohol intake (g/day)</i>			<i>Aged ≥55 years</i>	
				<2.5 (median 1.1)	65	1.0		
				2.5–4.3 (median 3.3)	10	0.8 (0.4–1.5)		
				>4.3 (median 6.0)	3	0.3 (0.1–1.1)		
				<i>All alcoholic beverages (servings/week)</i>				
				<1	69	1.0		
				≥1	9	0.44 (0.22–0.88)		
				<i>Wine (servings/week)</i>				
				<1	76	1.0		
				≥1	2	0.23 (0.06–0.95)		
				<i>Beer* (servings/month)</i>				
				<1	73	1.0		
≥1	5	0.7 (0.3–1.6)						
<i>Hard liquor (servings/week)</i>								
<1	71	1.0						
≥1	7	0.48 (0.22–1.04)						

Table 2.79 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lee <i>et al.</i> (2006), USA, Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) [included in Lee <i>et al.</i> (2007)]	NHS: 121 700 female registered nurses, aged 30–55 years, returning a mailed questionnaire in 1976; HPFS: 51 529 health professionals (all men), aged 40–75 years, responding to a mailed questionnaire in 1986; follow-up of 88 759 women (NHS) from 1980, 47 828 men (HPFS) from 1986 with follow-up rate >90%; follow-up ended in 2000, on 31/05 for NHS, on 31/01 for HPFS	Semiquantitative food-frequency questionnaires sent in 1980 and 1984 to NHS participants, and in 1986 and every 4 years after to both cohorts; questions on extent and frequency of alcohol use and total intake of fluids (including water)	Renal-cell carcinoma self-reported and then verified by histological data	NHS	132 cases	Pooled multivariate	NHS: body mass index, history of hypertension (yes/no), history of diabetes (yes/no), parity, smoking status, total energy intake; HPFS: body mass index, history of hypertension (yes/no), smoking status, multi-vitamin use, total energy intake *Additionally adjusted for the two other alcoholic beverages	Alcohol use divided into quartile groups
				HPFS	116 cases			
				<i>Total alcohol (g/day)</i>	58	1.0		
				0	88	1.0 (0.7–1.3)		
				0.1–4.9	61	0.9 (0.5–1.6)		
				5.0–14.9	41	0.7 (0.4–1.0)		
				≥15		<i>p</i> -trend=0.07		
				<i>Beer</i>				
				No beer	164	1.0*		
				Beer drinkers	82	0.7* (0.4–1.2)		
<i>Wine (servings)</i>								
<1/month	93	1.0*						
1/month–<2/week	96	1.2* (0.9–1.6)						
≥2/week	59	1.1* (0.7–1.8)						
<i>Liquor (servings)</i>								
<1/month	129	1.0*						
1/month–<2/week	58	0.9* (0.7–1.2)						
≥2/week	60	0.9 (0.6–1.2)						

Table 2.79 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Case definition (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lee <i>et al.</i> (2007), Pooled analysis including 12 cohorts; includes four previously published studies (Nicodemus <i>et al.</i> , 2004; Mahabir <i>et al.</i> , 2005; Rashidkhani <i>et al.</i> , 2005; Lee <i>et al.</i> , 2006)	530 469 women and 229 575 men with maximum follow-up of 7–20 years	Self-administered questionnaires	Cases ascertained by follow-up questionnaires and subsequent review of medical records, linkage to cancer registries, or both; histologically confirmed renal-cell cancer (ICD-0-2, C64.9); 61% renal-cell carcinoma, not otherwise specified (code 8312)	<i>Total alcohol (g/day)</i>	1430 cases (711 women, 719 men)	1.0 0.97 (0.85–1.11) 0.82 (0.69–0.96) 0.72 (0.60–0.86) <i>p</i> -trend<0.001	Age, hypertension, body mass index, smoking, parity, age at first birth, energy intake	Relative risks similar for men and women with significant inverse trends in both sexes
				0		1.0		
				0.1–4.9		0.98 (0.85–1.12)		
				5.0–14.9		0.87 (0.68–1.11)		
				≥15		1.0		
				<i>Beer(g/day)</i>		0.93 (0.79–1.08)		
				0		0.72 (0.59–0.87)		
				1.0–4.9		1.0		
				≥5.0		1.02 (0.88–1.17)		
				<i>Wine(g/day)</i>		0.88 (0.75–1.03)		
		0						
				<i>Liquor(g/day)</i>				
				0				
				1.0–4.9				
				≥5.0				

CI, confidence interval; ICD, International Classification of Diseases

Table 2.80 Case-control studies of alcoholic beverage consumption and cancer of the kidney

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Schwartz <i>et al.</i> (1962), France, 1954–58	69 cases of renal cell cancer	69 accident victims); age-matched in 5-year age groups	Interviewed in the hospital on alcohol drinking	Cases, 10.8 cL/day Controls, 12.6 cL/day	NR			Average consumption according to age (5-year age groups) varied from 9.6 to 14.0 cL pure alcohol/day
Williams & Horm (1977), USA, Third National Cancer Survey, 1969–71	101 kidney cancer cases (53 men, 48 women) among 7518 cancer patients		Interviewed to collect data on the amount and the duration of alcohol and tobacco use	<i>Men</i>	11	1.07	Age, race, smoking	Oz-years = units/week × years drinking
				<50 oz-years	14	0.76		
				>50 oz-years				
				<i>Women</i>	6	0.80		
				<50 oz-years	3	0.76		
				>50 oz-years				

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Goodman <i>et al.</i> (1986), USA, 1977–83	267 patients (189 men, 78 women) with newly diagnosed primary adenocarcinoma of the kidney in 18 hospitals in 6 cities, aged 20–80 years; 100% histologically confirmed; refusal rate, 11%	267 patients (189 men, 78 women) with diseases not tobacco-/obesity-related, diagnosed and interviewed ≤ 1 year after the case interview; matched 1:1 on age, sex, race, hospital, time of admission; refusal rate, 12%	Standardized interview on medical history, life-style drinking/smoking habits, demographic information, job history, leisure time and worksite energy expenditure	Men and women				* Alcohol score: years of drinking \times average daily consumption (in alcohol equivalents)
				<i>Alcohol use</i>				
				Never	65	1.0		
				Ever	193	0.6 (0.4–1.0)		
				<i>Alcohol score*</i>				
				1–9	60	0.5 (0.3–0.8)		
				10	69	0.9 (0.5–1.7)		
				<i>Beer</i>				
				Never	134	1.0		
				Ever	133	0.8 (0.5–1.1)		
				<i>Wine</i>				
				Never	129	1.0		
				Ever	138	0.7 (0.5–0.96)		
				<i>Hard liquor</i>				
Never	122	1.0						
Ever	144	0.7 (0.5–1.01)						
Yu <i>et al.</i> (1986), USA	6 renal-cell carcinoma; aged <55 years; 100% histologically confirmed	160 population-based; matched by age, sex	Personal interviews using questionnaire	Men only				Cases and controls did not differ significantly by consumption of alcoholic beverages (no data given)
				<i>Former use of beer</i>				
				Never	89	1.0		
				1–3 years	8	0.3 (0.0–1.1)		
>4 years	5	0.2 (0.0–0.5)						

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments		
Asal <i>et al.</i> (1988), USA, 1981–84	315 (209 men, 106 women; 34 non-white) incident renal-cell carcinomas in 29 Oklahoma hospitals; 300 histologically confirmed, 15 radiologically confirmed	313 (208 men, 105 women) patients; psychiatric illnesses or kidney disease excluded; 12% had cancer; matched by age (within 5 years), sex, race, hospital, time of interview; 336 (195 men, 141 women) selected by random-digit dialling from the Oklahoma population; frequency-matched by age (within 10 years), sex	Interviews in hospital, at home or at work on medication, medical history, radiation therapy, main occupation, tobacco/alcohol use, height and weight, family history of disease	Wine (glass/week)						
				<i>Ever</i>						
				Men	85	0.5 (0.4–0.8)	Age, weight, smoking	One alcohol unit = 1 oz (28.4 g) hard liquor, 4 oz (113 g) wine, 8 oz (227 g) beer; 'ever' drinkers included subjects who drank unknown amounts (6 cases, 3 controls)		
				Women	30	0.5 (0.3–0.9)	Age, weight			
				<i>Men</i>						
				Never	124	1.0				
				<1	48	0.4 (0.3–0.7)				
				1–4	15	0.7 (0.3–1.9)				
				>4	16	0.7 (0.3–1.6)				
				<i>Women</i>						
Brownson (1988), USA, 1984–86	326 (205 men, 121 women; all white) Missouri residents with primary adenocarcinoma of the kidney, identified via the Missouri Cancer Registry, aged ≥20 years; 100% histologically confirmed	978 (615 men, 363 women) patients in the Registry with cancers of the small intestine colon, rectum, prostate, skin, nervous, reticulo-endothelial and haematopoietic systems and lymph nodes	Information on smoking, alcohol use, job history recorded at the time of diagnosis	<i>Men</i>	NR					
				Never drank		1.0	Age, smoking			
				Ever drank		0.9 (0.6–1.3)	Age, smoking, sex			
				Unknown		1.1 (0.6–2.1)				
				<i>Women</i>						
				Never drank		1.0				
				Ever drank		1.1 (0.6–2.0)				
				Unknown		0.8 (0.3–2.0)				
<i>Both sexes</i>										
Never drank		1.0								
Ever drank		1.0 (0.7–1.4)								
Unknown		1.0 (0.6–1.7)								

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Kadamani <i>et al.</i> (1989), USA, 1981–83	210 (142 men, 68 women; 90% white) newly diagnosed renal-cell carcinomas in 23 Oklahoma hospitals, aged ≥ 20 years; 197 histologically confirmed, 13 radiologically confirmed	210 (142 men, 68 women) selected by random-digit dialling from the Oklahoma population; frequency-matched by age (within 5 years), sex; refusal rate, 45%	Interviews on demographics, job history, use of tobacco/alcohol; exposure to hydrocarbons (HC) estimated from job history by industrial hygienists	No HC exposure	NR	Odds ratio	Men: weight, education; women: weight	No CIs given; this study focused primarily on effects of occupational exposure to hydrocarbons on the risk for renal-cell carcinoma.
				<i>Never wine use</i>		<i>Men (women)</i>		
				<i>Ever wine use</i>		1.0 (1.0)		
				Low HC exposure		1.3 (0.8)		
				<i>Never wine use</i>		2.3 (0.5)		
				<i>Ever wine use</i>		0.56 (1.00)		
Maclure & Willett (1990), Massachusetts, USA	203 incident renal adenocarcinomas diagnosed in 37 hospitals in the Boston area, aged ≥ 30 years; 100% histologically confirmed	605 neighbourhood controls; not matched	Questionnaire administered by interviewer on diet, medication, smoking and alcohol, occupational history, physical activity	<i>Wine</i>			Age, sex, drinking	
				Low		1.0		
				Moderate		0.7 (0.4–1.2)		
				High		1.0 (0.3–3.0)		
				<i>Beer</i>				
				Low		1.0		
				Moderate		1.1 (0.7–1.7)		
				High		1.4 (0.8–2.5)		
				<i>Spirits</i>				
				Low		1.0		
Moderate		1.1 (0.7–1.6)						
High		1.1 (0.6–1.9)						

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Talamini <i>et al.</i> (1990b), Italy, 1986–89	240 (150 men, 90 women) renal-cell cancers in hospitals in northern Italy (Veneto, Pordenone, Milan area), aged 20–74 years; 100% histologically confirmed; renal pelvis cancers excluded; refusal rate for interview, 3%	665 (445 men, 220 women) patients in the same hospitals for acute conditions not related to alcohol, tobacco or hormones; matched 3:1 on sex, age (\pm 5 years), area of residence; refusal rate, 4%	Interviews on lifestyle, occupation, medical history (urologic, hormone-related, infectious diseases), socio-demographic factors, smoking, alcohol drinking	<i>Highest category of intake per day:</i> Alcohol, \geq 100 g Wine, \geq 4 drinks Beer, \geq 1 drink Spirits, \geq 1 drink	18 98 53 77	0.7 (0.4–1.3) 0.9 (0.6–1.3) 1.0 (0.7–1.5) 1.2 (0.8–1.7)	Age, sex, education, body mass index, area of residence	
Benhamou <i>et al.</i> (1993), France, 1987–91	196 (138 men, 58 women) renal-cell cancers in 10 French hospitals; mean age, 61.7 and 61.3 years, respectively; 100% histologically confirmed after nephrectomy; refusal rate, 0.5%	347 (235 men, 112 women) hospital patients; mean age, 62.8 and 62.5 years; matched on sex, age at interview (within 5 years), hospital, interviewer; 107 men and 54 women had non-alcohol-related malignancies; refusal rate, 0.5%	Questionnaire and interview on smoking, use of alcohol, coffee drinking, height, weight.	Men Women	NR	0.9 (0.5–1.6) 1.1 (0.5–2.1)		Exposure categories not defined; no trend in association of daily consumption of alcoholic beverages with cancer

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Kreiger <i>et al.</i> (1993), Canada, 1986–87	513 (312 men, 201 women) newly diagnosed renal-cell carcinomas resident in the province of Ontario, aged 25–69 years; 100% histologically confirmed; response rate, 81%	1369 (664 men, 705 women) selected from the 1986–87 Enumeration Composite Records of the Ministry of Revenue; matched 1:1 (men) or 2:1 (women) on age, sex, place of residence; response rate, 72%	Questionnaire on diet habits, socio-demographic data, smoking habits, medical history, job exposures and history, diuretic or analgesic use, hormonal and reproductive information (women only)	Alcohol intake			Age, active cigarette smoking, Quetelet index (combined for two time points: at 25 years of age, and at 5 years prior to the study)	*High = top 10% of the distribution	
				<i>Men</i>	None	43			1.0
				Moderate	173	0.9 (0.6–1.3)			
				High*	36	1.3 (0.7–2.4)			
				<i>Women</i>	None	65			1.0
				Moderate	84	0.7 (0.5–1.0)			
High*	18	0.7 (0.4–1.4)							
Mellempgaard <i>et al.</i> (1994), Denmark, 1989–91	368 (226 men, 142 women) renal-cell carcinomas of 482 diagnosed, born and living in Denmark, identified via the Danish Cancer Registry, aged 20–79 years; 100% histologically confirmed; refusal rate, 6.8%	396 (237 men, 159 women) of 500 identified from Central Population Register via the personal identification number, born and living in Denmark, aged 20–79 years; refusal rate, 14.4%	Questionnaire on education, jobs, height, weight, medical history, family history of cancer, smoking, alcohol use and diet; data recorded for the period ≥ 1 year prior to interview	Weekly intake			Age, socioeconomic status, body mass index, cigarette pack-years		
				<i>Men</i>	Not regularly	43		1.0	
				<75 mL	68	1.0 (0.6–1.8)			
				75–300 mL	68	0.8 (0.5–1.5)			
				>300 mL	45	0.8 (0.4–1.6)			
				<i>Women</i>	Not regularly	89		1.0	
				<40 mL	31	1.0 (0.5–1.8)			
				40–100 mL	12	0.5 (0.2–1.2)			
				>100 mL	9	0.4 (0.2–0.9)			

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments			
Muscat <i>et al.</i> (1995), USA, 1977–93	788 (543 men, 245 women; >90% white) newly diagnosed renal-cell cancers in 7 hospitals; 100% histologically confirmed; mean age, 58.7 years for men, 59.3 years for women	779 (529 men, 250 women; >90% white) patients hospitalized for non-tobacco-related conditions: 52% histologically confirmed cancers (excluding kidney, lung, upper aerodigestive tract, stomach, bladder and pancreas), 7% benign prostatic hypertrophy; excluding emphysema, hepatitis, cirrhosis, bronchitis, stroke and heart disease patients; frequency-matched by age (± 5 years), race, year of diagnosis	Interview with questionnaire on demographics, tobacco/alcohol consumption, medical history, occupational exposures	<i>Wine (oz/day)*</i>							
				Never/occasionally	510	1.0	Age, education, years of smoking	*Alcohol intake expressed in oz of whisky equivalents: 8 oz beer = 4 oz wine = 1 oz hard liquor			
				1–<4	27	0.9 (0.5–1.7)					
				>4	6	0.9 (0.8–1.0)					
				<i>Beer (oz/day)</i>							
				Never/occasionally	409	1.0					
				1–<4	87	0.9 (0.6–1.2)					
				4–7	19	0.8 (0.4–1.5)					
				>7	27	1.1 (0.6–2.0)					
				<i>Hard liquor (oz/day)</i>							
				Never/occasionally	428	1.0					
				1–<4	73	1.0 (0.7–1.4)					
				4–7	22	1.9 (0.9–4.3)					
>7	20	0.6 (0.3–1.1)									
<i>Wine (oz/day)</i>											
Never/occasionally	219	1.0									
1–<4	23	1.2 (0.6–2.3)									
<i>Beer (oz/day)</i>											
Never/occasionally	237	1.0									
1–<4	8	0.6 (0.2–1.4)									
<i>Hard liquor (oz/day)</i>											
Never/occasionally	227	1.0									
1–<4	18	1.1 (0.6–2.2)									

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Wolk <i>et al.</i> (1996), multi-centre, Australia, Denmark, Sweden, USA, 1989–91	1185 incident renal-cell adenocarcinomas newly diagnosed identified in cancer registries in Sidney, Denmark, Uppsala and Minnesota; mean age, 62 years (men), 63 years (women); 100% histologically confirmed	1526 selected from population registers (Denmark, Uppsala, electoral rolls (Sidney), Health Care beneficiary lists (Minnesota, 65–79-year age group) or by random-digit dialling (Minnesota, 20–64-year age group) chosen from the same area as cases; mean age, 62 years (men), 63 years (women); frequency-matched on sex, 5-year age group	Personal interview on use of tobacco, diuretics, analgesics, diet pills, anti-hypertension drugs, hormones and alcohol, height, weight, physical activity, reproductive and medical history, family history of cancer, job history; dietary intake assessed in a questionnaire (part of interview in Uppsala)	Total alcohol (drinks/week)	NR		Age, sex, study centre, body-mass index, smoking, total calories	* Sweden not included due to lack of data on specific alcoholic beverages; data for beer, port/sherry and spirit included
				<i>Men</i>	<1	1.0		
				1–3	1.1 (0.8–1.5)			
				4–7	1.0 (0.7–1.3)			
				8–14	0.9 (0.6–1.3)			
				≥15	1.0 (0.7–1.4)			
				<i>Women</i>	<1	1.0		
				1–2	0.8 (0.5–1.4)			
				2–4	0.6 (0.4–0.9)			
				5–9	0.5 (0.3–0.9)			
				≥10	0.5 (0.3–0.8)			
				Wine (glass/week)*				
				<i>Men</i>	0	1.0		
				<0.5	0.7 (0.5–1.2)			
0.5–0.6	0.8 (0.6–1.1)							
0.7–1.2	0.5 (0.3–1.0)							
≥1.3	0.8 (0.5–1.3)							
<i>Women</i>	0	1.0						
<0.5	0.5 (0.3–0.8)							
0.5–0.6	0.7 (0.5–1.1)							
0.7–2.9	0.3 (0.1–0.6)							
≥3.0	0.2 (0.1–0.4)							

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Lindblad <i>et al.</i> (1997), Sweden, 1989–91	379 of 542 eligible newly diagnosed renal-cell cancers among individuals born in Sweden and residing in any of eight counties in central Sweden between 1/6/89 and 31/12/91, identified via Regional Cancer Registries, aged, 20–79 years; mean age, 63.6 years (men), 64.4 years (women); 100% histologically confirmed; refusal rate, 12%	353 of 493 selected from the register of the same population; mean age, 62.7 years (men), 63.4 years (women); frequency-matched by sex, age (within 5 years); refusal rate, 26%	Interview with questionnaire on usual diet (63 items) prior to 1987, alcohol use, demographics, height, weight, physical activity, medical history, reproductive history, occupation and smoking; specific data collected on dietary habits 20 years ago	<i>Alcohol intake (g/day)*</i> <0.23 0.23 1.60 2.75	84 117 90 87	1.0 1.4 (0.8–2.3) 1.1 (0.6–2.0) 1.0 (0.6–1.7)	Age, sex, body mass index, smoking, level of education, total energy intake	*Alcohol intake defined in quartiles

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Mattioli <i>et al.</i> (2002), Italy, 1986–94	219 renal-cell carcinomas, registered in 1987–94 at the University Hospital of Bologna; 100% histologically confirmed; response rate, 67.6%	219 patients in the same hospital, admitted in 1991 with any disease but renal-cell carcinoma; matched on sex, age (within 5 years), birthplace, residence area; response rate, 67.6%	Questionnaire interview by telephone on height, weight, lifelong use of tobacco, alcohol, coffee and meat; job history	Alcohol intake (g/day)			Age, gender, birthplace, residence	
				<i>Men</i>				
				0	22	1.0		
				1–12	43	4.0 (1.1–14.8)		
				13–24	56	3.4 (1.1–10.3)		
				25–36	19	7.3 (1.2–44.6)		
				37–48	9	0.5 (0.1–2.5)		
				>48	16	1.0 (0.3–4.0)		
				<i>Women</i>				
0	20	1.0						
1–12	17	2.2 (0.3–16.1)						
>12	15	4.2 (0.3–53.5)						

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Parker <i>et al.</i> (2002), Iowa, USA	406 of 463 (261 men, 145 women) residents of Iowa with incident renal-cell carcinoma identified via the Iowa Cancer Registry, aged 40–85 years; 100% histo-logically confirmed; response rate, 88%	2429 controls (1598 men, 831 women); aged <65 years selected from Iowa driver's licence records; aged ≥65 years randomly selected from listings of Health Care Financing; matched by sex, 5-year age group; those with a history of cancer excluded; response rates, 82% (<65 years) and 79% (≥65 years)	Mailed questionnaire followed by telephone inter-view on demo-graphics, height and weight at various times in life, smoking history and status, medical history, job history, physical activity, family history of cancer; usual use of alcohol over all adult years ascertained in a food-frequency questionnaire	<i>Alcohol intake</i>		<i>Men</i>		Men: age, pack-years of smoking, family history of kidney cancer, history of hypertension, history of bladder infection, exercise, intake of red meat and fruit; women: age, pack-years of smoking, family history of kidney cancer, body mass index, history of hypertension, intake of red meat, vegetables and fruit
				Never	98	1.0		
				Ever	163	1.0 (0.7–1.5)		
				<i>Servings/week</i>				
				0	98	1.0		
				≤3	80	1.2 (0.8–1.8)		
				>3	83	0.9 (0.6–1.3)		
				<i>Ethanol (g/week)</i>				
				0	98	1.0		
				≤35	77	1.3 (0.9–1.9)		
				>35	86	0.9 (0.6–1.3)		
				<i>Wine (units/week)</i>				
				0	197	1.0		
				≤0.5	32	0.8 (0.5–1.3)		
>0.5	32	1.2 (0.7–2.0)						
<i>Beer (units/week)</i>								
0	127	1.0						
≤1	56	1.4 (0.9–2.0)						
>1	78	1.0 (0.7–1.4)						
<i>Liquor (units/week)</i>								
0	153	1.0						
≤1	57	1.4 (1.0–2.1)						
>1	51	1.1 (0.7–1.6)						

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Parker <i>et al.</i> (2002) (contd)				<i>Alcohol intake</i>			<i>Women</i>	
				Never	93	1.0		
				Ever	52	0.8 (0.5–1.2)		
				<i>Servings/week</i>				
				0	93	1.0		
				≤3	43	1.0 (0.6–1.5)		
				>3	9	0.4 (0.2–1.0)		
							<i>p for trend 0.04</i>	
				<i>Ethanol (g/week)</i>				
				0	93	1.0		
≤35	41	1.0 (0.6–1.5)						
>35	11	0.4 (0.2–0.9)						
			<i>p for trend 0.04</i>					
Pelucchi <i>et al.</i> (2002b), Italy, 1985–92	348 (236 men, 112 women) renal-cell cancers in general hospitals and university clinics in Milan and the Pordenone province, aged 25–77 years (median, 60 years); 100% histologically confirmed; refusal rate for interview, 4%	1048 (753 men, 295 women) patients admitted to the same hospitals and clinics for acute, non-neoplastic, non-urological and non-genital problems, aged 23–79 years (median, 60 years); refusal rate for interview, 4%	Questionnaire on personal characteristics, socio-demographic and lifestyle details (smoking, coffee drinking), intake of selected food items, medical history, alcohol intake	<i>Alcohol (drinks/day)</i>			Age, sex, study centre, education, body mass index, history of bladder infection, cigarette smoking, intake of vegetables, meat and fruit	Among women, 69% of the cases and 72% of the controls were drinkers; among men, these percentages were 88% and 91%, respectively.
				Never	64	1.0		
				Ever	284	0.8 (0.6–1.2)		
				<3	101	0.8 (0.5–1.1)		
				3–5	98	1.0 (0.6–1.5)		
				≥6	85	0.8 (0.5–1.3)		
				<i>Duration (years)</i>				
				<30	53	0.5 (0.3–0.7)		
				≥30	229	1.0 (0.7–1.5)		
				<i>Wine (drinks/day)</i>				
				0	68	1.0		
				<3	109	0.9 (0.6–1.3)		
				3–5	105	0.9 (0.6–1.4)		
				≥6	66	0.9 (0.6–1.5)		
<i>Beer</i>								
Never	270	1.0						
Ever	99	1.0 (0.7–1.4)						
<i>Spirits</i>								
Never	249	1.0						
Ever	99	1.1 (0.8–1.4)						

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments			
Hu <i>et al.</i> (2003), Canada, 1994–97	1279 (691 men, 588 women) incident renal-cell cancers in 8 provinces; 100% histologically confirmed; response rate, 79.9% of those contacted	5370 population, age-stratified; response rate, 71.3% of those contacted	Mailed questionnaire on socio-economic status, job history, residential history, height, weight, smoking history, physical activity, alcohol use, dietary history, food-frequency questionnaire	<i>Alcohol (servings/week)</i>				Age, province, education, smoking (not body mass index)			
				Never	217	1.0	<i>Men</i>				
				1–6	253	0.8 (0.6–1.0)					
				7–17	116	0.7 (0.5–0.9)					
				≥18	104	0.7 (0.5–0.9)	<i>p</i> -trend=0.006				
											<i>Women</i>
				Never	342	1.0					
				1–6	191	0.7 (0.6–0.9)					
				7–17	36	0.6 (0.4–0.8)					
				≥18	19	0.6 (0.4–1.1)	<i>p</i> -trend=0.0003				

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Bravi <i>et al.</i> (2007), Italy, 1992–2004	767 (494 men, 273 women) renal-cell carcinomas admitted to major hospitals, aged 24–79 years; median age, 62 years; 100% histologically confirmed; cancers of renal pelvis and ureter not included; refusal rate, <5%	1534 (988 men, 546 women) patients admitted to the same hospitals for acute non-neoplastic conditions, aged 22–79 years; (median age, 62 years; matched 2:1 by study centre, sex, age (5-year groups); refusal rate, <5%	Hospital-based interview with questionnaire on anthropometric measures, socio-demographic and lifestyle details, use of alcohol, tobacco, coffee, medical history, family history of cancer in first-degree relatives; food-frequency questionnaire on 78 items	<i>Drinks per week</i> Never <21 ≥21 Former drinkers*	131 361 212 63	1.0 0.88 0.80 0.97	None	*Former drinkers had not had a drink for ≥1 year

Table 2.80 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Hsu <i>et al.</i> (2007), multicentre, eastern Europe, 1999–2003	1065 newly diagnosed renal-cell cancers, aged, 20–79 years; 100% histologically confirmed; response rate, 90–98.6% across centres	1509 patients admitted to the same hospitals as cases with diagnoses unrelated to smoking or genitourinary disorders; frequency-matched on age, response rate, 90.3–96.1% across centres	In-person interview on usual weekly alcohol consumption during five periods of life; average lifetime consumption was calculated	<i>Intake (g/alcohol/week)</i>			Age, country, gender, tobacco use, education, body mass index, hypertension, medication, consumption of vegetables, white meat, red meat	Data for wine, beer and liquor separately also presented in article
				None	274	1.0		
				<36.5	310	1.18 (0.93–1.49)		
				36.5–137.5	290	1.15 (0.88–1.48)		
				137.5	191	0.83 (0.61–1.12)		
				Top decile of alcohol intake	27	0.39 (0.24–0.66)		

CI, confidence interval; NR, not reported

the results of the pooled analysis, although no formal meta-analysis of these studies is available.

2.16.4 *Type of alcohol*

In the Pooling Project of cohort studies (Lee *et al.*, 2007), inverse trends were seen for beer, wine and liquor, but only the trend for wine was statistically significant. However, the relative risks for different beverages did not differ significantly from each other.

The data from the case–control studies also did not provide clear evidence that the inverse association with kidney cancer was limited to a specific beverage.

2.16.5 *Interactions*

The associations between alcoholic beverage intake and kidney cancer did not vary appreciably by body mass index, history of hypertension, smoking status or age at diagnosis.

2.17 **Cancers of the lymphatic and haematopoietic system**

Lymphomas and haematopoietic malignancies comprise a heterogeneous group of malignancies and their etiology is not fully understood. There is a growing number of epidemiological studies that have examined the associations of alcoholic beverage consumption with the risk for these cancers.

2.17.1 *Cohort studies*

(a) *Special populations (Table 2.81)*

Five studies among heavy alcoholic beverage users or brewery workers have investigated the risk for lymphatic and/or haematopoietic cancers (Hakulinen *et al.*, 1974; Jensen, 1979; Robinette *et al.*, 1979; Schmidt & Popham, 1981; Carstensen *et al.*, 1990). Among the three studies that examined lymphatic/haematopoietic cancers combined, one showed no significant differences between the observed number of cases among Danish brewery workers, compared with the expected number of cases computed from age-, sex- and area-specific rates (Jensen, 1979); one showed a slightly increased risk for these cancers among Swedish brewery workers compared with the expected number of cases calculated using age-, follow-up time- and area-standardized rates for the Swedish male population (Carstensen *et al.*, 1990); and another showed a non-significant decreased risk among chronic alcoholic male US veterans compared with expected numbers computed from age- and time-specific rates for US men (Robinette *et al.*, 1979).

Table 2.81 Cohort studies of alcoholic beverage consumption and cancers of the lymphatic and haematopoietic system in special populations

Reference, location	Cohort description	Organ site (ICD code)	No. of cases/deaths Obs (Exp)	SIR/SMR (95% CI)	Adjustment factors	Comments
Hakulinen <i>et al.</i> (1974), Helsinki, Finland	Approximately 205 000 male alcohol misusers and a mean of 4370 male chronic alcoholics, aged >30 years, registered as chronic alcoholics between 1967 and 1970; morbidity during same period determined from Finnish Cancer Registry	Lymphoma, Hodgkin disease Leukaemia	1 (1.67) 1 (1.22)	[0.60 (0.02–3.34)] [0.82 (0.02–4.57)]	None	The expected numbers of cases were calculated from data from the Finnish Cancer Registry (1965–68). The exact amount of alcohol consumed by these men was unknown.
Jensen (1979), Denmark	14 313 Danish brewery workers employed at least 6 months in 1939–63; followed for cancer incidence and mortality in 1943–73; age not given; workers were allowed 2.1 L of free beer/day (77.7 g pure alcohol).	Lymphatic and haematopoietic Leukaemia	68 (65.98) 25 (26.33)	SIR 1.03 (0.80–1.31) SMR 0.95 (0.61–1.40)	Age, sex, area (capital/provincial towns)	Expected numbers were computed from age-, sex- and area-specific rates and corresponding perso–years at risk.

Table 2.81 (continued)

Reference, location	Cohort description	Organ site (ICD code)	No. of cases/deaths Obs (Exp)	SIR/SMR (95% CI)	Adjustment factors	Comments
Robinette <i>et al.</i> (1979), USA	4401 chronic alcoholic male veterans, hospitalized in 1944–45 and followed in 1946–74 for mortality; 29 years follow-up, age not given	Lymphatic and haematopoietic (ICD-8 200–209)	13 (17.3)	[0.75 (0.40–1.28)]	Age	Expected mortality was computed from age- and time-specific rates for US males that were applied to the actual numbers of person–years at risk at each age and in each calendar year.
		Leukaemia (ICD-8 204–207)	3 (6.4)	[0.47 (0.10–1.37)]		
		Haemato-poietic (ICD-8 200–203, 208–209)	10 (10.9)	[0.92 (0.44–1.69)]		
Schmidt & Popham (1981), Ontario, Canada	9889 alcoholic men, aged ≥ 15 years, admitted to the clinical service of the Addiction Research Foundation of Ontario between 1951 and 1970; maximum 21 years of follow-up	Malignant lymphoma (ICD-7 200, 201, 203)	5 (10.67)	0.47 [0.15–1.09]	Age	Expected deaths were calculated using the age-specific death rates for the general male population.
		Leukaemia (ICD-7 204)	3 (6.94)	0.43 [0.09–1.26]		

Table 2.81 (continued)

Reference, location	Cohort description	Organ site (ICD code)	No. of cases/deaths Obs (Exp)	SIR/SMR (95% CI)	Adjustment factors	Comments
Carstensen <i>et al.</i> (1990), Sweden	6230 men occupied in the Swedish brewery industry at the time of the 1960 census and followed between 1961 and 1979, aged 20–69 years	Lymphatic and haematopoetic (ICD-7 200–205) Leukaemias (ICD-7 204)	60 (46.9) 30 (19.1)	1.28 (0.98–1.65) 1.57 (1.06–2.24)	Age, follow-up period, region	Expected numbers of cases were calculated using the total male population as a reference and with standardization for year of birth, follow-up period and region of residence in 1960.

CI, confidence interval; ICD, International Classification of Diseases; Obs (Exp), observed (expected); SIR, standardized incidence ratio; SMR, standardized mortality ratio

In two studies, the observed number of cases of lymphoma among alcoholics was lower than that expected based on rates for the general population (Hakulinen *et al.*, 1974; Schmidt & Popham, 1981).

In studies among alcoholics, the observed number of cases of leukaemia did not differ significantly from those expected in one study (Hakulinen *et al.*, 1974), and was non-significantly lower in two other studies (Robinette *et al.*, 1979; Schmidt & Popham, 1981). Among brewery workers, a Danish study found no significant difference between the observed and expected number of leukaemia deaths (Jensen, 1979), while a Swedish study found a 1.6-fold higher risk of mortality among brewery workers compared with that expected from the local population (Carstensen *et al.*, 1990).

(b) *General population (Table 2.82)*

Four prospective cohort studies examined associations between alcohol intake and the risk for the lymphatic and/or haematopoietic cancers (Boffetta *et al.*, 1989; Kato *et al.*, 1992c; Chiu *et al.*, 1999; Lim *et al.*, 2006).

For non-Hodgkin lymphoma specifically, Chiu *et al.* (1999) found a non-significant inverse association with alcoholic beverage intake among postmenopausal women in the USA. This relationship persisted after adjustment for several potential confounding factors including age, total energy intake, residence (farm, no farm), education, marital status, history of transfusion and diabetes, and intake of red meat and fruit. [The Working Group noted that the level of alcohol intake was very low in this study.] In the only other cohort study of non-Hodgkin lymphoma and alcoholic beverage consumption, Lim *et al.* (2006) found weak evidence of an inverse association among male Finnish smokers in a multivariate analysis.

In a study among American men of Japanese ancestry that also considered several potential lifestyle, medical and dietary confounding factors, results were presented for lymphoma and leukaemia combined. A threefold higher risk for lymphoma/leukaemia was associated with consumption of ≥ 30 mL alcohol per day compared with non-drinkers (Kato *et al.*, 1992c).

In the two prospective cohort studies that assessed the association between alcoholic beverage intake and the risk for multiple myeloma, one study found no association (Lim *et al.*, 2006) and one found a lower risk among ever regular drinkers compared with never regular drinkers (Boffetta *et al.*, 1989).

2.17.2 *Case-control studies*

(a) *Lymphoma (Hodgkin disease, non-Hodgkin lymphoma and other lymphomas) (Table 2.83)*

Sixteen published case-control studies examined associations between alcoholic beverage intake and the risk for lymphomas (Williams & Horm 1977; Cartwright *et al.*, 1988; Brown *et al.*, 1992; Nelson *et al.*, 1997; Tavani *et al.*, 1997; De Stefani *et al.*,

Table 2.82 Cohort studies of alcoholic beverage consumption and cancers of the lymphatic and haematopoietic system in general populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Boffetta <i>et al.</i> (1989), USA, American Cancer Society (ACS) Cancer Prevention Study II	Case-control study nested within a prospective cohort of 508 637 men and 676 613 women, aged ≥ 30 years, who completed a questionnaire in 1982 and were followed up for mortality for 4 years; cause of death determined from the death certificate; 282 multiple myeloma cases (128 incident, 154 prevalent) matched 1:4 to controls on sex, ACS division, year of birth, ethnic group	Self-administered questionnaire that asked about drinking history	Multiple myeloma (incident)	Ever regular drinker	20	0.6 (0.3–1.0)	Age, sex, ethnic group	Analyses were presented using incident cases only.

Table 2.82 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments	
Kato <i>et al.</i> (1992c), Oahu, Hawaii, USA, Honolulu Heart Study	6701 American men of Japanese ancestry, born in 1900–19, residents of Oahu with no personal history of cancer at baseline who were identified by the Selective Service draft file of 1942; interviewed in 1965–68; 19-year follow-up for cancer incidence using SEER Registry	24-h diet recall during in-person interview to obtain usual monthly and actual intake of beer, spirits and wine (including sake)	Lymphoma, leukaemia (ICD-8 200–202, 204–207)	<i>Ethanol (mL/day)</i>		19	1.0	Age, cigarette smoking	Of the total alcohol consumed by participants, 69% was beer, 24% spirits, 7% wine.
				<30		25	1.0 (0.6–1.9)		
				≥30		21	3.1 (1.6–5.9)		
							<i>p</i> -trend<0.01		
				<i>Beer (mL/day)</i>		20	1.0		
				<500		26	1.5 (0.9–2.8)		
≥500		19	2.8 (1.5–5.3)						
			<i>p</i> -trend<0.01						

Table 2.82 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chiu <i>et al.</i> (1999), Iowa, USA, Iowa Women's Health Study	35 156 postmenopausal women, aged 55–69 years, who completed a mailed questionnaire in 1986, had no personal history of cancer and a total calorie intake of 600–5000 Kcal; followed through 1994 for cancer incidence using Iowa SEER data; 143 incident NHL cases developed	Mailed food-frequency questionnaire including usual intake of beer, wine and spirits over the last year	NHL (ICD-O 9590, 9670–3, 9675, 9680–2, 9684–6, 9690–3, 9695–6, 9698, 9700)	<i>Ethanol (g/day)</i> 0 ≤3.4 >3.4	96 27 20	1.0 0.78 (0.51–1.21) 0.59 (0.36–0.97) <i>p</i> -trend=0.03	Total energy, age, residence, education, marital status, transfusion history, diabetes history, intake of red meat, fruit	Inverse associations also seen for wine, liquor intake and beer intake

Table 2.82 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Lim <i>et al.</i> (2006), Finland, α -Tocopherol β Carotene Cancer Prevention (ATBC) Study	27 111 healthy Finnish male smokers (≥ 5 cigarettes per day), aged 50–69 years, with no personal history of cancer who completed a baseline dietary questionnaire, randomized to a supplement that contained α -tocopherol, β -carotene, both or placebo; followed up to 16.4 years for cancer incidence using the Finnish Cancer Registry; 195 NHL, 11 HL and 32 MM cases developed	Self-administered dietary questionnaire to assess intake over the previous 12 months	NHL (ICD-O2 9590-9595, 9670–9677, 9680–9688, 9690–9698, 9700–9715, 9823), MM (9732), HL (9650, 9652–9655, 9657–9667)	Ethanol (g/day) <i>NHL</i> 0 0.04–5.2 5.3–13.3 13.4–27.6 27.7–278.5	19 55 43 46 32	0.67 (0.40–1.14) 1.0 (reference) 0.83 (0.56–1.24) 0.97 (0.65–1.45) 0.76 (0.49–1.20)	Age, calories, education, smoking history, serum high-density lipoprotein	Alcohol non-significantly inversely associated with DL, FL, TCL and non-significantly positively associated with CLL, SLL; No association between alcohol intake and MM (data not shown)

CI, confidence interval; CLL, chronic lymphocytic leukemia; DL, diffuse lymphoma; FL, Follicular lymphoma; HL, Hodgkin lymphoma; ICD, International Classification of Diseases; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; SEER, Surveillance, Epidemiology, and End Results; SLL, small lymphocytic lymphoma; TCL, T-cell lymphoma

Table 2.83 Case-control studies of alcoholic beverage consumption and lymphomas

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Williams & Horm (1977), Multicentre, USA	42 exposed men, 54 exposed women; 46 exposed men, 23 exposed women with incident, invasive cancer from the Third National Cancer Survey	1746 men, 3134 other cancers; 1742 men, 3165 other cancers; from the Third National Cancer Survey; excluding cancers of the lung, larynx, mouth, oesophagus, bladder	Interviewer-administered standardized questionnaire	Lympho-sarcoma; HD	Lymphosarcoma			Age, race, smoking	Controls excluded cancers of the lung, larynx, mouth, oesophagus, urinary bladder; for other lymphomas, fewer than 11 cases for women and fewer than 18 for men; results presented only for lymphosarcoma and Hodgkin disease
					<i>Men</i>				
					None		1.0		
					<51 oz/years	5	0.40		
					≥51 oz/years	8	0.53		
					<i>Women</i>				
					None		1.0		
					<51 oz/years	8	0.94		
					≥51 oz/years	3	0.75		
					Hodgkin disease				
					<i>Men</i>				
					None		1.0		
					<51 oz/years	7	0.45		
					≥51 oz/years	7	0.82		
<i>Women</i>									
None		1.0							
<51 oz/years	4	0.87							
≥51 oz/years	0	-							
Other lymphomas									
<i>Men</i>									
None		1.0							
<51 oz/years	4	0.19							
≥51 oz/years	1	0.74							
<i>Women</i>									
None		1.0							
<51 oz/years	1	0.50							
≥51 oz/years	0	-							

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments	
Cartwright <i>et al.</i> (1988), Yorkshire, United Kingdom, 1979–84	437 cases (244 men, 193 women) from hospitals in Yorkshire, aged ≥ 15 years; 100% histologically confirmed; response rate, 31%	724 hospital-based with diseases unrelated to smoking; matched 2:1 by sex, age (± 3 years), residential district; response rate not given	Interviewer-administered standardized questionnaire	NHL	Wine drinker	50	<2.0 ($p>0.05$)	Not given	27 cases and 22 controls had had a previous non-skin cancer.	
Brown <i>et al.</i> (1992), Iowa, Minnesota, USA, 1981–84	622 white men (438 living, 184 deceased) from Iowa Health Registry and Minnesota surveillance network, aged ≥ 30 years; 100% histologically confirmed; response, 89%	1245 white male population-based (820 alive, 425 deceased) selected by RDD (alive and <65 years), HCFA (≥ 65 years) or death certificate (deceased); frequency-matched to cases on age (± 5 years), vital status at time of interview, state; response rate, 78%	Interviewer-administered standardized questionnaire	NHL	Drinker versus non-drinker	461	0.9 (0.7–1.1)	Age, state, tobacco use	Drinkers were subjects who had ever consumed any alcoholic beverage at least weekly; no significant associations with lymphoma subtype (follicular, diffuse, small lymphocyte) or with intake of liquor only or beer or wine only; farming, education, family history of cancer and exposure to high-risk jobs or chemicals did not confound results; population overlaps with Chiu <i>et al.</i> (2002).	
					<i>Drinks/week</i>					
					Non-drinker	357	1.0			
					<5	117	0.7 (0.5–1.0)			
					5–11	120	1.0 (0.7–1.4)			
12–23	121	0.9 (0.6–1.2)								
>23	103	0.9 (0.7–1.3)								

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Nelson <i>et al.</i> (1997), Los Angeles County, USA, 1989–92	378 (185 men, 193 women) from a population-based cancer registry in Los Angeles, CA, aged 18–75 years; 100% histologically confirmed; response rate, 35%	378 population-based controls (185 men, 193 women); matched 1:1 on sex, age (± 3 years), race/ethnicity, language of interview, neighbourhood; response rate not given	Interviewer-administered standardized questionnaire that asked about weekly alcohol use before the reference date	NHL	Men			Matching factors adjusted for using conditional logistic regression	All cases and controls HIV negative; no significant differences in associations according to alcoholic beverage type
					<i>Drinks/week</i>				
					Non-drinker	69	1.0		
					Current drinker	46	0.68 (0.43–1.08)		
					0.1–4	37	0.61 (0.34–1.12)		
					5–11	29	0.45 (0.24–0.84)		
					≥ 12	50	1.09 (0.60–1.98)		
							<i>p</i> -trend=0.82		
					Women				
					<i>Drinks/week</i>				
Non-drinker	122	1.0							
Current drinker	71	0.63 (0.40–1.00)							
0.1–4	45	0.74 (0.43–1.27)							
5–11	13	0.51 (0.24–1.06)							
≥ 12	13	0.50 (0.23–1.09)							
		<i>p</i> -trend=0.03							
Tavani <i>et al.</i> (1997), Milan and Pordenone, Italy, 1983–92	829 cases (158 HD, 429 NHL, 141 MM, 101 STS); aged 17–79 years; 100% histologically confirmed; response rate, >97%	1157 hospital-based, aged 17–79 years; response rate, >97%	Interviewer-administered structured questionnaire	HD, NHL	Alcohol drinking			Centre, age, sex	This study partially overlaps with Tavani <i>et al.</i> (2001b)
					HD				
					Tertile 1	33	1.0		
					Tertile 2	68	1.1 (<i>p</i> >0.05)		
					Tertile 3	57	0.9 (<i>p</i> >0.05)		
					NHL				
					Tertile 1	67	1.0		
Tertile 2	172	0.8 (<i>p</i> >0.05)							
Tertile 3	190	0.8 (<i>p</i> >0.05)							
De Stefani <i>et al.</i> (1998b), Uruguay, 1988–95	160 (85 men, 75 women) from a single oncology institution in Uruguay, aged 20–84 years; histological confirmation not given; response rate, 36.7%	163 hospital-based (86 men, 77 women); frequency-matched to cases on sex, age (± 10 years), residence, urban/rural status	Interviewer-administered standardized questionnaire	NHL	Men			Age, year of diagnosis, residence, urban/rural status, 'mate' years, salted meat intake, type of tobacco	No significant association with wine or liquor intake, but a positive association with ≥ 61 mL/day beer intake (odds ratio, 5.5; 95% CI, 1.1–26.7)
					Never drinker	30	1.0		
					1–60 mL alcohol/day	20	1.4 (0.5–3.9)		
					≥ 61 mL alcohol/day	35	1.1 (0.5–2.5)		

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Matsuo <i>et al.</i> (2001), Nagoya, Japan, 1988–97	333 (202 men, 131 women) adults from a single cancer centre hospital; 100% histologically confirmed; response rate, 98.6%	55 904 non-cancer hospital outpatients (15 811 men, 40 093 women); response rate, 98.6%	Self-administered standardized questionnaire	Malignant lymphoma: HD + NHL + TCL (ICD-10, C81-85)	Never drinker	183	1.00	Age, sex	
					Former drinker	14	1.01 (0.85–1.77)		
					<1.5 drinks/day	13	1.57 (0.87–2.82)		
					≥1.5 drinks/day	1	0.18 (0.02–1.28)		
					Current drinker	136	0.67 (0.52–0.85)		
<1.5 drinks/day	87	0.63 (0.48–0.83)							
≥1.5 drinks/day	49	0.74 (0.52–1.04)							
Tavani <i>et al.</i> (2001b), Milan and Pordenone, Italy, 1981–94	446 cases (256 men, 190 women) from hospitals in Pordenone, aged 17–79 years; 100% histologically confirmed; response rate, 97%	1295 hospital-based (791 men, 504 women), aged 17–79 years; 97% response rate	Interviewer-administered standardized questionnaire	Incident NHL (200, 202)	<i>Total alcohol (drinks/day)</i>			Age, sex, centre, education, marital status, blood transfusions, diabetes, intake of milk, meat, green vegetables and fruit	Test for trend for spirit intake ($p=0.08$); no significant associations for total alcohol, wine, beer or spirit intake were associated with a borderline significantly increased risk.
					Non-drinker	68	1.0		
					<3	155	0.92 (0.65–1.30)		
					3–6	135	0.98 (0.66–1.45)		
					≥7	86	1.02 (0.64–1.63)		
		p trend=0.84							
Briggs <i>et al.</i> (2002), USA, 1984–88	960 living men identified from eight US population-based cancer registries, aged 32–60 years; 100% histologically confirmed; response rate, 88%	1717 male population-based (living) selected by RDD; frequency-matched to cases on date of birth (± 5 years), geographical region; response rate, 83%	Interviewer-administered standardized questionnaire	NHL (ICD-O 9591, 9600, 9602, 9611–13, 9621, 9630, 9640, 9642, 9691, 9694, 9696, 9750)	Never drinkers	300	1.0	Age, race/ethni-city, cancer registry, smoking history, education	No associations with beer or spirit intake; an inverse dose–response association of wine intake with risk for NHL ($p=0.02$), particularly for those who started drinking wine at age ≤ 16 years (p -trend= 0.004)
					All drinkers	660	0.9 (0.8–1.1)		
					Current drinker	490	0.9 (0.8–1.1)		
					Former drinker	170	1.0 (0.8–1.3)		
					Wine drinker				
					1–6 drinks/week	178	0.8 (0.5–1.3)		
					≥1 drink/day	46	0.4 (0.2–0.9)		
		p -trend = 0.02							

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Chiu <i>et al.</i> (2002), pooled analysis USA, Kansas, 1979–81; Iowa, Minnesota, USA, 1980–83	170 white men (79 living, 91 deceased) from Kansas statewide tumour registry, aged ≥ 21 years; 100% histologically confirmed; 622 white men (429 living, 193 deceased) from Iowa Health Registry and Minnesota surveillance network; aged ≥ 30 years; 100% histologically confirmed; response rate, 89%–96%	2193 white population-based men (1278 living, 915 deceased) selected by RDD (< 65 years), HCFA (≥ 65 years), or death certificate (deceased); frequency-matched to cases on age (± 5 years), vital status at time of interview, state; response rate, 77–93%	Interviewer-administered standardized questionnaire	NHL	<i>Ethanol (g/week)</i> Non-drinker Tertile 1 Tertile 2 Tertile 3	364 121 152 152	1.0 0.8 (0.6–1.0) 0.9 (0.7–1.1) 0.8 (0.7–1.1) <i>p</i> -trend=0.25	Age, state, marital status, type of respondent, first degree relative with HLPC, use of herbicides, tobacco use	Significant interaction of alcohol intake with family history of HLPC: positive association of alcohol with risk for NHL in those with a family history; no association in those with no family history

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Morton <i>et al.</i> (2003), Connecticut, USA, 1995–2001	601 living women identified from the Connecticut Tumor Registry, aged 21–84 years; 100% histologically confirmed; 72% response rate	718 female population-based (living) selected by RDD (<65 years), HCFA (≥65 years); frequency-matched to cases on age (± 5 years); response rate, 69% (RDD), 47% (HCFA)	Interviewer-administered standardized questionnaire	NHL (ICD-O 9590–9642, 9690–9701, 9740–9750)	Never drinker	230	1.0	Age, education	Race, family history of cancer, body mass index, smoking, menopausal status, daily fruit, fat, protein and animal protein intake did not confound results; no significant associations with beer or liquor consumption; significantly reduced risk for NHL associated with >40 years of wine drinking (<i>p</i> -trend=0.02) and ≥25 years at initiation of wine drinking.
					Ever drinker	371	0.82 (0.65–1.04)		
					<i>Ethanol (g/month)</i>				
					<70	124	0.82 (0.61–1.10)		
					70–300	126	0.83 (0.62–1.13)		
					>300	121	0.82 (0.60–1.10)		
					<i>Duration (years)</i>				
					1–24	138	1.05 (0.76–1.43)		
25–40	122	0.89 (0.65–1.22)							
>40	111	0.62 (0.46–0.85)	<i>p</i> -trend=0.01						

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Chang <i>et al.</i> (2004), Sweden, 2000–02	613 living (364 men, 249 women) identified from a network of physicians and the regional cancer registries, aged 18–74 years; 99% histologically confirmed; response rate, 75.5%	480 living (279 men, 201 women) identified using population registries, aged 18–74 years; frequency-matched to cases on sex, age (± 10 years); response rate, 66.8%	Self-administered standardized questionnaire	NHL (ICD-10 C82–85, 88.0, 91.3–5, 91.7), CLL (91.1)	Men			Age, smoking status	All subjects HIV-free; body mass index, height, education, history of rheumatoid arthritis, blood transfusion or skin cancer, occupational exposure to pesticides, dietary intake of dairy products, fried red meat and vegetables did not confound results; for all NHL, no associations for any specific type of alcohol; significant positive association of CLL (a subtype of NHL) with two highest categories of wine intake (p -trend=0.03)
					Never drinker	15	1.0		
					Current drinker	329	1.1 (0.5–2.4)		
					<i>Total alcohol(g/day)</i>				
					0–2.2	43	1.0		
					>2.2–8.4	61	1.5 (0.8–2.5)		
					>8.4–19.1	108	1.7 (1.0–2.9)		
					>19.1	147	1.8 (1.1–2.9)		
							p -trend=0.06		
					Women				
					Never drinker	26	1.0		
					Current drinker	213	1.0 (0.6–2.0)		
					<i>Total alcohol(g/day)</i>				
					0–2.2	103	1.0		
>2.2–8.4	66	0.8 (0.5–1.3)							
>8.4–19.1	57	0.8 (0.5–1.4)							
>19.1	22	0.7 (0.3–1.4)							
		p -trend=0.33							
			Sex, age, smoking status	Current versus never drinker					
Diffuse B-cell	NR	0.7 (0.3–1.4)							
CLL	NR	2.4 (0.9–6.5)							
Follicular	NR	1.0 (0.4–2.3)							
T-cell	NR	0.3 (0.1–0.9)							

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Willett <i>et al.</i> (2004), United Kingdom, 1988–2001	700 Caucasians (362 men, 338 women) identified through the Leeds General Infirmary or haematological departments in other hospitals, aged 18–64 years; 100% histologically confirmed; response rate, 75%	915 living (495 men, 420 women) identified from the same general practice as the case, aged 18–64 years; individually matched on sex, date of birth, residence; response rate, 71%	Interviewer-administered standardized questionnaire	NHL (ICD03 9679–84, 9690–98, 9689, 9699, 9673, 9700–19, 9827, 9659)	<i>Drinks/day</i> Never >0–1 >1–2 >2–4 >4–6 >6	34 315 198 85 33 35	0.91 (0.57–1.47) 1.0 0.79 (0.62–1.02) 0.89 (0.64–1.25) 0.81 (0.50–1.31) 0.84 (0.52–1.35)	Sex, age, region	Alcohol consumption defined as ever drinking wine, spirits, beer or lager \geq once a year in the 20 years preceding diagnosis/ pseudo-diagnosis; no evidence of an interaction between smoking status and alcohol intake; no associations for any specific beverage type or NHL subtype.
Morton <i>et al.</i> (2005), pooled analysis of nine case-control studies, Italy, Sweden, United Kingdom, USA, 1988–2002	6492 completed a questionnaire between 1990 and 2004, with electronic data available, data for alcohol intake, age 17–84 years; 100% histologically confirmed; participation rates, 68%–>97%	8683 RDD-, hospital-, population-based; participation rates, 47%–>97%	Standardized questionnaires	NHL	Non-drinker Ever drinker 1–6 drinks/week 7–13 drinks/week 14–27 drinks/week \geq 28 drinks/week	1804 4688 2027 958 951 745	1.0 0.83 (0.76–0.89) 0.81 (0.74–0.88) 0.83 (0.74–0.92) 0.85 (0.76–0.95) 0.87 (0.76–0.99) <i>p</i> -trend=0.97	Sex, age, ethnic origin, socioeconomic status	Associations did not differ by beverage type: significant or borderline significantly decreased risks; lowest risk observed for Burkitt lymphoma

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Besson <i>et al.</i> (2006a), Czech Republic, France, Germany, Ireland, Italy, Spain, 1998–2004	1742; 100% histologically confirmed; response rate, 82.1–91%	2465 hospital-based and population-based; matched by sex, age, residence/region; response rate, 44.4%–96.4%	In-person interview using standardized questionnaires	NHL (NR)	Regular drinking Never Ever <i>Ethanol (g/week)</i> ≤194 >194–≤730 >730	584 627 79 225 219	1.0 0.99 (0.84–1.18) 0.84 (0.62–1.15) 1.19 (0.94–1.49) 0.90 (0.71–1.15) <i>p</i> -trend=0.90	Sex, age, educational level, smoking status, centre	No association with any specific alcoholic beverage type; no significant differences in associations by histological subtype; generally lower risk of NHL for men but not for women; no interaction between alcohol drinking status and smoking status
Besson <i>et al.</i> (2006b), Czech Republic, France, Germany, Ireland, Italy, Spain, 1998–2004	340 (185 men, 155 women); aged ≥17 years, 100% histologically confirmed; response rate, 87.7%	2465 population- or hospital-based (1322 men, 1143 women); matched on sex, age (±5 years of birth), study region; response rates, 81.2% for hospital controls, 51.5% for population controls	Interviewer-administered standardized questionnaire	Hodgkin lymphoma	Regular drinking Never Ever	876 866	1.0 0.61 (0.43–0.87)	Sex, age, education, smoking status, centre	Stronger inverse association in older (≥35 years) versus younger (<35 years) individuals; inverse association strongest for wine for subjects <35 years; no interaction between alcohol and smoking for younger or older groups

Table 2.83 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD-9 code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment for potential confounding factors	Comments
Nieters <i>et al.</i> (2006), Germany, 1999–2002	710 (390 men, 320 women) recruited from physician offices and hospitals in six regions of Germany; aged 18–80 years; 46% histologically confirmed; response rate, 87.4%	710 population-based (390 men, 320 women); matched 1:1 on sex, age (± 1 years of birth), study region; response rate, 44.3%	Interviewer-administered standardized questionnaire	Lymphoma	Men			Education, pack-years of smoking	Non-drinker defined as <2 g ethanol/day for men and <0.5 g ethanol/day for women; alcohol intake assessed for 5–10 years prior to diagnosis; among men, significant inverse associations observed for all beverage types and for follicular, B-cell and Hodgkin lymphoma; among women, significant inverse associations observed for Hodgkin lymphoma.
					Non-drinker	101	1.0		
					Drinker	287	0.47 (0.31–0.71)		
					<i>Ethanol (g/day)</i>				
					2–<10	117	0.52 (0.33–0.81)		
					10–<40	129	0.41 (0.26–0.65)		
					≥ 40	41	0.50 (0.28–0.91)		
					Women				
					Non-drinker	85	1.0		
					Drinker	233	0.68 (0.45–1.03)		
<i>Ethanol (g/day)</i>									
0.5–<2	87	0.67 (0.42–1.07)							
2–<10	93	0.66 (0.41–1.08)							
≥ 10	53	0.73 (0.42–1.27)							

CI, confidence interval; CLL, chronic lymphocytic leukaemia; HCFA, Health Care Financing Administration; HD, Hodgkin disease; HIV, human immunodeficiency virus; HLPC, haematolymphoproliferative cancer; ICD, International Classification of Diseases; MM, multiple myeloma; NR, not reported; RDD, random-digit dialling; NHL, non-Hodgkin lymphoma; STS, soft tissue sarcoma; TCL, T-cell lymphoma

1998b; Matsuo *et al.*, 2001; Tavani *et al.*, 2001b; Briggs *et al.*, 2002; Chiu *et al.*, 2002; Morton *et al.*, 2003; Chang *et al.*, 2004; Willett *et al.*, 2004; Besson *et al.*, 2006a,b; Nieters *et al.*, 2006).

Most case–control studies of alcoholic beverage consumption and lymphoma focused specifically on non-Hodgkin lymphoma and/or its histological subtypes. In the study of Chang *et al.* (2004), a positive association was observed only for men and only for the histological subtype chronic lymphocytic leukaemia. In that study, all cases and controls were free of human immunodeficiency viral infection and careful consideration was given to several potential confounding factors including age, tobacco smoking and occupational exposure to pesticides. Most other studies of non-Hodgkin lymphoma observed an inverse association with alcoholic beverage intake. The largest of these studies (Briggs *et al.*, 2002) included 960 male (living only) cases and more than 1700 population-based controls and found no difference in the risk for non-Hodgkin lymphoma between drinkers and non-drinkers after adjustment of age, ethnicity and smoking status.

Most individual studies of non-Hodgkin lymphoma had limited power to conduct detailed analyses of alcoholic beverages and risk for this disease, particularly for specific beverage types and histological subtypes. Therefore, data from nine case–control studies conducted in Italy, Sweden, the United Kingdom and the USA were pooled to include 6492 cases of non-Hodgkin lymphoma and 8683 controls (Morton *et al.*, 2005). Results of that analysis showed a significantly lower risk for non-Hodgkin lymphoma for ever drinkers compared with non-drinkers; however, there was no consistent dose–response relationship between frequency of alcoholic beverage intake and risk for the disease. There was also no consistent evidence of an association with duration of alcoholic beverage drinking or with the age at starting drinking; moreover, the risk for non-Hodgkin lymphoma for current drinkers was lower than that for former drinkers in a subset of the pooled data. No difference in the association by alcoholic beverage type or a combination of beverage types consumed was observed. For specific subtypes of non-Hodgkin lymphoma, no significantly elevated risks were found. The lowest risk associated with ever drinking was that for Burkitt lymphoma (odds ratio, 0.51; 95% CI, 0.33–0.77 for ever versus non-drinker). Lower risks for diffuse B-cell, follicular and T-cell lymphomas were also associated with ever drinking. The authors noted that all disease misclassification was probably non-differential and therefore unlikely to explain a significant inverse association; findings were similar when analyses were restricted to studies that had a high response rate.

A multicentre case–control study of non-Hodgkin lymphoma and alcoholic beverage intake included data from five European countries and comprised 1742 cases and 2465 controls (Besson *et al.*, 2006a). Overall, there were no associations observed for ever drinking, age at starting drinking, duration of drinking or monthly consumption with risk for all non-Hodgkin lymphomas or with any histological subtype; similarly, no associations with risk for non-Hodgkin lymphoma were found for any specific type of alcoholic beverage. However, a lower risk associated with regular alcoholic beverage

intake was observed for men (odds ratio, 0.76; 95% CI, 0.62–0.93; 691 exposed cases) and for non-Mediterranean countries (odds ratio, 0.7; 95% CI, 0.6–0.9).

Among the four studies that examined Hodgkin lymphoma specifically (Williams & Horm, 1977; Tavani *et al.*, 1997; Besson *et al.*, 2006b; Nieters *et al.*, 2006), there was a consistent inverse association. For example, in the large multicentre European study, the odds ratio for Hodgkin lymphoma associated with ever regular drinking compared with never regular drinking was 0.61 (95% CI, 0.43–0.87; 81 exposed cases); this association was consistent for younger and older adults (Besson *et al.*, 2006b).

(b) *Leukaemia (Table 2.84)*

The association of alcoholic beverage intake with risk for adult leukaemia was examined in six epidemiological case–control studies (Williams & Horm, 1977; Brown *et al.*, 1992; Wakabayashi *et al.*, 1994; Pogoda *et al.*, 2004; Rauscher *et al.*, 2004; Gorini *et al.*, 2007). No consistent patterns of association between total alcoholic beverage intake and risk for all leukaemias combined were observed. Two studies showed a non-significant two- to threefold higher risk for acute lymphocytic leukaemia associated with heavy drinking (Wakabayashi *et al.*, 1994) or with any drinking (Brown *et al.*, 1992), a third found no association of drinking with risk for this type of leukaemia (Gorini *et al.*, 2007). Similarly, there was no consistent evidence of associations with acute non-lymphocytic, chronic lymphocytic or chronic myeloid leukaemias among studies. The available evidence also did not support an association for any specific alcoholic beverage type.

(c) *Multiple myeloma (Table 2.85)*

Five case–control studies (four in the USA and one in Canada) examined associations between alcoholic beverage intake and the risk for multiple myeloma (Williams & Horm, 1977; Gallagher *et al.*, 1983; Linet *et al.*, 1987; Brown *et al.*, 1992, 1997). In the largest study, there was a lower risk for multiple myeloma among drinkers compared with non-drinkers in white men and to a lesser extent in black men and white women (Brown *et al.*, 1997). There was a non-significant 2.8-fold higher risk for multiple myeloma for white women who consumed ≥ 22 drinks per week (Brown *et al.*, 1997). Among the other case–control studies, no consistent patterns of association were observed. It should be noted that most studies collected data on alcoholic beverage consumption from proxy respondents, and that some included prevalent cases. In addition, not all studies controlled for the potential confounding effects of tobacco smoking, and only one controlled for other factors such as farming, family history of cancer and occupational exposure to high-risk chemicals (Brown *et al.*, 1992).

2.17.3 *Parental exposure and childhood cancers (Table 2.86)*

Six case–control studies in Australia, Canada, Europe and the USA examined associations of paternal alcoholic beverage intake before pregnancy and/or maternal

Table 2.84 Case-control studies of alcoholic beverage consumption and leukaemia

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Williams & Horm (1977), Multicentre, USA	33 exposed men, 29 exposed women with incident, invasive cancer from the Third National Cancer Survey	1755 men, 3159 women with other cancers (excluding lung, larynx, mouth, oesophagus, urinary bladder) from the Third National Cancer Survey	Interviewer-administered standardized questionnaire	CLL	<i>Men</i>		1.0	Age, race, smoking	For other histological subtypes, fewer than 16 cases for women, and less than 17 cases for men; results are presented only for CLL.
					None	9	2.0 (NR)		
					<51 oz/year	8	1.10 (NR)		
					≥51 oz/year				
					<i>Women</i>		1.0		
					None	3	0.71 (NR)		
					<51 oz/year	2	1.20 (NR)		
					≥51 oz/year				

Table 2.84 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Brown <i>et al.</i> (1992), Iowa, Minnesota, USA, 1981–84	578 white men (340 living, 238 deceased) from Iowa Health Registry and Minnesota surveillance network, aged ≥ 30 years; 100% histologically confirmed; response rate, 86%	820 white population-based men selected by RDD (alive and < 65 years), HCFA (≥ 65 years) or death certificate (deceased); frequency-matched to cases on age (± 5 years), vital status at time of interview, state; response rate, 78%	Interviewer-administered standardized questionnaire	Leukaemia	<i>Drinker versus non-drinker</i>			Age, state, tobacco use	Drinkers were subjects who had ever consumed any alcoholic beverage at least weekly; farming, education, family history of cancer and exposure to high-risk jobs or chemicals did not confound results; no meaningful associations with any specific beverage type.
					All leukaemia	333	1.3 (0.8–1.3)		
					ANLL	72	0.8 (0.5–1.1)		
					CML	31	1.0 (0.6–1.9)		
					CLL	138	1.0 (0.7–1.3)		
					ALL	12	3.0 (0.9–9.9)		
Myelodysplasia	41	1.6 (0.9–2.7)							
Other	39	1.5 (0.8–2.6)							

Table 2.84 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Wakabayashi <i>et al.</i> (1994), Hyogo, Japan, 1981–90	142 (87 men, 55 women) ALL, ANL or CLL treated at a single institution in Hyogo, Japan, aged ≥18 years; histological confirmation not given; response rate not given	284 hospital-based (174 men, 110 women) from the Department of Ophthalmology; matched 2:1 on sex, age; response rate not given	Clinical chart abstraction	Leukaemia	Ethanol (g/day)			None		
						<i>ANLL</i>				
						0	48			1.0
						1–21	18			2.52 (1.08–5.89)
						22–43	3			2.52 (0.35–18.36)
						≥44	6			1.89 (0.52–6.91)
						<i>ALL</i>				
						0	65			1.0
						1–21	22			2.44 (1.14–5.25)
						22–43	4			1.09 (0.28–4.27)
						≥44	8			2.44 (0.72–8.32)
						<i>CLL</i>				
						0	35			1.0
1–21	6	2.87 (0.56–14.7)								
22–43	2	0.38 (0.07–2.04)								
≥44	–	–								
Pogoda <i>et al.</i> (2004), Los Angeles County, CA, USA, 1992–94	164 (88 men, 76 women) from a population-based cancer registry in Los Angeles, CA, aged 25–75 years; histological confirmation not given; response rate, 57%	164 population-based (88 men, 76 women); matched 1:1 on sex, birth (± 5 years), race/ethnicity, neighbourhood; response rate not given	Interviewer-administered standardized questionnaire	AML (ICD-O 9861, 9864, 9866, 9867, 9891)	<i>Ethanol (g/day)</i>			Education, pack-years of smoking		
						0	24			1.0
						1–3	9			0.7 (0.3–1.5)
						4–10	10			0.7 (0.3–1.4)
						>10	6			0.8 (0.4–1.6)
										<i>p</i> -trend=0.2

Table 2.84 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Rauscher <i>et al.</i> (2004), Multicentre, USA, 1986–89	765 incident from clinical sites throughout the USA; median age, 48 years; histological confirmation not given; response rate, 84%	618 population-based identified by RDD; frequency-matched by sex, age (\pm 10 years), race, region of residence; response rate, 66%	Interviewer-administered questionnaire	Acute leukaemia	Regular versus non-regular drinker <i>Drinks/week</i>	NR	0.75 (0.60–93)	Age, race, sex, region, education	524 cases and 540 controls were self-respondents; smoking, solvent and exposure to ionizing radiation exposure did not confound results; significant inverse associations for light and moderate beer intake.
					<1	383	1.0		
					1–5	148	0.69 (0.52–0.92)		
					6–8	62	0.59 (0.40–0.87)		
					>8	172	0.88 (0.66–1.2)		

Table 2.84 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Gorini <i>et al.</i> (2007), Italy, 1990–93	649 (381 men, 268 women) from population-based cancer registries and clinical, pathology records in 11 areas; aged 20–74 years; 100% histologically confirmed; response rate, 88%	1771 population-based (913 men, 858 women) randomly selected through computerized demographic files or from National Health Service files, aged 20–74 years; frequency-matched to cases on sex, age, area of residence; response rate, 81%	Interviewer-administered standardized questionnaire	Leukaemia (ICD-O 204–208)	Ethanol (g/day)			Age, gender, smoking status, area of residence, educational level, type of interview	No associations between total alcohol intake and risk for ALL or CLL; no significant associations with beer or liquor consumption; wine consumption associated with a borderline significantly increased risk for all leukaemias, ALL and CLL (tests for trend, $p=0.001$, $p=0.004$, $p=0.01$, respectively).	
					<i>All leukaemias</i>	Ever versus never	519			0.97 (0.74–1.26)
						Non-drinker	119			1.0
						<9.0	83			0.73 (0.51–1.03)
						9.1–7.9	152			1.05 (0.77–1.43)
						18.0–1.7	126			1.03 (0.74–1.45)
						>1.7	158			1.15 (0.82–1.63)
			<i>p</i> -trend=0.007							
			<i>ALL</i>	Ever versus never	37	0.88 (0.40–1.93)				
			<i>CLL</i>	Ever versus never	168	0.86 (0.58–1.28)				

ALL, acute lymphocytic leukaemia; AML, acute myeloid leukaemia; ANLL, acute non-lymphocytic leukaemia; CI, confidence interval; CLL, chronic lymphocytic leukaemia; CML, chronic myeloid leukaemia; HCFA, Health Care Financial Administration; ICD, International Classification of Diseases; NR, not reported; RDD, random-digit dialling

Table 2.85 Case-control studies of alcoholic beverage consumption and multiple myeloma

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Williams & Horm (1977), Multicentre, USA	37 exposed men, 34 exposed women with incident invasive cancer from the Third National Cancer Survey	1751 men, 3154 women with other cancers (excluding lung, larynx, mouth, oesophagus, bladder) from the Third National Cancer Survey	Interviewer-administered standardized questionnaire	Multiple myeloma	Men		1.0	Age, race, smoking	
					None				
					<51 oz/years	1	0.19 (NR)		
					≥51 oz/years	10	0.74 (NR)		
					Women		1.0		
					None				
					<51 oz/years	2	0.42 (NR)		
					≥51 oz/years	3	0.93 (NR)		
Gallagher <i>et al.</i> (1983). Vancouver, Canada, 1972–81	84 living (49 men, 35 women) incident and prevalent from a single clinic, aged 34–83 years; histological confirmation not given; response rate, 100%	84 patients with non-head and neck cancers (26 gastrointestinal, 10 basal-cell carcinoma, 27 breast/female genital, 7 male genital, 1 brain, 12 haematopoietic); diagnosed in 1977–80; matched 1:1 on sex, age (±5 years), year of diagnosis (±5 years); response rate, 100%	Interviewer-administered standardized questionnaire	Multiple myeloma	NR	NR	No association (data not shown)	Matching factors adjusted for using conditional logistic regression	

Table 2.85 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Linet <i>et al.</i> (1987), Baltimore, MD, USA, 1975–82	100 (19 direct, 81 proxy) ascertained from seven Baltimore area hospitals; whites who were residents of the area; 100% histologically confirmed; response rate, 83%	100 hospital-based randomly selected from non-cancer patients (53 direct, 47 proxy); matched (1:1) on sex, age (± 5 years), year of diagnosis; response rate, 68%	Interviewer-administered standardized questionnaires by telephone	Multiple myeloma (ICD-8/9 203)	Ever beer drinker versus non-drinker	NR	0.8 (0.4–1.6)	Matched pair analysis used with no adjustment for other covariates	
					Ever hard liquor drinker versus non-drinker	NR	1.7 (0.9–3.3)		

Table 2.85 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Brown <i>et al.</i> (1992), Iowa, USA, 1980–83	173 white men (101 living, 72 deceased) from Iowa Health Registry, aged ≥ 30 years; 100% histologically confirmed; response rate, 84%	452 living white population-based men selected by RDD (alive and <65 years) or HCFA (≥ 65 years); frequency-matched to cases on age (± 5 years), vital status at time of interview; response rate, 78%	Interviewer-administered standardized questionnaire	Multiple myeloma	Non-drinker	76	1.0	Age	Drinkers were subjects who had ever consumed any alcoholic beverage at least weekly; farming, education, family history of cancer and exposure to high-risk jobs or chemicals did not confound results.
					Drinker	97	1.3 (0.9–1.9)		
					<i>Drinks/week</i>				
					<5	23	1.0 (0.6–1.8)		
					5–11	36	1.8 (1.1–3.1)		
					12–23	20	1.0 (0.6–1.8)		
					>23	17	1.4 (0.7–2.6)		
					<i>Beverage type</i>				
Beer or wine only	38	1.1 (0.7–1.7)							
Hard liquor	17	1.2 (0.6–2.3)							
Other combinations	42	1.7 (1.0–2.7)							

Table 2.85 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Brown <i>et al.</i> (1997), Georgia, Michigan, New Jersey, USA, 1986–89	365 white (192 men, 173 women) and 206 black (91 men, 115 women) (101 living, 72 deceased) from the regional tumour registry rapid case-ascertainment system, aged 30–79 years; histological confirmation not given; response rate, 63% for whites and 67% for blacks	1155 white (736 men, 419 women), 967 black (614 men, 353 women) selected by RDD (<65 years), HCFA (≥65 years); frequency matched to cases on sex, race, age, area; response rate, 75% for HCFA and 78% for RDD	Interviewer-administered standardized questionnaire	Multiple myeloma	<i>White men</i>			Age, education, study area	Duration (years) of alcohol drinking was associated with a non-significant decreased risk in black men and white women and had no association in black women; beverage type was not associated with risk.
					Never drinker	55	1.0		
					Ever drinker	137	0.6 (0.4–0.9)		
					<i>Drinks/week</i>				
					<8	55	0.7 (0.5–1.1)		
					8–21	42	0.6 (0.3–0.9)		
					22–56	31	0.6 (0.4–1.1)		
					≥57	9	0.6 (0.3–1.3)		
					<i>Years drinking</i>				
					<30	26	0.6 (0.4–1.1)		
					30–39	43	0.9 (0.5–1.4)		
					≥40	65	0.5 (0.3–0.8)		
					<i>Beverage type</i>				
					Liquor	96	0.7 (0.4–1.0)		
					Beer	110	0.6 (0.4–0.9)		
Wine	58	0.6 (0.4–1.0)							
<i>Black men</i>									
Never drinker	24	1.0							
Ever drinker	67	0.8 (0.5–1.3)							
<i>Drinks/week</i>									
<8	18	0.8 (0.4–1.5)							
8–21	22	0.7 (0.4–1.3)							
22–56	21	0.9 (0.5–1.8)							
≥57	6	0.7 (0.3–1.8)							

Table 2.85 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Brown <i>et al.</i> (1997) (contd)					<i>White women</i>				
					Never drinker	112	1.0		
					Ever drinker	61	0.7 (0.5–1.0)		
					<i>Drinks/week</i>				
					<8	38	0.6 (0.4–1.0)		
					8–21	14	0.6 (0.3–1.2)		
					≥22	8	2.8 (0.9–8.2)		
					<i>Black women</i>				
					Never drinker	75	1.0		
					Ever drinker	40	1.0 (0.6–1.6)		
					<i>Drinks/week</i>				
					<8	23	1.0 (0.6–1.8)		
				8–21	12	1.1 (0.5–2.2)			
				≥2	4	0.6 (0.2–2.0)			

CI, confidence interval; HCFA, Health Care Financial Administration; ICD, International Classification of Diseases; RDD, random-digit dialling

Table 2.86 Case-control studies of parental alcoholic beverage consumption and childhood haematopoietic cancer

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
McKinney <i>et al.</i> (1987), United Kingdom, 1980–83	234 (139 boys, 95 girls; 171 leukaemia, 63 lymphoma) in three regions from a single clinic, aged <15 years; 100% histologically confirmed; response rate not given	468 hospital-based; matched (2:1) on age, sex, hospital; response rate not given	Interviewer-administered standardized questionnaire for alcohol intake during pregnancy	Leukaemia or lymphoma		NR	No association (data not shown)	None	
van Duijn <i>et al.</i> , (1994), Netherlands, 1981–82	80 ANLL (47 boys, 33 girls) and 517 ALL cases (288 boys, 229 girls), ascertained from Dutch Childhood Leukaemia Group, aged <15 years, 100% histologically confirmed; response rate for ALL and ANLL, 86%	240 population-based (141 boys, 99 girls) randomly selected from census lists; matched (3:1) on sex, age (± 3 months), residence; response rate, 67%	Mailed standardized questionnaires for frequency of parental alcohol intake before or during pregnancy	ANLL, ALL	Maternal alcohol intake during pregnancy (yes versus no) <i>ANLL</i> Age at diagnosis 0–4 years 5–9 years 10–14 years <i>ALL</i> Age at diagnosis 0–4 years 5–9 years 10–14 years	42 21 15 6 115 51 22	2.6 (1.4–4.6) 2.8 (1.2–6.5) 3.0 (1.1–8.4) 0.8 (0.3–2.3) 1.1 (0.8–1.9) 0.8 (0.5–1.5) 1.0 (0.4–2.1)	Age, gender, social class, maternal smoking, prescription drug use, ultrasound, exposure to radiation or viral infection during pregnancy, occupational exposure to hydrocarbons	No associations for parental alcohol intake 1 year before pregnancy

Table 2.86 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Severson <i>et al.</i> (1993), Canada, USA, 1980–84	187 (94 boys, 93 girls) identified through the Children's Cancer Group, aged ≤17 years; 100% histologically confirmed; response rate, 78%	187 (97 boys, 90 girls) population-based selected by RDD; matched (2:1) to cases on date of birth (±6 months–2 years), race, telephone area code, exchange; response rate, 78.5%	Interviewer-administered standardized questionnaire to assess parental intake before or during pregnancy	AML	Maternal alcohol intake			Unclear	Maternal age at birth of child, education, use of mind altering drugs, sex of child and race of the child did not confound the results; paternal alcohol intake 1 month before conception was not associated with risk for AML.
					Current drinker	41	1.02 (0.65–1.63)		
					Ever drank	32	1.07 (0.63–1.82)		
					Drank during pregnancy	51	1.42 (0.91–2.23)		
					<i>Age at diagnosis</i>				
0–2 years	21	3.00 (1.23–8.35)							
3–10 years	13	0.81 (0.36–1.80)							
11–17 years	17	1.13 (0.53–2.44)							

Table 2.86 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Shu <i>et al.</i> (1996), Australia, Canada, USA, 1983–88	302 infant leukaemia (203 ALL, 88 AML, 11 other) identified through the Children's Cancer Group, aged ≤18 months; 100% histologically confirmed; response rate, 79%	558 population-based selected by RDD; matched 1–4:1 on year of birth, telephone area code, exchange; response rate, 75%	Interviewer-administered (by telephone) standardized questionnaire to assess parental alcohol intake before, during or after pregnancy	AML, ALL	Maternal intake during pregnancy			Sex, maternal age, education, maternal smoking during pregnancy	Maternal alcohol intake during pregnancy: no specific associations for drinking during nursing period or by beverage type except for AML associated with 1-4 drinks/month of liquor (odds ratio, 6.37; 95% CI, 1.95–20.80; $p < 0.01$); paternal alcohol intake 1 month before pregnancy: no associations with total alcohol or with specific beverage types for ALL or AML	
					<i>ALL</i>	Ever	NR			1.43 (1.00–2.04)
						versus never				
						2nd and/or 3 rd trimester	NR			2.28 (1.26–4.13)
						None				1.0
						1–20 drinks	NR			1.76 (1.14–2.72)
						>20 drinks	NR			0.93 (0.53–1.62) p -trend=0.40
					<i>AML</i>	Ever	NR			2.64 (1.36–5.06)
						versus never				
						2nd and/or 3 rd trimester	NR			10.48 (2.79–39.33)
	None	NR	1.0							
	1–20 drinks	NR	2.36 (1.11–5.03)							
	>20	NR	3.13 (1.20–8.06) p -trend<0.01							

Table 2.86 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments
Infante-Rivard <i>et al.</i> , (2002) Québec, Canada, 1980–93	491 incident (275 boys, 216 girls) identified from tertiary care centres; aged 0–9 years; histological confirmation not given; response rate, 96%	491 (275 boys, 216 girls) selected from family allowance files (government files); matched to cases (1:1) on age, sex, region of residence at the time of diagnosis; response rate, 84%	Interviewer-administered (by telephone) standardized questionnaire that referred to maternal alcohol intake 1 month prior to pregnancy through to the nursing period and paternal intake 1 month prior to pregnancy	ALL	<i>Maternal intake</i>		1.0	Mother's age, education	For maternal alcohol intake, patterns of association similar across alcohol type; appeared to be potential interactions of maternal alcohol intake with the <i>GSTM1</i> null genotype and with <i>CYP2E1</i> *5 allele
					None	NR	0.8 (0.6–1.1)		
					1 month before pregnancy	180	0.7 (0.5–0.9)		
					During pregnancy	151	0.7 (0.5–1.0)		
					<1.0 drink/day	20	0.8 (0.5–1.6)		
					≥1 drink/day	46	0.5 (0.3–0.8)		
					<i>Paternal intake</i>				
					1 month before pregnancy				
					None	NR	1.0		
					Any	420	1.4 (1.0–2.0)		
<1.0 drink/day	189	1.4 (1.0–2.0)							
1–2 drinks/day	143	1.6 (1.1–2.5)							
≥3 drink/day	79	1.7 (1.1–2.7)							
			<i>p</i> -trend=0.01						

Table 2.86 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjustment factors	Comments	
Menegaux <i>et al.</i> (2005), France, 1995–99	280 (166 boys, 114 girls) newly diagnosed with acute leukaemia, aged <15 years; response rate, 95%	288 (168 men, 120 women) hospitalized for conditions other than cancer or birth defects; frequency-matched on age, gender, hospital, ethnic origin; response rate, 99%	Interviewer-administered standardized questionnaire assessed maternal alcohol intake during pregnancy and breastfeeding	ANLL, ALL	Maternal intake during pregnancy			Age, gender, hospital, ethnic origin	No differences in associations according to beverage type; wine and spirits significantly increased the risk of ALL but was not significantly associated with ANLL.	
					<i>ALL</i>	Never	87			1.0
						Ever	153			2.0 (1.4–3.0)
						1 glass/week	103			2.0 (1.3–3.0)
						2 glasses/week	25			2.8 (1.3–6.0)
						≥3 glasses/week	25			1.9 (0.9–3.5)
					<i>ANLL</i>	Never	12			1.0
						Ever	28			2.6 (1.2–5.8)
						1 glass/week	21			2.8 (1.2–6.6)
						2 glasses/week	–			–
	≥3 glasses/week	7	2.4 (0.8–7.1)							

ALL, acute lymphocytic leukaemia; AML, acute myeloid leukaemia; ANLL, acute non-lymphocytic leukaemia; CI, confidence interval; CYP, cytochrome P-450; GST, glutathione S-transferase; ICD, International Classification of Diseases; NR, not reported; RDD, random-digit dialling

alcoholic beverage intake during pregnancy with risk for haematopoietic cancers in children (McKinney *et al.*, 1987; van Duijn *et al.*, 1994; Severson *et al.*, 1993; Shu *et al.*, 1996; Infante-Rivard *et al.*, 2002; Menegaux *et al.*, 2005). Three of four studies reported no association between paternal alcoholic beverage intake 1 month or 1 year before pregnancy and risk of any childhood leukaemia or lymphoma (van Duijn *et al.*, 1994; Severson *et al.*, 1993; Shu *et al.*, 1996), whereas a positive association between a higher number of drinks per day and the risk for acute lymphocytic leukaemia was observed in the fourth study (Infante-Rivard *et al.*, 2002). For maternal alcoholic beverage intake during pregnancy, one study showed no association with leukaemia or lymphoma (McKinney *et al.*, 1987), while another showed a reduced risk for acute lymphocytic leukaemia when comparing any intake with no intake (Infante-Rivard *et al.*, 2002). Statistically significant two- to 2.4-fold higher risks for acute non-lymphocytic leukaemia were associated with any maternal alcoholic beverage intake during pregnancy in two studies (van Duijn *et al.*, 1994; Menegaux *et al.*, 2005). Similarly, statistically significant positive associations between maternal alcoholic beverage intake and risk for acute lymphocytic (Shu *et al.*, 1996; Menegaux *et al.*, 2005) and acute myeloid (Severson *et al.*, 1993; Shu *et al.*, 1996) leukaemias were observed. The strongest associations observed in the studies of alcoholic beverages and acute myeloid leukaemia were for children diagnosed at 10 years of age or younger (Severson *et al.*, 1993; Shu *et al.*, 1996). Overall, there was no consistent evidence of dose–response relationships for maternal or paternal alcoholic beverage intake or for intake of any specific type of alcohol beverage and risk for any childhood haematopoietic cancer. Most studies adjusted for potential confounding factors including maternal age, maternal smoking and child’s gender. Importantly, it is unclear whether any of the observed associations between maternal or paternal alcoholic beverage intake and risk for childhood haematopoietic cancers are attributed to recall bias.

2.18 *Cancer at other sites*

2.18.1 *Testis (Table 2.87)*

(a) Parental exposure

Among two cohort (Robinette *et al.*, 1979; Jensen, 1980) and three case–control studies (Schwartz *et al.*, 1962; Brown *et al.*, 1986; Weir *et al.*, 2000) conducted in the general population, only one case–control study suggested a possible association between testicular cancer in adults and maternal drinking during pregnancy (Brown *et al.*, 1986). The association was of borderline significance for the consumption of more than one drink per week relative to no drinking (odds ratio, 2.3; 95% CI, 1.0–5.2), but no association was observed for one drink (odds ratio, 1.1; 95% CI, 0.6–2.2), and no clear trend was apparent with the amount of alcohol consumed.

Table 2.87 Case-control studies of alcoholic beverage consumption and testicular cancer

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Parental exposure								
Brown <i>et al.</i> (1986), USA, 1979–81	225 mothers (pre- and perinatal cancer); response rate, 88%	213 mothers; response rate, 90%	Standardized telephone questionnaire	Never drinker		1.0	Tobacco smoking	
				1 drink/week		1.1 (0.6–2.2)		
				>1 drink/week		2.3 (1.0–5.2)		
						<i>p</i> -trend=0.14		
Weir <i>et al.</i> (2000), Ontario, Canada, 1987–89	346 case mothers/502 cases, aged 16–59 years; response rate, 80.8%	522 control mothers/ 975 controls; aged 16–59 years; response rate, 67.8%	Self-administered questionnaire	<i>Drinks/ week during pregnancy</i>			Age (5-year age group)	
				0	232	1.0		
				<2	83	1.2 (0.9–1.7)		
				≥2	24	0.8 (0.5–1.3)		
Chen <i>et al.</i> (2005b), USA, 1993–2001	278 incident childhood germ-cell; response rate, 80.8%	422; response rate, 66.6%; 1:2 match	Telephone interview; self-administered questionnaire	<i>Ever drank ≥6 months</i>			Gender of children, age, maternal education, race, family income	
				Never	182	1.0		
				Yes	92	0.9 (0.7–1.2)		
				<i>Ever drank during 1 month before pregnancy to nursing</i>				
				Never	126	1.0		
Yes	148	0.9 (0.7–1.2)						

Table 2.87 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments
Adult exposure								
Swerdlow <i>et al.</i> (1989), Oxford and West Midlands, United Kingdom 1977–81	259 cases of histologically confirmed testis cancer, aged ≥10 years	2 sets of controls: 238 radiotherapy controls treated in the same centres as cases; 251 non-radiotherapy controls who were general surgical, orthopaedic ENT and dental in-patients	Interview	Ever drank <i>Alcohol regularly?</i> Wine No Yes	NR	1.0 1.7 (1.21–2.43)	Social class	There was no dose–response relationship between risk for the tumour in relation to mean or to maximal wine consumption
UK Testicular Cancer Study Group (1994), United Kingdom, 1984–86	794, aged 15–49 years; response rate, 92%	609; 1:2 match (case/controls); response rate, 83.1%	Face-to-face interview	<i>Alcohol (g/week)</i> None <68.8 68.8–124.6 124.6–<211.2 211.2–<364.7 ≥364.7	92 150 147 130 135 140	1.0 1.26 (0.86–1.83) 1.23 (0.85–1.79) 0.87 (0.60–1.28) 1.06 (0.72–1.56) 1.13 (0.97–1.66) <i>p</i> -trend=0.41	Cryptorchidism, inguinal hernia at age <15 years	No evidence of an effect of testicular temperature on cancer risk

CI, confidence interval

One additional cohort study conducted among male and female cirrhotics in Denmark found a slightly increased risk for testicular cancer of all histological types (SIR, 2.3; 95% CI, 1.0–4.5) that varied little with type of cirrhosis and disappeared after 10 years of follow-up (Sørensen *et al.*, 1998).

One case–control study investigated the association of childhood germ-cell tumours (seminoma, embryonal carcinoma, yolk-sac tumour, choriocarcinoma, immature teratoma and mixed germ-cell tumours) and parental alcohol drinking (Chen *et al.*, 2005b). Results showed no association between germ-cell cancer overall and alcoholic beverage drinking by either parent before pregnancy, or during pregnancy or nursing; odds ratios were 0.9 (95% CI, 0.7–1.2) and 1.0 (95% CI, 0.8–1.3) for ever drinking, for mothers and fathers, respectively. Additional stratified analyses by sex, histological type and anatomical site did not show any association.

(b) *Adult exposure*

Two case–control studies in the United Kingdom investigated the association between alcoholic beverage drinking and testicular cancer. Swerdlow *et al.* (1989) found no association for regular alcoholic beverage drinking, duration of drinking or consumption of beer, cider or spirits; however, a significant association was found with regular consumption of wine, with an odds ratio of 1.71 (95% CI, 1.21–2.43), but no dose–response relation. The other case–control study found no association with alcohol intake at the time of diagnosis or at age 20 years (UK Testicular Cancer Study Group, 1994).

2.18.2 *Cancer of the brain*

(a) *Parental exposure and childhood brain cancer (Table 2.88)*

Only one cohort study found an association between alcoholic beverage consumption and brain cancer (Robinette *et al.*, 1979). Three additional studies with suboptimal methodology did not provide evidence of an association between increased alcoholic beverage consumption and brain cancer (IARC, 1988). However, a descriptive study based on cancer registries and national mortality data in France (Remontet *et al.*, 2003) showed a large increase in the incidence of and mortality from brain cancer between 1980 and 2000, during which time alcohol consumption decreased markedly.

Five case–control studies have assessed the association between alcoholic beverage consumption of parents and childhood brain cancer. Two of the studies were conducted in the USA and Canada (Bunin *et al.*, 1994; Yang *et al.*, 2000), one in China (Hu *et al.*, 2000), one in Germany (Schüz *et al.*, 2001) and one in the USA (Kramer *et al.*, 1987). Three of the studies examined the association between neuroblastoma and parental alcoholic beverage consumption (Kramer *et al.*, 1987; Yang *et al.*, 2000; Schüz *et al.*, 2001). Kramer *et al.* (1987) found a weak, non-significant association for any maternal alcoholic beverage drinking during pregnancy, with a suggestive increase

Table 2.88 Case–control studies of parental alcoholic beverage consumption and childhood brain tumours

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Kramer <i>et al.</i> (1987), Great Delaware Valley, USA, 1970–79	104 incident from the Great Delaware Valley Pediatric Tumor registry and the Cancer Research Center between 1970 and 1979; response rate, 74.8%	101; selection through RDD; response rate, 57.1%	Telephone interview	<i>Maternal drinking during pregnancy</i>			Not specified	90% CI reported; 1 drink=1 serving of beer, wine or liquor
				Any drinking	36	1.44 (0.94–2.21)		
				≥1 drink/day (frequent)	9	9.0 (2.16–37.56)		
				≥3 drinks/day (binge)	6	6.0 (1.26–28.54)		
Bunin <i>et al.</i> (1994), Canada, USA, 1986–89	322 diagnosed before 6 years of age in 1986–89; identified through the Children’s Cancer Group; response rate, 65%	321; selected through RDD; 1:1 match; response rate, 74%	Telephone interview of the mother or father	≥1 drink/day or ≥3 drinks occasionally	12	12.0 (3.14–45.82)	Income	*Crude odds ratio reported
				<i>Maternal exposure to beer during pregnancy</i>				
				Astrocytoma	10	1.4 (0.5–3.7)		
				Primitive neurectoderma tumour	12	4.0 (1.1–22.1)*		

Table 2.88 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hu <i>et al.</i> (2000), Northeast, Heilongjiang Province, China, 1991–96	82 consecutive incident (43 boys, 39 girls) intracranial primary brain tumours, ≤18 years of age; 100%; residing in Heilongjiang Province at the time of diagnosis; 100% histologically confirmed; participation rate	3 individually matched per case; participation rate, 100%	Structured questionnaire (interview) administered to parents of all study subjects; history of parental liquor drinking obtained	<i>Lifetime paternal liquor consumption (L)</i> Never ≤200 ≥201	41 20 21	1.00 3.21 (1.43–7.22) 4.43 (1.94–10.14) <i>p</i> for trend=0.0001	Family income, mother's education, father's education	Similar associations for paternal age when started to drink liquor and numbers of years of drinking liquor; only one mother in the case group and two mothers in the control group reported drinking hard liquor.

Table 2.88 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Yang <i>et al.</i> (2000), Canada, USA, 1992–94	538 children newly diagnosed with neuroblastoma in 1992–94, ≤19 years old; 100% histologically confirmed; response rate, 73%	504 mothers selected by RDD; 304 fathers directly interviewed; proxy interviews obtained for 142 (28%); 1:1 match; response rate, 72%	Structured telephone questionnaire to parents	<i>Maternal drinking</i>	253	0.9 (0.7–1.1)	Child's gender, mother's race and education, household income in the birth year	No association for paternal lifetime alcohol consumption, or before mother's pregnancy
				Lifetime	235	1.1 (0.8–1.4)		
				Around pregnancy ^a	205	1.1 (0.8–1.4)		
				1 month before conception	96	1.2 (0.9–1.7)		
				1st trimester	60	1.6 (1.0–2.4)		
				2nd trimester	58	1.4 (0.9–2.1)		
3rd trimester	54	1.0 (0.5–2.0)						
				Breastfeeding				

Table 2.88 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Schüz <i>et al.</i> , (2001), Germany, 1988–94	Pooled analysis of 2 case–control studies (1988–93; 1992–94); total of 192; children; response rate, 83.1%	2537; 2:1 match by gender and date of birth within 1 year; response rate, 71%	Questionnaire and telephone interview; same exposure assessment in both studies	Maternal alcohol consumption			Socioeconomic status, degree of urbanization	Odds ratio from a matched logistic regression on age, gender, birth year
				<i>Overall</i>				
				Never	140	1.0		
				1–7 glasses/week	38	0.84 (0.56–1.26)		
				>7 glasses/week	3	3.04 (0.75–12.2)		
				<i>Stage I/II</i>				
				Never	73	1.0		
				1–7 glasses/week	12	0.90 (0.45–1.80)		
>7 glasses/week	0	–						
<i>Stage III/VI</i>								
Never	39	1.0						
1–7 glasses/week	23	0.88 (0.53–1.45)						
>7 glasses/week	3	5.23 (1.33–20.6)						

CI, confidence interval; RDD, random-digit dialling

^a Exposure category includes drinking 1 month before pregnancy, during pregnancy and during breastfeeding

in risk with amount and frequency. However, these results were based on very small numbers of controls. A case–control study based on the Children’s Cancer Group and Paediatric Oncology Group institutions in the USA and Canada (Yang *et al.*, 2000) found no associations between the risk for neuroblastoma and either maternal or paternal alcoholic beverage consumption, while the combined analysis of two case–control studies used in the German study observed no overall association between maternal alcoholic beverage consumption during pregnancy and neuroblastoma or stage I/II neuroblastoma. However, an association was observed between advanced stage (III/IV) neuroblastoma and high alcoholic beverage consumption either during lifetime or around the time of pregnancy (Schüz *et al.*, 2001).

One study conducted in the USA and Canada found that maternal beer consumption during pregnancy was associated with primitive neuroectoderm tumours, but no association was found between alcoholic beverage consumption and astrocytoma (Bunin *et al.*, 1994), while the Chinese study reported that paternal hard liquor consumption before the pregnancy was associated with brain cancer (Hu *et al.*, 2000). [The Working Group considered that there was a possibility of recall bias in this study.]

(b) *Adult brain cancers (Table 2.89)*

One cohort study (Efird *et al.*, 2004) assessed associations between cigarette smoking and other lifestyle factors, including alcohol, and the occurrence of glioma in adults. There was no association with consumption of alcoholic beverages, beer or wine in the past year, although a slight non-significant association was observed for liquor consumption in the past year.

Nine case–control studies assessed the association between alcoholic beverage consumption and brain cancer in adults (Table 2.89). In studies conducted in Australia (Ryan *et al.*, 1992; Hurley *et al.*, 1996), Germany (Boeing *et al.*, 1993) and the USA (Preston-Martin *et al.*, 1989; Hochberg *et al.*, 1990; Lee *et al.*, 1997), no significant associations or trends were observed with the consumption of alcoholic beverages and the occurrence of glioma or meningioma. However, three studies, one conducted in Canada and two conducted in China, did find an association between the consumption of alcoholic beverages and brain cancer. The Canadian study found an elevated risk for ‘ever use’ of wine, but not of beer or spirits (Burch *et al.*, 1987) and one Chinese study (Hu *et al.*, 1998) found that consumption of liquor was associated with the occurrence of glioma in men with significant trends for the number of years of drinking, lifetime consumption and average consumption. However, no associations were seen for beer in adjusted analyses. In a separate report of the same study (Hu *et al.*, 1999), higher levels of consumption of beer, liquor and total alcohol were all associated with brain cancer, with respective adjusted odds ratios of 2.9 (95% CI, 1.1–7.6), 3.8 (95% CI, 1.6–9.2) and 3.2 (95% CI, 1.5–7.0) in the third tertile of consumption.

Table 2.89 Case-control studies of alcoholic beverage consumption and adult brain cancer

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Choi <i>et al.</i> (1970), Minneapolis-St Paul Metropolitan area, USA, 1963-64	All (157) histologically proven primary tumours diagnosed in 4 hospitals between June and January 1963, and from June 1963 to June 1964; 126 histologically confirmed	157 patients admitted with conditions other than tumour of any site, neurological, psychiatric, ophthalmological or lymphatic disorders; matched on hospital of admission, sex, age, race, geographic area of residence, location of residence	Questionnaire interview	Central nervous system	<i>Verified tumours</i>			Age	Odds ratios and confidence intervals not presented; for subjects <20 years of age, his/her mother was approached for an interview; a proxy was interviewed when a subject could not provide proper responses.	
					Never	39	$p=0.008$			
					Ever	65				
					<i>Gliomas</i>					
					Never	20				
					Ever	35				
					<i>Astrocytoma</i>					
					Never	14				
					Ever	10				
					<i>Glioblastoma</i>					
Never	5									
Ever	23									
<i>Meningioma</i>										
Never	10	$p=0.007$								
Ever	14									

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Musicco <i>et al.</i> (1982); Milan, Italy, 1979–80	51 patients hospitalized with gliomas, >20 years of age; mean age, 47 years; 15 astrocytomas, grades I and II; 10 oligodendrogliomas; and 26 astrocytomas, grades III and IV, and/or glioblastoma multiforme	201 admitted to the same hospital for meningioma, intervertebral disc prolapse or radiculitis, neuraxitis or multiple sclerosis, epilepsy, cerebrovascular disease, other neurological diseases; mean age 49 years; 2:1 matched for age, sex, place of residence	Interview	Central nervous system	Drinkers	24	1.0 <i>p</i> =1.000		Analyses based on 42 case–control pairs; patients who drank alcoholic beverages daily were considered drinkers; some diseases included in the control group may be linked to alcoholic beverage consumption; CI not reported.

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Burch <i>et al.</i> (1987), southern Ontario, Canada, 1979–82	247 astrocytomas and glioblastomas (no meningiomas), aged 25–80 years; residents of metropolitan Toronto and southern Ontario; histologically confirmed through medical records; response rate, 75%	228 hospital-based, free of cancer; patients admitted to any hospital in the study area and who had a condition other than cancer at any site; response rate, 56%	Interviewer-administered questionnaire at home	Brain	<i>Beer</i>		1.0	Age, sex, proxy status, residence	Matched pair analysis
					Never		2.68 (1.18–6.07)		
					Low		0.49 (0.23–1.05)		
					Medium		1.47 (0.71–3.03)		
					High				
					<i>Spirits</i>		1.0		
					Never		1.29 (0.74–2.25)		
					Low		1.35 (0.50–3.65)		
					Medium		0.83 (0.41–1.71)		
					High				
					<i>Wine</i>		1.0		
					Never		1.06 (0.46–2.43)		
Low		2.07 (0.91–4.73)							
Medium		2.92 (1.20–7.07)							
High									
Preston-Martin <i>et al.</i> (1989), Los Angeles, USA, 1980–84	277 black and white men residing in Los Angeles County in 1980–1984, aged 25–49 years; first diagnosed with glioma or meningioma; response rate, 74%	272 neighbourhood; response rate, 98.2%	Face-to-face or telephone	Brain	<i>Glioma</i>			No adjustment specified	
					Beer at least once a month	32	0.7 (0.5–1.2)		
					Wine at least once a month	39	0.7 (0.5–1.1)		
					Liquor at least once a month	55	1.3 (0.8–1.9)		
					<i>Meningioma</i>				
					Beer at least once a month	7	0.4 (0.1–0.9)		
					Wine at least once a month	14	0.7 (0.3–1.4)		
Liquor at least once a month	15	0.7 (0.3–1.4)							

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hochberg <i>et al.</i> (1990), USA, 1977–81	160 newly diagnosed glioblastoma or astrocytoma identified in collaborating hospitals in Boston, Providence and Baltimore	128 friends of cases, excluding blood relatives; matched for sex, age (± 5 years), place of residence	Self-administered questionnaire, with telephone follow-up	Brain	Regular consumption of beer	67	0.7 (0.4–1.1)	Age, sex, socioeconomic status	Proxy interviews for 20% of cases and 2% of controls
Ryan <i>et al.</i> (1992), Adelaide, Australia, 1987–90	190 incident gliomas or meningiomas in 1987–90, aged 25–74 years; identified through the South Australian Central Cancer Registry; response rate, 90.5%	419 selected from the Australian electoral poll; 2:1 match; response rate, 63.3%	Face-to-face questionnaire at home or at work	Brain (191, 192)	<i>Glioma</i> Non-drinkers All sources 0–6.9 g/day 7–19.9 g/day ≥ 20 g/day <i>Meningioma</i> Non-drinkers All sources 0–6.9 g/day 7–19.9 g/day ≥ 20 g/day		1.0 0.94 (0.57–1.55) 0.86 (0.47–1.60) 0.74 (0.39–1.40) 1.00 (0.53–1.91) 1.0 0.59 (0.33–1.05) 0.63 (0.31–1.30) 0.49 (0.22–1.09) 0.58 (0.22–1.49)	Sex, age	Never drinkers were subjects who never drank at least once a month for a year; similar associations for beer, wine and spirit consumption.

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Boeing <i>et al.</i> (1993), Southwest Germany, 1987–88	115 gliomas, 81 meningiomas and 30 acoustic neuromas, aged 25–75 years; 100% histopathologically confirmed; participation rate, 97.8%	418 randomly selected from the residential registries of the study area; participation rate, 72%	Standardized interview	Brain (191.0, 192.0, 192.1)	Consumption of alcoholic beverages assessed by lifelong history				No numerical data on alcohol presented; alcohol consumption was assessed by lifelong history; no significant association of risk for glioma or meningioma with lifelong consumption of a single alcoholic beverage or total alcohol.

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hurley <i>et al.</i> (1996), Australia (state of Victoria), 1987–91	416 incident (250 men, 166 women) primary gliomas, aged 20–70 years; identified through medical records from 14 Melbourne hospitals; 100% histologically confirmed; participation rate, 66% of eligible and 86% of the contacted cases	Selected from the electoral roll; 422 interviewed (252 men, 170 women); participation rate, 43.5% of those identified as eligible and 64.7% of the contacted controls	Structured questionnaire (interview); subjects sent a section of the questionnaire on details of some other variables	Brain (ICD-0 938–946)	Drank any alcoholic beverages	318	1.00 0.96 (0.67–1.37)	Age, gender, reference date	No increase in risk when average daily alcohol consumption considered
					<i>All</i>				
					Never Ever <i>Men</i> Never Ever				
					<i>Women</i> Never Ever				
Lee <i>et al.</i> (1997), California, USA 1991–1994	494 incident gliomas from 1991 to 1994, aged ≥20 years; identified through hospital records in the San Francisco Bay area; response rate, 82%	462 (random-digit dialling telephone number); frequency matched by age, gender, race/ethnicity; response rate, 63%	Structured questionnaire face-to-face	Brain (glioma) (ICD-0-2 9380–9481)	Mean consumption levels		No levels presented	Age, education, income	Only mean consumption levels of cases and controls presented; no significant differences noted

Table 2.89 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Hu <i>et al.</i> (1998), China (Northeast, Heilongjiang Province), 1989–95	218 incident primary gliomas (139 astrocytomas and 79 other brain gliomas) identified from the Department of Neurosurgery of 6 major hospitals, aged 20–74 years; 100% histologically confirmed; participation rate, 100%	436 subjects with non-neoplastic, non-neurological diseases; 2:1 matched for sex, age, area of residence; participation rate, 100%.	Structured questionnaire (interview)	Brain	Liquor			Income, education, occupational exposure, consumption of vegetables and fruit; liquor also controlled for number of years of beer drinking, and beer controlled for number of years of liquor consumption	Only subjects directly interviewed included; associations for liquor similar for numbers of years drinking and lifetime liquor consumption; no associations noted for similar measures of beer consumption in the Hu <i>et al.</i> (1998) analysis, but were seen in an expanded analysis (Hu <i>et al.</i> , 1999, see text).
					<i>Age started to drink</i>				
					Never	55	1.00		
					≤20	54	1.98 (1.05–3.72)		
					≥21	31	1.40 (0.70–2.78)		
							<i>p</i> for trend=0.28		
<i>Average oz/day</i>									
Never	55	1.00							
≤2	38	1.54 (0.77–3.06)							
>2	47	1.87 (0.98–3.58)							

CI, confidence interval; ICD, International Classification of Diseases

2.18.3 *Cancer of the thyroid*

The association of alcoholic beverage consumption and thyroid cancer was examined in four cohort (Table 2.90) and six case–control (Tables 2.91) studies.

One cohort study among alcoholics in Sweden reported no significant excess risk for thyroid cancer compared with the general population (Adami *et al.*, 1992a). Two cohort studies conducted in the general population also reported no significant association of increasing alcohol consumption with risk for thyroid cancer (Iribarren *et al.*, 2001; Navarro Silvera *et al.*, 2005).

A pooled analysis of the case–control studies (Table 2.91), based on 1732 cases, found no association with increasing intake of beer and wine (relative risk, 0.9 (95% CI, 0.7–1.1) for more than 14 drinks per week) (Mack *et al.*, 2003). No difference was found for wine or beer separately or between men or women.

No data were available on the effect of duration of alcoholic beverage drinking or cessation of drinking on the risk for thyroid cancer.

2.18.4 *Melanoma*

(a) *Cohort studies (Table 2.92)*

Two cohort studies, one in a group of radiological technologists exposed to ionizing radiation in the USA (Freedman *et al.*, 2003) and one in alcoholic women in Sweden (Sigvardsson *et al.*, 1996), found no significant associations between the risk for melanoma and alcoholic beverage intake.

(b) *Case–control studies (Table 2.93)*

Six of nine case–control studies reported no significant association between alcoholic beverage intake and the risk for melanoma (Østerlind *et al.*, 1988; Bain *et al.*, 1993; Kirkpatrick *et al.*, 1994; Westerdahl *et al.*, 1996; Naldi *et al.*, 2004; Vinceti *et al.*, 2005). These studies were conducted in Australia, Italy, Denmark, Sweden and the USA.

Three case–control studies in the USA reported some increase in risk for melanoma associated with alcoholic beverage intake (Stryker *et al.*, 1990; Millen *et al.*, 2004; Le Marchand *et al.*, 2006). None of these were adjusted for exposure to ultraviolet light and thus the possibility of confounding can not be excluded.

2.18.5 *Other female cancers (vulva and vagina)*

(a) *Cohort studies (Table 2.94)*

Two cohort studies have examined the association between alcoholic beverage intake and risk for other female cancers. These studies were carried out in special populations, namely women being treated for alcohol abuse or alcoholism in Sweden (Sigvardsson *et al.*, 1996; Weiderpass *et al.*, 2001b). One study indicated an elevated

Table 2.90 Cohort studies of alcoholic beverage consumption and thyroid cancer

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment factors	Comments
Special populations								
Hakulinen <i>et al.</i> (1974), Finland	Chronic alcoholic men (mean annual number in registry, 4370), aged >30 years, registered in 1967–70 when under custody of alcohol-misuse supervision, or when sent to a labour institute because of the vagrant law		Thyroid	Alcoholics	1 death observed/0.4 expected			No information regarding alcohol consumption, relative risk or CI was reported

Table 2.90 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment factors	Comments
Adami <i>et al.</i> (1992a), Uppsala, Sweden	9353 patients (8340 men; mean age at entry, 49.8 years; at diagnosis, 68.1 years; 1013 women; mean age at entry, 49.4 years; at diagnosis, 60.0 years) with a hospital discharge diagnosis of alcoholism in 1965–83	Follow-up through to 1984 (average follow-up, 7.7 years; maximum, 19 years)	Thyroid	No data on individual alcohol or tobacco use	Men: 3 Women: 0	SIR <i>Men</i> 1.7 (0.3–4.9) <i>Women</i> 0.0 (0.0–8.0)	Sex	

Table 2.90 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment factors	Comments
General population								
Iribarren <i>et al.</i> (2001), California, USA, Kaiser-Permanente Medical Care Program Cohort	94 549 men and women, aged 10–89 years, subscribers to the Kaiser Permanente Medical Care Program, northern California, who underwent regular health check-ups in 1964–73; follow-up based on the Cancer Incidence File (San Francisco Bay Area) through to 1997; median follow-up, 19.9 years	Self-administered questionnaire	Thyroid	<i>Alcohol consumption (drinks/day)</i> 0 1–2 3–5 ≥6		0.9 (0.6–1.3) 1.0 1.0 (0.5–1.8) 1.0 (0.3–3.0)	Age, sex, race, education, goitre, treatment to neck with X-rays, family history	Alcohol intake of 1–2 drinks/day = referent category; 73 cases of thyroid cancer in men and 123 cases in women; relative risk by gender not given

Table 2.90 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment factors	Comments
Navarro Silvera <i>et al.</i> (2005), Canada, Canadian National Breast Screening Study Cohort	49 613 women, aged 40–59 years, from the general Canadian population, recruited into the cohort between 1980 and 1985; average follow-up, 15.9 years	Self-administered questionnaire	Thyroid	<i>Alcohol intake (g/day)</i> None Any 1–3 3–10 ≥10	103 total	<i>Hazard ratio</i> 1.0 1.2 (0.7–1.8) 1.2 (0.7–2.0) 0.7 (0.4–1.2) 0.8 (0.5–1.4) <i>p</i> -trend=0.56	Age, education, pack–years of smoking, body mass index	No association for papillary or follicular subtype

CI, confidence interval; ICD, International Classification of Diseases

Table 2.91 Case-control studies of alcoholic beverage consumption and thyroid cancer

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Ron <i>et al.</i> (1987), Connecticut, USA, 1978–80	159 identified via Connecticut Tumor Registry; 100% histologically confirmed; response rate, 80%	285 population (random-digit dialling, Medicare records); 2:1 frequency-matched by sex, age; response rate, 65%	Interviewer-administered questionnaire	<i>Alcohol use</i> Non-user Any beer Any wine Any hard liquor	87 37 56 59	1.0 0.7 (0.4–1.3) 0.8 (0.5–1.3) 0.9 (0.6–1.5)	Age, sex, prior radiotherapy to the head and neck, thyroid nodules, goitre	Non-user: consumer of <1 drink per week
Kolonel <i>et al.</i> (1990), Hawaii, USA, 1980–97	191 (140 women, 51 men), identified through Hawaii Tumor registry, aged ≥ 18 years; 100% histologically confirmed; response rate, 79%	441 from Health Surveillance of the Department of Health; matched by age, sex; response rate, 74%	Self-administered questionnaire plus diet history	Regular alcohol use <i>Men</i> Never Ever <i>Women</i> Never Ever		1.0 0.6 (0.3–1.4) 1.0 1.0 (0.6–1.6)	Age, ethnicity	Number of cases not reported

Table 2.91 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Galanti <i>et al.</i> (1997), Norway/Sweden, 1993–94	Norway: 87 identified through Norwegian Cancer Register, born in Norway and living in the Tromsø Health Care Region, aged 18–75 years; response rate, 75% Sweden: 165 identified through registry, aged 18–75 years; response rate, 86%	Norway: 192 from population register; matched by age, sex; response rate, 56% Sweden: 248 from population register; matched by age, sex, county of residence; response rate, 69%.	Self-administered questionnaire	No. of drinks/month		Odds ratio (univariate analysis)		Not adjusted; results not changed after adjustment for smoking status, education
				<i>Wine (1.5 dL)</i>				
				<1	107	1.0		
				1–3	54	1.1 (0.7–1.7)		
				>3	52	0.7 (0.4–1.1)		
				<i>Light beer (2–5 dL)</i>				
				<1	113	1.0		
				1–4	61	1.0 (0.7–1.6)		
				>4	49	0.8 (0.5–1.2)		
				<i>Strong beer (2–5 dL)</i>				
				<1	181	1.0		
				>1	35	0.9 (0.5–1.6)		
				<i>Mild liquor (0.4 dL)</i>				
<1	184	1.0						
>1	34	0.8 (0.5–1.2)						
<i>Hard liquor (0.4 dL)</i>								
<1	147	1.0						
>1	71	0.8 (0.5–1.1)						
<i>Ethanol (g/day)</i>								
<1	89	1.0						
1–3.95	80	0.8 (0.6–1.2)						
>3.95	67	0.7 (0.5–1.1)						

Table 2.91 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Chatenoud <i>et al.</i> (1999), Italy, 1983–93	428, aged <75 years; 100% histologically confirmed; refusal rate for interview, <3%	3526 hospital patients (non-malignant); excluded alcohol and tobacco- or dietary-related diseases	Interviewer-administered questionnaire	<i>Alcohol intake 2 years before</i> Lowest Highest		Odds ratio 1.0 1.7 (1.3–2.3)	Age, sex	The main focus of this study was on refined-cereal intake and risk for cancer; the quantity of alcohol consumed was not specified.

Table 2.91 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments	
Rossing <i>et al.</i> (2000), Washington State, USA, 1988–94	410 papillary tumours identified via the Washington State Cancer Surveillance System, aged 18–64 years; response rate, 84%	574 population (random-digit dialling); matched by age, county of residence; response rate, 74%	Interviewer-administered questionnaire	Alcohol intake			Odds ratio	Age	* Never drank ≥ 12 alcoholic drinks within 1 year; cases and controls were only women
				Never*	126	1.0			
				>10 years ago	28	1.0 (0.5–1.7)			
				6–10 years ago	23	0.8 (0.5–1.5)			
				≤ 5 years ago	33	1.0 (0.6–1.8)			
				Amount (drinks/week)					
				Current drinkers					
				Never*	128	1.0			
				≤ 1	59	0.7 (0.4–1.0)			
				2–3	55	0.6 (0.4–0.9)			
				4–7	44	0.6 (0.4–0.9)			
				>7	42	0.9 (0.5–1.4)			
				Former drinkers					
				Never*	128	1.0			
≤ 1	42	1.2 (0.7–1.9)							
2–3	16	0.9 (0.5–1.9)							
4–7	6	0.3 (0.1–0.8)							
>7	18	1.2 (0.6–2.4)							
Pooled analyses									
Franceschi <i>et al.</i> (1991), 4 hospital-based case-control studies	385, aged <75 years; 100% histologically confirmed; response rate, ~97%	798 hospital patients (non-malignant)	Interviewer-administered questionnaire	Alcohol intake			Odds ratio	Age, sex, education, study centre	CI not reported
Low	103	1.0							
Intermediate	122	1.1							
High	160	1.3							
						χ^2 (trend), 2.72			

Table 2.91 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No of cases	Relative risk (95% CI)	Adjustment factors	Comments
Mack <i>et al.</i> (2003), 10 case-control studies	370 men, 1296 women; six studies provided information on wine and beer combined	702 men, 2106 women	Pooled analysis	<i>Weekly drinks of wine and beer</i> None ≤2 >2–7 7–14 >14	787 263 321 146 149	<i>Men</i> 1.0 0.8 (0.6–1.0) 0.8 (0.7–1.0) 1.0 (0.8–1.3) 0.9 (0.7–1.1) <i>p</i> for trend 0.12	Stratification on study, age, sex, ethnicity, current smoking	No difference in cancer risk between men and women

CI, confidence interval

Table 2.92 Cohort studies of alcoholic beverage consumption and melanoma

Reference, location, name of study	Cohort description	Exposure assesment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Swedish Cancer Registry Study	15 508 alcoholic women individually matched for region and age with one non-alcoholic women; incidence data from the Swedish Cancer Registry	Alcoholic women from the records of the Temperance boards in Sweden	Reference Alcoholic women	28 14	1.0 0.5 (0.3–1.0)		[May be confounded by differences in smoking, dietary habits and/or other factors.]

Table 2.92 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Freedman <i>et al.</i> (2003), USA, 1926–98 Radiologic Technologists Study	68 588 white cancer-free radiological technologists (54 045 women, 14 543 men); follow-up, 698 028 person-years; cases identified through SEER	Baseline questionnaire 1983–89 on height, weight, smoking, alcohol use, female hormonal factors, work history, other factors; participation rate, 86%; Second questionnaire 1994–98 updated information on risk factors, skin pigmentation, hair and eye colour, family medical history; participation rate, 83%	Alcohol (drinks/week)			Gender, years smoked, skin pigmentation, hair colour, personal history of non-melanoma skin cancer, decade of starting work as a technologist, education, proxy measures for residential childhood and adult exposure to sunlight	
			<i>Women</i>	159			
			Never	23	1.0		
			Ever	136	1.2 (0.8–1.9)		
			<1–6	114	1.2 (0.7–1.9)		
			7–14	19	1.7 (0.9–3.1)		
			>14	3	2.1 (0.6–7.0)		
					<i>p</i> for trend 0.05		
			<i>Men</i>	48			
			Never	8	1.0		
			Ever	40	1.5 (0.7–3.3)		
			<1–6	32	1.5 (0.7–3.4)		
			7–14	4	0.9 (0.2–3.0)		
			>14	4	2.4 (0.7–8.2)		
		<i>p</i> for trend 0.61					
<i>All</i>	207						
Never	31	1.0					
Ever	176	1.3 (0.9–1.9)					
<1–6	146	1.2 (0.8–1.8)					
7–14	23	1.4 (0.8–2.5)					
>14	7	2.1 (0.9–4.8)					
		<i>p</i> for trend 0.08					

CI, confidence interval, SEER, Surveillance, Epidemiology and End Result

Table 2.93 Case-control studies of alcoholic beverage consumption and melanoma

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Østerlind <i>et al.</i> (1988), East Denmark	474 incident, identified in the Danish Cancer Registry, aged 20–79 years; response rate, 92%	926 selected from National Population Register; response rate, 82%	Face-to-face structured questionnaire at home	<i>Alcoholic beverage</i>			Sunbathing, socioeconomic status
				Beer	0.7 (0.5–1.1)		
				Wine	0.7 (0.5–1.1)		
				Fortified wine	0.8 (0.5–1.2)		
				Distilled liquor	0.7 (0.5–1.1)		
				<i>Alcohol (kg/year)</i>			
0–1.1	1.0						
1.2–3.3	0.8 (0.6–1.1)						
3.4–8.4	0.8 (0.5–1.1)						
≥8.5	0.6 (0.4–0.9)						
Stryker <i>et al.</i> (1990), Massachusetts, USA, 1982–85	196 Caucasians; biopsy-confirmed cases older than 18 years; response rate, 92%	232 Caucasians; response rate, 92%	Face-to-face food-frequency questionnaire	Alcoholic bev.			Age, sex, hair colour, ability to tan
				<i>Beer</i>			
				None	1.0		
				<10 g/day	1.1		
				≥10 g/day	1.6		
					<i>p</i> trend=0.2		
				<i>Red wine</i>			
				None	1.0		
				<10 g/day	0.9		
				≥10 g/day	1.1		
					<i>p</i> trend=0.9		
				<i>White wine</i>			
None	1.0						
<10 g/day	0.9						
≥10 g/day	0.8						
	<i>p</i> trend=0.9						

Table 2.93 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Stryker <i>et al.</i> (1990) (contd)				<i>Liquor</i>			
				None		1.0	
				<10 g/day		1.3	
				≥10 g/day		1.2	
						<i>p</i> trend=0.7	
				<i>All types</i>			
None		1.0					
<10 g/day		1.2					
≥10 g/day		1.8 (1.0–3.3)					
		<i>p</i> trend=0.03					
Bain <i>et al.</i> (1993), Brisbane, Queensland, Australia, 1983–85	41 women, aged <80 years; histologically confirmed; [response rate, 63%]	297, aged <80 years; response rate not given	Mailed food-frequency questionnaire plus home interview	<i>Alcohol drinking (g/day)</i>			Age, hair colour, number of painful sunburns, total energy intake, number of years of schooling
			None		1.0		
			0.1–9.9		0.78 (0.32–1.94)		
			10.0–19.9		1.40 (0.46–4.30)		
			≥20.0		2.50 (0.87–7.40)		
Kirkpatrick <i>et al.</i> (1994), Washington State, USA, 1984–87	256 white, aged 25–65 years, identified from SEER cancer registry; response rate, 80%	234 identified by random-digit dialling to approximate age, sex, county of cases; response rate, 73%	Mailed food-frequency questionnaire plus telephone interview	<i>Drinks/month</i>			
				≤1	103	1.0	
				2–10	69	1.55	
				>10	62	1.18 (0.52–2.62)	
				≤1	103	1.0	
				2–10	69	1.31	
		>10	62	1.16 (0.53–2.59)			

Table 2.93 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Westerdahl <i>et al.</i> (1996), southern Sweden, 1988–90	400 men and women, aged 15–75 years, from Regional Tumour Registry; histopathological diagnosis; response rate, 88.1%	640 population-based, selected by random sampling, matched 2:1 by sex, age, parish; response rate, 70.1%	Mailed comprehensive questionnaire	Any versus none		1.0 (0.7–1.4)	History of sunburn, hair colour, number of raised naevi
				Distilled alcohol >1/month		1.4 (1.0–1.9)	
				<i>Total alcohol intake (g/day)</i>			
				0	84	1.0	
				1–9	160	0.8 (0.6–1.1)	
10–19	37	0.9 (0.5–1.5)					
≥20	25	0.9 (0.5–1.8)	<i>p</i> trend>0.05				
Millen <i>et al.</i> (2004), Philadelphia, California, USA, 1991–92	497 newly diagnosed invasive cutaneous melanoma in two clinics, aged 20–79 years; 100% histologically confirmed; response rate, 84%	561 hospital-based; dermatological or psychiatric problems for clinic visit excluded; response rate, 66%	Food-frequency questionnaire	<i>Alcohol (times/week)</i>			Education, skin response after repeated sun exposure, age, sex, study site, presence of dysplastic nevi
				0	154	1.0	
				0.7	77	1.04 (0.69–1.57)	
				1.4–7.0	160	1.55 (1.09–2.20)	
				7.7–59	106	1.53 (1.03–2.29)	
				<i>p</i> for trend		0.04	

Table 2.93 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Naldi <i>et al.</i> (2004), 27 centres in Italy, 1992–94	542 (226 men, 316 women), aged 15–87 years; 100% histologically confirmed; participation rate 99%	538 hospital-based (230 men, 308 women), aged 15–92 years; participation rate, 99%	Structured questionnaire, standardized examination	<i>Alcohol (drinks/week)</i> Never <1 1–13 14–27 ≥28	131 89 132 132 58	1.0 0.81 (0.53–1.22) 0.91 (0.62–1.33) 1.26 (0.83–1.91) 0.83 (0.49–1.40)	Age, sex, education, body mass index, history of sunburns, propensity to sunburn, number of naevi, number of freckles, skin, hair and eye colour, tobacco smoking

Table 2.93 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Vinceti <i>et al.</i> (2005), Modena, Italy, 3 years	59 (28 men, 31 women newly diagnosed cutaneous melanomas attending the Dermatologic Clinic of Modena University Hospital (only centre for diagnosis, therapy and follow-up); 100% histologically confirmed; participation rate, 72%)	59 randomly selected residents of Modena; matched on sex, age	Self-administered questionnaire on diet and lifestyle habits	<i>Alcohol (g)</i> <1.6 ≥1.6–23.3 >23.3		1.0 1.86 (0.64–5.42) 0.97 (0.17–5.50)	Dietary factors, energy intake

Table 2.93 (continued)

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Number of exposed cases	Odds ratio (95% CI)	Adjustment factors
Le Marchand <i>et al.</i> (2006), Hawaii, USA, 1986–92	278 prevalent and incident (167 men, 111 women) invasive or in situ identified through Hawaii Tumor Registry with four grandparents of pure Caucasian origin; aged 18–79 years 100% histopathologically confirmed; participation rate, 67.5%	278 Caucasians randomly selected from local residential; registries matched to each case on sex, age; participation rate, 60.6%	Standardized interview by trained interviewers, including demographics, sun exposure, vacations, lifetime smoking, alcohol use, quantitative food-frequency questionnaire, skin colour, naevi, hair colour	Alcohol drinking status			Height, education, hair and eye colour, number of blistering sunburns at ages 10–17 years, ability to tan, family history
				<i>Men</i>			
				Never	22	1.0	
				Former	35	1.6 (0.8–3.4)	
				Current	110	1.9 (1.0–3.4)	
				<i>Women</i>			
				Never	35	1.0	
				Former	30	1.3 (0.6–2.6)	
				Current	46	1.5 (0.7–2.9)	
				Lifetime ethanol intake (kg)			
<i>Men</i>							
≤45	47	1.0					
>45–265	52	1.2 (0.6–2.2)					
>265	68	2.3 (1.2–4.4)					
<i>Women</i>							
≥0	35	1.0					
1–48.6	36	1.1 (0.5–2.4)					
>48.6	40	1.7 (0.7–3.8)					

CI, confidence interval; SEER, Surveillance, Epidemiology and End Result

Table 2.94 Cohort studies of alcoholic beverage consumption and other female cancers

Reference, location, name of study	Cohort description	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson <i>et al.</i> (1996), Sweden, Temperance Boards Study	Nested case–control study; 15 508 alcoholic women born in 1870–1961 obtained from Temperance Boards; controls matched for region and day of birth; case ascertainment, Swedish Cancer Registry	Vulva, vagina and other female genital (ICD-7 176)	Alcohol abusers	16	4.0 (1.3–12)	Age, region	Estimate not adjusted for smoking
Weiderpass <i>et al.</i> (2001b), Sweden, National Board of Health and Welfare/Study of Alcoholic Women	36 856 women registered and hospitalized with alcoholism between 1965 and 1994; data from Inpatients Register; linkages to nationwide Registers of Causes of Death and Emigration and national Register of Cancer; mean age, 42.7 years; average follow-up time, 9.4 years	Vulva (ICD-7 176.0) Vagina (ICD-7 176.1)	Total <i>Age at cancer diagnosis</i> <50 years ≥50 years Total <i>Age at cancer diagnosis</i> <50 years ≥50 years	8 0 8 10 1 9	SIR 1.0 (0.4–2.0) – 1.2 (0.5–2.4) 4.6 (2.2–8.5) 2.5 (0.1–14.1) 5.1 (2.3–9.7)		Using expected rates specifically for squamous-cell carcinoma of the vulva, the overall SIR was 1.1 (0.5–2.2)

CI, confidence interval; ICD, International Classification of Diseases; SIR, standardized incidence ratio

risk for vaginal cancer but not for vulvar cancer (Weiderpass *et al.*, 2001b). The other study presented high relative risk estimates for both vulvar and vaginal cancers combined. The cohort studies could not adjust risk estimates for factors that may have confounded the association between alcoholic beverage and vulvar and vaginal cancers, such as HPV infections, number of sexual partners and tobacco smoking. It is possible that women who abuse alcohol have other behavioural patterns that may affect risks for vulvar and vaginal cancer.

(b) *Case-control studies (Table 2.95)*

Three case-control studies investigated the association between alcoholic beverage consumption and risk for vulvar cancer in Italy (Parazzini *et al.*, 1995b) and in the USA (Mabuchi *et al.*, 1985b; Sturgeon *et al.*, 1991). Two of these were hospital-based (Mabuchi *et al.*, 1985b; Parazzini *et al.*, 1995b) and one was population-based (Sturgeon *et al.*, 1991).

Confounding factors were considered in two studies (Sturgeon *et al.*, 1991; Parazzini *et al.*, 1995b), but only one provided risk estimates adjusted for smoking and sexual behaviour (Sturgeon *et al.*, 1991), which are potential confounders.

The three case-control studies reported no association between alcoholic beverage consumption and risk for vulva cancer.

(c) *Evidence of a dose-response*

One case-control study (Parazzini *et al.*, 1995b) and the cross-sectional study (Williams & Horm, 1977) presented information on dose-response for alcoholic beverage consumption and vulvar cancer. Neither study found evidence of a dose-response.

(d) *Types of alcoholic beverage*

Three studies (Williams & Horm, 1977; Mabuchi *et al.*, 1985b; Sturgeon *et al.*, 1991) investigated differences in risk according to the type of beverage and found no evidence of an effect.

Table 2.95 Case–control studies of alcoholic beverage consumption and other female cancers

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), The Third National Cancer Survey (cross-sectional study), USA, 1967–71	3856 cancer patients (all sites); age range not given; response rate, 57%	Randomly selected patients with cancers thought to be unrelated to tobacco and alcohol use	Personal interview	Vulva	Wine	0.63	Age, race, smoking	None of the values were significantly increased ($p>0.05$) *less/more than one drink per week during a year
					$\leq 51^*$	–		
					>51			
					Beer			
					≤ 51	1.61		
					>51	0.84		
					Hard liquor			
					≤ 51	1.67		
>51	0.43							
Total alcohol								
≤ 51	1.20							
>51	0.39							

Table 2.95 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Mabuchi <i>et al.</i> (1985b), New York, Michigan, Florida, Minnesota, USA, 1972–75	149 patients with vulvar carcinoma from 155 hospitals; patient identification abstracted from hospital records; 100% histologically confirmed; participation rate, 79.7%	149 patients, admitted to the hospital for circulatory, digestive, nervous system, musculoskeletal, respiratory, genitourinary, endocrine, orthopaedic diseases, accidents and others; free of any cancer; matched to cases on hospital, sex, race, age (in 3-year range), marital status	Interview by blinded interviewers, mostly at hospital	Vulva	No association between alcohol consumption or specific alcoholic beverages and risk for vulvar cancer			

Table 2.95 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Sturgeon <i>et al.</i> (1991), Chicago and Upstate New York, USA, 1985–87	201 incident cancer obtained from 34 hospitals in Chicago and Upstate New York, aged 53.9 years; 100% pathologically confirmed; participation rate, 61%	342 randomly selected using digit dialling techniques for controls <65 years and Health Care Financing Administration for women ≥65 years; mean age, 52.6 years; matched to cases by age in 5-year groups, race, residence; participation rate, 51%	Structured interview and food-frequency questionnaire at home	Vulva	No association between overall ethanol consumption and vulvar cancer; specific types of alcoholic beverage showed no appreciably increased risk with increasing intake.		Age, sexual behaviour, cigarette smoking	

Table 2.95 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Parazzini <i>et al.</i> (1995b), Milan, Italy, 1987–93	125 admitted to general and teaching hospitals in the greater Milan area, aged 30–80 years; invasive vulvar cancer histologically confirmed	541 patients randomly selected, admitted to the same hospitals for acute conditions, not hormonal, gynaecological or neoplastic, aged 27–79 years; matched by age, interview year	Standard questionnaire; interview during hospital stay	Vulva	<i>Alcohol drinking</i> Never Occasional Regular	1.0 0.7 (0.4–1.2) 1.1 (0.7–1.7) χ^2 trend=0.17 $p=0.68$	Age, education, body mass index	Limited statistical power due to small study sample size; possible information bias

CI, confidence interval; ICD, International Classification of Diseases

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