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 *et al*. (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 *et al*. (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 *et al*. (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)	60 (46.9)	1.28 (0.98–1.65)	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.
		Leukaemias (ICD-7 204)	30 (19.1)	1.57 (1.06–2.24)		

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, ocation, 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 *et al.* (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, ocation, 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 *et al*. (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)	*Ethanol (mL/day)* 0 <30 ≥30 *Beer (mL/day)* 0 <500 ≥500	 19 25 21 20 26 19	 1.0 1.0 (0.6–1.9) 3.1 (1.6–5.9) *p*-trend<0.01 1.0 1.5 (0.9–2.8) 2.8 (1.5–5.3) *p*-trend<0.01	Age, cigarette smoking	Of the total alcohol consumed by participants, 69% was beer, 24% spirits, 7% wine.

Table 2.82 (continued)

Reference, ocation, 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 *et al.* (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)	*Ethanol (g/day)* 0 ≤3.4 >3.4	 96 27 20	 1.0 0.78 (0.51–1.21) 0.59 (0.36–0.97) *p*-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, ocation, 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 *et al.* (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)** *NHL* 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** *Men* None <51 oz/years ≥51 oz/years *Women* None <51 oz/years ≥51 oz/years **Hodgkin disease** *Men* None <51 oz/years ≥51 oz/years *Women* None <51 oz/years ≥51 oz/years **Other lymphomas** *Men* None <51 oz/years ≥51 oz/years *Women* None <51 oz/years ≥51 oz/years	 5 8 8 3 7 7 4 0 4 1 1 0	 1.0 0.40 0.53 1.0 0.94 0.75 1.0 0.45 0.82 1.0 0.87 – 1.0 0.19 0.74 1.0 0.50 –	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

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 *et al*. (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 *et al*. (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 *Drinks/week* Non-drinker <5 5–11 12–23 >23	461 357 117 120 121 103	0.9 (0.7–1.1) 1.0 0.7 (0.5–1.0) 1.0 (0.7–1.4) 0.9 (0.6–1.2) 0.9 (0.7–1.3)	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 *et al*. (2002).

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 *et al*. (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** *Drinks/week* Non-drinker Current drinker 0.1–4 5–11 ≥12 **Women** *Drinks/week* Non-drinker Current drinker 0.1–4 5–11 ≥12	 69 46 37 29 50 122 71 45 13 13	 1.0 0.68 (0.43–1.08) 0.61 (0.34–1.12) 0.45 (0.24–0.84) 1.09 (0.60–1.98) *p*-trend=0.82 1.0 0.63 (0.40-1.00) 0.74 (0.43–1.27) 0.51 (0.24–1.06) 0.50 (0.23–1.09) *p*-trend=0.03	Matching factors adjusted for using conditional logistic regression	All cases and controls HIV negative; no significant differences in associations according to alcoholic beverage type
Tavani *et al*. (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 HD Tertile 1 Tertile 2 Tertile 3 NHL Tertile 1 Tertile 2 Tertile 3	 33 68 57 67 172 190	 1.0 1.1 (p>0.05) 0.9 (p>0.05) 1.0 0.8 (p>0.05) 0.8 (p>0.05)	Centre, age, sex	This study partially overlaps with Tavani *et al*. (2001b)
De Stefani *et al*. (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* Never drinker 1–60 mL alcohol/day ≥61 mL alcohol/day	30 20 35	1.0 1.4 (0.5–3.9) 1.1 (0.5–2.5)	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)

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 *et al*. (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 Former drinker <1.5 drinks/day ≥1.5 drinks/day Current drinker <1.5 drinks/day ≥1.5 drinks/day	183 14 13 1 136 87 49	1.00 1.01 (0.85–1.77) 1.57 (0.87–2.82) 0.18 (0.02–1.28) 0.67 (0.52–0.85) 0.63 (0.48–0.83) 0.74 (0.52–1.04)	Age, sex	
Tavani *et al*. (2001b), Milan and Pordenone, Italy, 1981–94	446 cases (256 men, 190 women) from hospitals in Pordeno, 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)	*Total alcohol (drinks/day)* Non-drinker <3 3–6 ≥7	 68 155 135 86	 1.0 0.92 (0.65–1.30) 0.98 (0.66–1.45) 1.02 (0.64–1.63) *p* trend=0.84	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; beer and spirit intake were associated with a borderline significantly increased risk.
Briggs *et al.* (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 All drinkers Current drinker Former drinker Wine drinker 1–6 drinks/week ≥1 drink/day	300 660 490 170 178 46	1.0 0.9 (0.8–1.1) 0.9 (0.8–1.1) 1.0 (0.8–1.3) 0.8 (0.5-1.3) 0.4 (0.2-0.9) *p*-trend = 0.02	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)

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 *et al.* (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	*Ethanol (g/week)* 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) *p*-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 *et al*. (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 Ever drinker *Ethanol (g/month)* <70 70–300 >300 *Duration (years)* 1–24 25–40 >40	230 371 124 126 121 138 122 111	1.0 0.82 (0.65-1.04) 0.82 (0.61–1.10) 0.83 (0.62–1.13) 0.82 (0.60–1.10) *p*-trend=0.79 1.05 (0.76–1.43) 0.89 (0.65–1.22) 0.62 (0.46–0.85) *p*-trend=0.01	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 (*p*-trend=0.02) and ≥25 years at initiation of wine drinking.

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 *et al*. (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)		
					Total alcohol(g/day)				
					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)		
					Total alcohol(g/day)				
					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		
					Current versus never drinker			Sex, age, smoking status	
					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 *et al*. (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)	*Drinks/day* 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 ≥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 *et al*. (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 ≥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) *p*-trend=0.97	Sex, age, ethnic origin, socioeco-nomic 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 *et al.* (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 *Ethanol (g/week)* ≤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) *p*-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 *et al*. (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 asssociation 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 *et al*. (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** Non-drinker Drinker *Ethanol (g/day)* 2–<10 10–<40 ≥40 **Women** Non-drinker Drinker *Ethanol (g/day)* 0.5–<2 2–<10 ≥10	 101 287 117 129 41 85 233 87 93 53	 1.0 0.47 (0.31–0.71) 0.52 (0.33–0.81) 0.41 (0.26–0.65) 0.50 (0.28–0.91) 1.0 0.68 (0.45–1.03) 0.67 (0.42–1.07) 0.66 (0.41–1.08) 0.73 (0.42–1.27)	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.

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	*Men* None <51 oz/year ≥51 oz/year *Women* None <51 oz/year ≥51 oz/year	 9 8 3 2	 1.0 2.0 (NR) 1.10 (NR) 1.0 0.71 (NR) 1.20 (NR)	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.

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 *et al.* (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	*Drinker versus non-drinker* All leukaemia ANLL CML CLL ALL Myelodysplasia Other	 333 72 31 138 12 41 39	 1.3 (0.8–1.3) 0.8 (0.5–1.1) 1.0 (0.6–1.9) 1.0 (0.7–1.3) 3.0 (0.9–9.9) 1.6 (0.9–2.7) 1.5 (0.8–2.6)	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.

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 *et al.* (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 Ophthalmo–logy; matched 2:1 on sex, age; response rate not given	Clinical chart abstraction	Leukaemia	**Ethanol (g/day)**			None	
					ANLL				
					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)		
					ALL				
					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)		
					CLL				
					0	35	1.0		
					1–21	6	2.87 (0.56–14.7)		
					22–43	2	0.38 (0.07–2.04)		
					≥44	–	–		
Pogoda *et al.* (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)	*Ethanol (g/day)*			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)		
							p-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 *et al.* (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 (± 10 years), race, region of residence; response rate, 66%	Interviewer-administered questionnaire	Acute leukaemia	Regular versus non-regular drinker *Drinks/week* <1 1–5 6–8 >8	NR 383 148 62 172	0.75 (0.60–93) 1.0 0.69 (0.52–0.92) 0.59 (0.40–0.87) 0.88 (0.66–1.2)	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.

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 *et al.* (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)** *All leukaemias* Ever versus never Non-drinker <9.0 9.1–7.9 18.0–1.7 >1.7 *ALL* Ever versus never *CLL* Ever versus never	 519 119 83 152 126 158 37 168	 0.97 (0.74–1.26) 1.0 0.73 (0.51–1.03) 1.05 (0.77–1.43) 1.03 (0.74–1.45) 1.15 (0.82–1.63) *p*-trend=0.007 0.88 (0.40–1.93) 0.86 (0.58–1.28)	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).

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* None <51 oz/years ≥51 oz/years *Women* None <51 oz/years ≥51 oz/years	 1 10 2 3	 1.0 0.19 (NR) 0.74 (NR) 1.0 0.42 (NR) 0.93 (NR)	Age, race, smoking	
Gallagher *et al*. (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 *et al*. (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 *et al.* (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 Drinker *Drinks/week* <5 5–11 12–23 >23 *Beverage type* Beer or wine only Hard liquor Other combinations	76 97 23 36 20 17 38 17 42	1.0 1.3 (0.9–1.9) 1.0 (0.6–1.8) 1.8 (1.1–3.1) 1.0 (0.6–1.8) 1.4 (0.7–2.6) 1.1 (0.7–1.7) 1.2 (0.6–2.3) 1.7 (1.0–2.7)	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.

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 *et al*. (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	*White men* Never drinker Ever drinker *Drinks/week* <8 8–21 22–56 ≥57 *Years drinking* <30 30–39 ≥40 *Beverage type* Liquor Beer Wine *Black men* Never drinker Ever drinker *Drinks/week* <8 8–21 22–56 ≥57	 55 137 55 42 31 9 26 43 65 96 110 58 24 67 18 22 21 6	 1.0 0.6 (0.4–0.9) 0.7 (0.5–1.1) 0.6 (0.3–0.9) 0.6 (0.4–1.1) 0.6 (0.3–1.3) 0.6 (0.4–1.1) 0.9 (0.5–1.4) 0.5 (0.3–0.8) 0.7 (0.4–1.0) 0.6 (0.4–0.9) 0.6 (0.4–1.0) 1.0 0.8 (0.5–1.3) 0.8 (0.4–1.5) 0.7 (0.4–1.3) 0.9 (0.5–1.8) 0.7 (0.3–1.8)	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.

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 *et al.* (1997) (contd)					*White women*				
					Never drinker	112	1.0		
					Ever drinker	61	0.7 (0.5–1.0)		
					Drinks/week				
					<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)		
					Black women				
					Never drinker	75	1.0		
					Ever drinker	40	1.0 (0.6–1.6)		
					Drinks/week				
					<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 *et al.* (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	NR	No association (data not shown)	None	
van Duijn *et al*., (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)** *ANLL* Age at diagnosis 0–4 years 5–9 years 10–14 years *ALL* 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 *et al.* (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)		
					Age at diagnosis				
					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 *et al.* (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** *ALL* Ever versus never 2nd and/or 3rd trimester None 1–20 drinks >20 drinks *AML* Ever versus never 2nd and/or 3rd trimester None 1–20 drinks >20	 NR NR NR NR NR NR NR NR	 1.43 (1.00–2.04) 2.28 (1.26–4.13) 1.0 1.76 (1.14–2.72) 0.93 (0.53–1.62) *p*-trend=0.40 2.64 (1.36–5.06) 10.48 (2.79–39.33) 1.0 2.36 (1.11–5.03) 3.13 (1.20–8.06) *p*-trend<0.01	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

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 *et al.*, (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	*Maternal intake* None 1 month before pregnancy During pregnancy <1.0 drink/day ≥1 drink/day Nursing period *Paternal intake 1 month before pregnancy* None Any <1.0 drink/day 1–2 drinks/day ≥3 drink/day	 NR 254 180 151 20 46 NR 420 189 143 79	 1.0 0.8 (0.6–1.1) 0.7 (0.5–0.9) 0.7 (0.5–1.0) 0.8 (0.5–1.6) 0.5 (0.3–0.8) 1.0 1.4 (1.0–2.0) 1.4 (1.0–2.0) 1.6 (1.1–2.5) 1.7 (1.1–2.7) *p*-trend=0.01	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 *GSTM1* null genotype and with *CYP2E1*5* allele

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 *et al.* (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** *ALL* Never Ever 1 glass/week 2 glasses/week ≥3 glasses/week *ANLL* Never Ever 1 glass/week 2 glasses/week ≥3 glasses/week	 87 153 103 25 25 12 28 21 – 7	 1.0 2.0 (1.4–3.0) 2.0 (1.3–3.0) 2.8 (1.3–6.0) 1.9 (0.9–3.5) 1.0 2.6 (1.2–5.8) 2.8 (1.2–6.6) – 2.4 (0.8–7.1)	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.

ALL, acute lumphocytic 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.