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 *et al*. (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	*Misusers* 82 *Alcoholics* 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	*PCMR* 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 *et al.*, (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	*Incidence*			Age, sex	Local male population
			50	48	1.0 (0.8–1.4)		
			85	84	1.0 (0.8–1.3)		
		Rectum	*Mortality*				
			63	58	1.1 (0.8–1.4)		
			62	54	1.1 (0.9–1.5)		
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	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 *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; 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) $p<0.001$		

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 *et al.* (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 *et al.* (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 *et al.* (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		58 men		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.
				Non-daily		1.0	
				1–30 mL ethanol/ day		2.2 (1.1–4.4)	
				≥30 mL ethanol/ day		2.4 (1.3–4.5)	
					68 women		
				Non-daily		1.0	
				1–30 mL ethanol/ day		1.1 (0.6–2.1)	
				≥30 mL ethanol/ day		1.4 (0.8–2.6)	
Klatsky *et al.* (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)	
						p-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)	
						p-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 Infrequent (1–2 times/month) Occasional (1–2 times/week) Daily Non-drinker Drinker	43 men 48 women	1.0 2.03 3.83 (p<0.05) 5.42 (p<0.01) p-trend<0.001 1.0 1.92 (p<0.05)	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.
Goldbohm *et al.* (1994)[a], Netherlands, 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	Abstainers 1–4.9 g ethanol/day 5–14.9 g ethanol/day 15–29.9 g ethanol/day ≥30 g ethanol/day	63 51 34 36 21	1.0 0.7 (0.5–1.0) 0.6 (0.4–0.9) 0.9 (0.5–1.6) 1.1 (0.3–3.6) p-trend=0.79	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.
			Rectum	Abstainers 1–4.9 g ethanol/day 5–14.9 g ethanol/day 15–29.9 ethanol/day ≥30 g ethanol/day	19 26 17 25 19	1.0 1.2 (0.6–2.4) 0.8 (0.4–1.6) 1.5 (0.7–3.2) 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 *et al.,* (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 <4 oz/month 4–<24 oz/month ≥24 oz/month	120 44 76 88	1.0 0.7 (0.5–9.0) 1.1 (0.8–1.4) 1.4 (1.0–1.8) *p*-trend=0.005	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
			Rectum	0 oz/month < oz/month 4–<24 oz/month ≥24	32 19 35 37	1.0 1.1 (0.6–2.0) 2.0 (1.2–3.2) 2.3 (1.4–3.7) *p*-trend=0.0001	
Glynn *et al.* (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-tochopherol, 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 Q2 >5.3–≤13.4 g ethanol/day Q3 >13.4–≤27.7 g ethanol/day Q4 >27.7 g ethanol/ day	5 7 8 15	1.0 1.5 (0.5–4.8) 1.8 (0.6–5.6) 3.6 (1.3–10.4) *p*-trend=0.01	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
			Rectum (ICD-9154)	Q1 ≤5.3 g ethanol/ day Q2 >5.3–≤13.4 g ethanol/day Q3 >13.4–≤27.7 g ethanol/day Q4 >27.7 g ethanol/ day	3 3 7 5	1.0 1.0 (0.2–5.1) 2.3 (0.6–9.0) 1.5 (0.3–6.7) *p*-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 *et al.* (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 0.1–1.0 cup/day 1.1–2.0 cups/day ≥2.1 cups/day	13 31 10 7	1.0 3.5 (p<0.01) 1.9 3.2 (p<0.05) p-trend <0.05	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
			Rectum (ICD-9154)	0 cup/day 0.1–1.0 cup/day 1.1–2.0 cups/day ≥2.1 cups/day	21 11 9 2	1.0 0.8 1.9 1.4 p-trend >0.05	
Thun *et al.* (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), Rectum (ICD-9154)	*Men* None Less than daily 1 drink/day 2–3 drinks/day ≥4 drinks/day	 211 216 111 182 131	*Men* 1.0 1.0 (0.9–1.3) 1.0 (0.8–1.3) 1.1 (0.9–1.4) 1.2 (1.0–1.5) p-trend=0.1	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.
				Women None Less than daily 1 drink/day 2–3 drinks/day ≥4 drinks/day	 305 131 40 76 24	*Women* 1.0 0.8 (0.7–1.0) 0.6 (0.4–0.8) 0.9 (0.7–1.2) 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 *et al.* (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) *p*-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 *et al.* (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 *et al*., 2004)
				≥20 g ethanol/day	26	1.1 (0.7–1.6)	
			Rectum (ICD-O20.0)	<20 g ethanol/day	116	1.0	
				≥20 g ethanol/day	7	0.9 (0.4–2.1)	
Otani *et al.* (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				*Men*	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
			Colon (ICD-O 180–189)	Non-drinker	62	1.0	
				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) *p*-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) *p*-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 *et al.* (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)	
						p-trend=0.58	
			Rectum (ICD-7 154 or ICD-10 20.0)	<1 drink/week	28	1.0	
				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)	
						p-trend=0.03	
Shimizu *et al.* (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			*Men*	Adjusted for age, height, body-mass index, smoking, years of education; significant dose–response relationship between alcohol consumption and colon cancer in both sexes
				No alcohol	5	1.0	
				≤36.7 g ethanol/day	45	1.8 (0.7–4.5)	
				>36.7 g ethanol/day	58	2.7 (1.1–6.8)	
						p-trend=0.01	
						Women	
				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)	
						p-trend=0.03	
			Rectum			*Men*	
				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)	
						p-trend=0.06	
						Women	
				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)	
						p-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 *et al.* (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 1–7 units/week >7 units/week	30 39 26	1.0 1.5 (0.9–2.5) 1.5 (0.9–2.7) *p*-trend=0.12	Adjusted for sex, age, smoking status; association with alcohol partially confounded by smoking
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 <1 drink/day ≥1 drink/day *Years drinking* 0 0–17 17–34 >34	63 22 26 52 3 17 39	1.0 1.1 (0.6–1.8) 1.7 (1.0–2.8) *p*-trend=0.04 1.0 0.7 (0.2–2.3) 1.3 (0.7–2.4) 1.7 (1.1–2.8) *p*-trend=0.02	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

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 *et al.* (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			*Men* - HPFS	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 *et al.*, 1995)
				0 g ethanol/day	37	1.0	
				<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	
						Women - NHS	
				0 g ethanol/day	200	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			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 *et al.* (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)	
				Daily	23	1.0 (0.5–1.8)	
			Rectum (ICD-O 154–154.1)	Non-drinker	73	1.0	
				Former drinker	0	NS	
				Occasional	28	1.2 (0.7–2.0)	
				Daily	34	1.2 (0.7–2.1)	
Wakai *et al.* (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	*Men*			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 ≈ 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.
				Non-drinker	24	1.0	
				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)	
						p-trend=0.85	
				Women			
				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)	
						p-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 *et al.* (2005) (contd)			Rectum			*Men*	
				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)	
						p-trend=0.027	
						Women	
				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)	
						p-trend=0.36	

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

[a]Studies 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 *et al*. (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	*Subgroups (no. of studies)* All (27) Men (13) Women (13) *Colon* (14) *Rectum* (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 *et al.* (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	*Total alcohol*			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) *p*-trend<0.001	
				Beer			
				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) *p*-trend=0.2	
				Wine			
				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) *p*-trend=0.001	
				Liquor			
				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) *p*-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 *et al*. (2004) (contd)			Colon	*Total alcohol*			
				0 g ethanol/day	Not reported	1.0	
				>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) *p*-trend<0.001	
			Rectum	*Total alcohol*			
				0 g ethanol/day	Not reported	1.0	
				> 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) *p*-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 *et al*. (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	*Subgroup (no. of studies)* All (7) Men (3) Women (3) Asia (4) Europe (2) USA (1) All (14) Men (7) Women (3) Asia (7) Europe (3) USA (4) All (12) Men (6) Women (3) Asia (7) Europe (3) USA (2)	*Colorectal* 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) *Colon* 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) *Rectum* 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	*Beer drinking* <Daily ≥Daily *Men* Abstainer Moderate drinker Heavy drinker *Women* Abstainer Moderate drinker Heavy drinker	 74 92 24 141 	Obs/Exp *Men* 1.0 1.4 (0.9–2.1) *Women* No association *Men* 1.0 1.1 2.1 *Women* 1.0 1.1 –	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				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	*Colon*	*Men*		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		
				Rectal			
				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)				*Colon*	*Women*		
				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		
				Rectal			
				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 *et al*. (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	*Colon* Men Women *Rectal* 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	*Colon* None <50 oz/year ≥50 oz/year None <50 oz/year ≥50 oz/year *Rectal* None <50 oz/year ≥50 oz/year None <50 oz/year ≥50 oz/year	 NG 52 96 NG 47 29 NG 27 42 NG 11 14	*Men* 1.0 1.4 1.5 (p<0.05) *Women* 1.0 1.2 1.4 *Men* 1.0 0.8 0.7 *Women* 1.0 0.8 2.0 (p<0.05)	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.
Graham *et al.* (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 *et al.* (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	*Colon* Non-consumer Consumer *Rectal* Non-consumer Consumer	 21 121 26 172	 1.0 1.4 (0.3–5.7) 1.0 1.6 (0.5–5.5)	Adjusted for sex, age
Manousos *et al.* (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	*Colorectal* 0 glasses of beer/ week 1–10 glasses of beer/week ≥11 glasses of beer/ week *Rectal* 0 glasses of beer/ week 1–10 glasses of beer/week ≥11 glasses of beer/ week	 68 24 8 27 5 3	 *p*-trend >0.25 *p*-trend >0.5	Matched on sex and age; futher 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

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 *et al.* (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	*Colon* 0 g ethanol/day 0.1–47.6 g ethanol/day >47.6 g ethanol/day 0 g ethanol/day 0.1–17.7 g ethanol/day >17.7 g ethanol/day *Rectal* 0 g ethanol/day 0.1–47.6 g ethanol/day >47.6 g ethanol/day 0 g ethanol/day 0.1–17.7 g ethanol/day >17.7 g ethanol/day		*Men* 1.0 1.2 1.4 *p*-trend=0.1 *Women* 1.0 1.0 1.0 *p*-trend=0.41 *Men* 1.0 0.5 ($p<0.05$) 1.3 *p*-trend=0.43 *Women* 1.0 1.3 0.8 *p*-trend=0.34	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

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 *et al.* (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** *Colon* Non-drinker >0 drink/week *Rectal* 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	*Colon* Non-drinker Drinker *Rectal* Non-drinker Drinker		*Men* 1.0 0.68 (p>0.5) *Men* 1.0 0.60 (p>0.5)	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
Kabat *et al.* (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	Never <1 oz/day 1–7.9 oz/day 8–31.9 oz/day ≥32 oz/day Never <1 oz/day 1–7.9 oz/day 8–31.9 oz/day ≥32 oz/day	30 31 26 21 22 67 12 7 2 0	*Men* 1.0 1.6 (0.9–2.8) 1.3 (0.7–2.4) 1.8 (0.9–3.5) 3.5 (1.8–7.0) *Women* 1.0 0.5 (0.3–1.0) 0.5 (0.2–1.2) 0.7 (0.1–3.2) –	Matched on sex, age, calendar year of hospital interview, religion, education; in men, heavy beer consumption associated with an increased risk for 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
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	*Colon* ≤0.1 g ethanol/day 0.1–4.0 g ethanol/day 4.1–12.8 g ethanol/day 12.9–31.8 g ethanol/day >31.8 g ethanol/day ≤0.1 g ethanol/day 0.1–0.95 g ethanol/day 0.96–3.9 g ethanol/day 4.0–12.9 g ethanol/day >12.9 g ethanol/day		*Men* 1.0 0.6 (0.3–1.3) 0.4 (0.2–1.0) 0.8 (0.4–1.7) 1.0 (0.5–2.1) *Women* 1.0 1.4 (0.7–2.7) 1.2 (0.5–2.6) 2.0 (0.9–4.4) 2.0 (0.9–4.5)	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.

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)				*Rectal*		*Men*	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; *p*-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)	
						Women	
				≤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 *et al.* (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	*Colon* 0 g ethanol/day 1–112 g ethanol/day 113–280 g ethanol/day ≥281 g ethanol/day 0 g ethanol/day 1–112 g ethanol/day 113–280 g ethanol/day ≥281 g ethanol/day *Rectal* 0 g ethanol/day 1–112 g ethanol/day 113–280 g ethanol/day ≥281 g ethanol/day 0 g ethanol/day 1–112 g ethanol/day 113–280 g ethanol/day ≥281 g ethanol/day		*Men* 1.0 1.4 1.0 1.0 *Women* 1.0 1.1 1.2 1.4 *Men* 1.0 1.5 1.1 1.5 *Women* 1.0 1.3 1.5 0.9	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; *p*-values and 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
Ferraroni *et al.* (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	*Colon* <3 drinks/day 3–6 drinks/day >6 drinks/day *Rectal* <3 drinks/day 3–6 drinks/day >6 drinks/day	 290 107 58 187 62 46	 1.0 1.1 1.2 p=0.67 1.0 0.8 0.9 p=0.46	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 *et al.*, 1993); 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
Peters *et al.* (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	*Colon* 0–9 g ethanol/day 10–39 g ethanol/day 40–69 g ethanol/day ≥70 g ethanol/day *Rectal* 0–9 g ethanol/day 10–39 g ethanol/day 40–69 g ethanol/day ≥70 g ethanol/day	 61 39 25 20 61 39 25 20	 1.0 1.0 (0.5–1.9) 0.8 (0.4–1.5) 1.6 (0.6–3.7) 1.0 1.2 (0.5–2.7) 0.6 (0.2–1.8) 1.4 (0.4–4.5)	Adjusted for age and education; no associations with any specific beverage type

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 *et al*. (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	*Drink–years (drinks/year × years drinking)* Quartile 1 Quartile 2 Quartile 3 Quartile 4 Tertile 1 Tertile 2 Tertile 3		*Men* 1.0 1.1 (0.7–1.8) 1.0 (0.6–1.7) 1.8 (1.1–2.9) *p*-trend=0.06 *Women* 1.0 0.9 (0.5–1.7) 1.9 (1.0–3.6) *p*-trend >0.05	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 *et al*., 1991).

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	*Right colon*			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	71	1.0	
				0.5 drink/day	59	0.9 (0.6–1.3)	
				1 drink/day	31	1.0 (0.6–1.5)	
				2 drinks/day	27	1.0 (0.6–1.7)	
				3–4 drinks/day	40	1.7 (1.1–2.7)	
				≥5.0 drinks/day	21	1.8 (1.0–3.2)	
						p-trend=0.007	
				Rectal			
				0 drink/day	97	1.0	
				0.5 drink/day	107	1.1 (0.8–1.5)	
				1 drink/day	46	0.9 (0.6–1.4)	
				2 drinks/day	48	1.2 (0.8–1.9)	
				3–4 drinks/day	64	1.7 (1.1–2.5)	
				≥5.0 drinks/day	30	1.5 (0.9–2.5)	
						p-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 *et al.* (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	*Men* Never 1–15 g ethanol/ week >15 g ethanol/week *Women* Never 1–15 g ethanol/ week >15 g ethanol/week	 60 26 26 100 15 4	*Men* 1.0 1.4 (0.7–3.0) 1.1 (0.5–2.4) *Women* 1.0 1.1 (0.5–2.1) 0.6 (0.2–1.9)	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).
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	*Colon* Non-drinker Light Moderate Medium–heavy Heavy *Rectal* Non-drinker Light Moderate Medium–heavy Heavy	 19 14 18 10 2 11 22 16 14 4	 1.0 0.6 (0.3–1.4) 1.1 (0.5–2.5) 1.0 (0.4–2.3) 0.7 (0.1–3.6) 1.0 2.2 (1.0–7.5) 2.0 (0.8–4.9) 2.5 (1.1–5.6) 4.7 (1.3–2.8)	Adjusted for age, marital status, education, cigarette smoking, diet; too few female drinkers so results limited to men

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 *et al.* (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	*Colon* <1.0 kg/year ≥1.0 kg/year *Rectal* <1.0 kg/year ≥1.0 kg/year		*Men and women* 1.0 6.42 ($p<0.01$) *Men* 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 *et al.* (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	*Colon* 0 mL ethanol/day 1–30.1 mL ethanol/day 30.2–53.9 mL ethanol/day 54–90.7 mL ethanol/day >90.7 mL ethanol/day 0 mL ethanol/day 1–9.9 mL ethanol/day 10–15.5 mL ethanol/day 15.6–25.8 mL ethanol/day >90.7 mL ethanol/day	 5 22 22 19 24 29 22 14 19 20	*Men* 1.0 0.9 0.9 0.8 1.0 *p*-trend=0.99 *Women* 1.0 1.4 0.9 1.3 1.4 *p*-trend=0.43	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.

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 *et al.* (1991) (contd)				*Rectal*		*Men*	
				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 *p*-trend=0.42	
						Women	
				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 *p*-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 *et al*. (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	*Colon* 0–9.9 g ethanol/day 10.0–19.9 g ethanol/day 20.0–29.9 g ethanol/day ≥30 g ethanol/day *Rectal* 0–9.9 g ethanol/day 10.0–19.9 g ethanol/day 20.0–29.9 g ethanol/day ≥30 g ethanol/day	 282 37 18 15 166 30 11 10	 1.0 0.7 (0.5–1.2) 1.2 (0.6–2.3) 0.9 (0.4–1.8) 1.0 1.0 (0.6–1.6) 1.2 (0.6–2.7) 1.1 (0.5–2.4)	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

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 *et al*. (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	*Colon* Never Past Occasional <50 mL ethanol/day ≥50 mL ethanol/day *Rectal* Never Past Occasional <50 mL ethanol/day ≥50 mL ethanol/day	 42 2 18 9 9 41 2 19 19 21	 1.0 0.4 (0.0–2.0) 0.6 (0.3–1.1) 0.3 (0.1–0.8) 0.3 (0.1–0.9) 1.0 0.3 (0.0–1.7) 0.5 (0.2–1.0) 0.5 (0.2–1.1) 0.6 (0.3–1.3)	Adjusted for sex and age; heavier drinking not associated with increased risk for colon or rectal cancer
Meyer & White (1993), Washington, USA, 1985–89	424 colon, men and women aged 30–62 years; identified through the Seattle-Pugent 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	 0 g ethanol/day 0.1–9.9 g ethanol/day 10–29 g ethanol/day ≥30 g ethanol/day Total consumption 0 g ethanol/day 0.1–9.9 g ethanol/day 10–29 g ethanol/day ≥30 g ethanol/day Total consumption	 	*Men* 1.0 1.9 1.7 2.6 (1.04–1.54) *p*-trend <0.05 *Women* 1.0 1.3 1.8 2.5 (1.03–1.72) *p*-trend <0.05	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.

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 *et al.* (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	*Colon* None 1–2 drinks/week 3–5 drinks/week 6–10 drinks/week ≥11 drinks/week *Rectum* None 1–2 drinks/week 3–5 drinks/week 6–10 drinks/week ≥11 drinks/week	 122 239 77 46 33 47 93 48 26 19	 1.0 1.0 (0.8–1.3) 0.9 (0.6–1.3) 0.9 (0.6–1.4) 1.3 (0.8–2.2) *p*-trend=0.61 1.0 0.9 (0.6–1.4) 1.5 (0.9–2.3) 1.3 (0.8–2.2) 1.9 (1.0–3.5) *p*-trend=0.01	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

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 Haemoccult 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 Haemoccult 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 Haemoccult 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 *et al.* (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	*Men* <10 g ethanol/day 10–19 g ethanol/day 20–39 g ethanol/day 40–59 g ethanol/day ≥60 g ethanol/day *Women* <5 g ethanol/day 5–9 g ethanol/day ≥10 g ethanol/day	 16 12 26 24 31 41 4 17	*Men* 1.0 1.5 (0.6–4.4) 1.2 (0.6–2.6) 1.9 (0.9–4.5) 1.3 (0.6–2.9) p >0.1 *Women* 1.0 0.6 (0.2–1.8) 0.9 (0.5–1.9) p>0.1	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
Le Marchand *et al*. (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	*Right colon* Never Past Current Never Past Current	 	*Men* 1.0 2.6 (1.4–5.2) 2.0 (1.0–3.4) *Women* 1.0 3.1 (1.0–9.4) 2.5 (0.9–7.0)	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.

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 *et al*. (1997) (contd)				*Left colon*		*Men*	
				Never		1.0	
				Past		1.7 (0.8–3.3)	
				Current		1.1 (0.7–2.0)	
						Women	
				Never		1.0	
				Past		1.3 (0.5–3.4)	
				Current		1.0 (0.5–2.3)	
				Rectal		*Men*	
				Never		1.0	
				Past		1.4 (0.8–2.4)	
				Current		1.1 (0.6–2.0)	
						Women	
				Never		1.0	
				Past		1.5 (0.6–4.1)	
				Current		1.0 (0.3–3.0)	
Yamada *et al*. (1997), Tokyo, Japan, 1991–93	66 colorectal (55 men, 11 women) (excluded *in situ*), 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	23	1.0	Adjusted for sex, age, body-mass index, cigarettes smoked per day
				1–20 g ethanol/day	24	1.1 (0.4–3.1)	
				21–40 g ethanol/day	55	0.7 (0.3–1.9)	
				≥41 g ethanol/day	30	2.0 (0.7–5.4)	
						p-trend=0.09	

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 *et al.* (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) *p*-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 *et al.* (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	*Colon* 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) *p*-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 *et al.* (1998) (contd)				*Rectum*			
				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) *p*-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 *et al.* (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	*Colon* Non-drinker Former drinker Current drinker Non-drinker Former drinker Current drinker *Rectum* Non-drinker Former drinker Current drinker Non-drinker Former drinker Current drinker	 248 41 173 448 6 15 255 34 174 390 4 17	*Men* 1.0 2.3 (1.4–3.7) 1.0 (0.8–1.3) *Women* 1.0 1.4 (0.4–4.3) 0.7 (0.4–1.3) *Men* 1.0 1.1 (0.9–1.4) 0.6 (0.4–1.0) *Women* 1.0 1.2 (0.7–2.3) 1.1 (0.3–4.1)	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.

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 *et al.* (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	*Proximal colon* Never drank weekly Drank weekly Drank daily *Distal colon* Never drank weekly Drank weekly Drank daily *Rectum* Never drank weekly Drank weekly Drank daily	 41 55 80 28 51 100 37 74 119	 1.0 1.1 (0.6–1.7) 1.0 (0.6–1.7) *p*-trend=0.9 1.0 1.4 (0.9–2.5) 2.3 (1.4–3.7) *p*-trend=0.001 1.0 1.5 (0.9–2.4) 1.6 (1.0–2.6) *p*-trend=0.06	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

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 *et al.* (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	*Colon* Never Former drinker Current drinker *Rectal* Never Former drinker Current drinker	 219 97 133 164 84 111	 1.0 1.0 (0.7–1.3) 1.5 (1.1–2.0) *p*-trend=0.02 1.0 1.1 (0.7–1.5) 1.3 (1.0–1.9) *p*-trend=0.1	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.

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 *et al.* (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	*Colon* <5 g ethanol/day 5–29 g ethanol/day ≥30 g ethanol/day *Rectal* <5 g ethanol/day 5–29 g ethanol/day ≥30 g ethanol/day	 58 23 30 81 24 27	 1.0 1.2 (0.6–2.7) 2.7 (1.2–6.1) 1.0 0.7 (0.4–1.5) 1.4 (0.7–3.0)	Adjusted for sex, age, total energy intake, family history of colorectal cancer, body mass index, smoking, vigorous physical activity, red meat intake, *MTHFR* genotype; no evidence of an interaction of alcoholic beverages with *MTHFR* genotype on risk for colon, rectal or colorectal 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
Murtaugh *et al*. (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			*Men*	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
				None	251	1.0	
				Low	183	0.9 (0.7–1.2)	
				High	172	1.3 (0.9–1.7)	
						Women	
				None	227	1.0	
				Low	116	1.1 (0.8–1.4)	
				High	72	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/m^2 but 1.08 for persons with a body-mass index of ≥25 kg/m^2 (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 sociodemographic 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.