2.13 Cancer of the ovary

2.13.1 *Cohort studies (Tables 2.70 and 2.71)*

Since 1988, four prospective cohort studies have examined the association between alcoholic beverage intake and the risk for ovarian cancer in special populations, namely women hospitalized or being treated for alcohol dependence (Adami *et al*., 1992a; Tønnesen *et al*., 1994, Sigvardsson *et al*., 1996; Lagiou *et al*., 2001; Table 2.70) and four have examined the association in the general population (Kushi *et al*., 1999; Kelemen *et al*., 2004; Schouten *et al*., 2004; Chang *et al*., 2007; Table 2.71). The studies were conducted in Europe (Denmark, the Netherlands and Sweden) and the USA. The studies in special populations presented results adjusted for age and calendar period only, whereas the population-based cohort studies presented results adjusted for a large variety of factors.

There was no evidence of an overall association between alcoholic beverage intake and the risk for ovarian cancer in these cohort studies.

Table 2.70 Cohort studies of ovarian cancer and alcoholic beverage consumption in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Comments
Adami *et al.* (1992a) Sweden, Cohort of people with a discharge diagnosis of alcoholism	Cohort of 9353 individuals (1013 women) with a discharge diagnosis of alcoholism in 1965–83; follow-up for 19 years (mean, 7.7 years); exclusion of cancer in the first year of follow-up	Registry-based	Women with diagnosis of alcoholism	4	**SIR** 1.9 (0.5–4.9)	
Tønnesen *et al.* (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 male and female alcohol abusers who entered an outpatient clinic in Copenhagen during 1954–198?; 3093 women observed for 9.4 years	Registry-based	Alcohol abusers	6	0.9 (0.3–1.8)	
Sigvardsson *et al.* (1996), Sweden, Alcoholic women from the records of the Temperance Boards	Ovarian and fallopian tube cancer detected among 65 women	Registry-based	Alcohol abusers	65	1.2 (0.9–1.8)	
Lagiou *et al.* (2001), Sweden, Cohort of alcoholic women	Cohort of 36 856 women diagnosed with alcoholism between 1965 and 1994; mean duration of follow-up, 9.6 years, 317 518 person–years; first year of follow-up excluded from all analysis.	Registry-based	All women	76	**SIR** 0.86 (0.68–1.08) p=0.19	Expanded population and follow-up of the cohort reported by Adami *et al.* (1992a)

CI, confidence interval; SIR, standardized incidence ratio

Table 2.71 Cohort studies of ovarian cancer and alcoholic beverage consumption in the general population

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kushi *et al.* (1999), Iowa, USA, Iowa Women's Health Study	29 083 women, aged 55–69 years (postmenopausal); follow-up 1986–95 (10 years); 139 incident cases of epithelial ovarian carcinoma; exclusions: cancer history other than skin, bilateral oopherectomy, incomplete questionnaire, energy intake implausibly high or low	Mailed self-administrated questionnaire (in 1986) and follow-up questionnaires (1987, 1989, 1992)	Ovary	*Alcohol consumption (g/day)* 0 0.9–3.9 4.0–10 >10	 78 43 8 10	 1.00 (reference) 1.37 (0.93–2.04) 0.61 (0.28–1.34) 0.49 (0.24–1.01) *p* trend=0.01	Age, total energy intake, number of live births, age at menopause, family history of ovarian cancer in a first degree relative, hysterectomy/ unilateral oopherectomy status, waist-to-hip ratio, level of physical activity, cigarette smoking, educational level	

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kelemen *et al.* (2004), Iowa, USA, Iowa Women's Health Study	27 205 women, aged 55–69 years (postmenopausal); follow-up, 1986–2000 (15 years); 147 incident epithelial ovarian cancers detected; association between ovarian cancer and alcohol in the context of folate consumption examined	Self-administered questionnaires	Ovary	*Alcohol consumption (g/day)* <0.01 0.01–3.9 4.00–9.9 ≥10	 48 75 12 12	 1.00 (reference) 0.78 (0.54–1.13) 0.75 (0.39–1.42) 0.58 (0.30–1.11) *p* trend=0.08	Age, folate, age at menopause, physical activity, postmenopausal hormone use, oral contraceptive use, family history of breast cancer, family history of ovarian cancer, known diabetes at baseline, smoking, carotene, vitamin C and vitamin E	

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Schouten *et al.* (2004), Netherlands, The Netherlands Cohort Study	62 573 Dutch postmenopausal women, aged 55–69 years; started September 1986; follow up of sub-cohort of 2211 members; exclusion criteria: any cancer diagnosis other than skin, women who had undergone oopherectomy; follow-up biennially by mail to December 1995 (9.3 years); 235 cases of epithelial ovarian cancer detected; analysis based on 214 cases	Self-administered questionnaire	Ovary	*Alcohol consumption (categorical mean)* No (0) g/day 0.1–4 (1.9) g/day 5–14 (9.3) g/day ≥15 (26.3) g/day Total increment per 10 g alcohol	 57 74 28 21 	 1.00 (reference) 1.13 (0.79–1.63) 0.85 (0.53–1.37) 0.92 (0.55–1.54) *p* trend=0.54 1.01 (0.84–1.21)	Age, use of oral contraceptives, parity, height, body mass index, energy intake, current cigarette smoking	Possible limitation: misclassification of alcohol consumption (if any, expected to be non-differential); former-drinkers not separated from abstainers (small proportion)

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chang *et al.* (2007), USA, California Teachers Study	90 371 teachers; baseline assessment 1995–96; follow-up to end of 2003; excluded: women >85 years of age, with previous history of ovarian cancer, bilateral oopherectomy before baseline, when information not provided or invalid; 253 women diagnosed with epithelial ovarian cancer (227 invasive, 26 borderline)	Mailed questionnaire	Ovary (invasive and borderline)	**Year before baseline** *Total alcohol intake (g/day)* None <10 10–20 ≥20 *Alcohol from wine (g/day)* None <11.1 ≥11.1	 77 81 72 23 91 99 63	 1.00 (reference) 1.04 (0.76–1.42) 1.47 (1.06–2.03) 1.15 (0.71–1.84) *p* trend=0.19 1.00 (reference) 1.09 (0.80–1.50) 1.57 (1.11–2.22) *p* trend=0.01	Race, total energy intake, parity, oral contraceptive use, strenuous exercise, menopausal status/hormone replacement therapy, stratified by age at baseline; other alcohol types, race, total energy intake, parity, oral contraceptive/ hormone-replacement therapy use, strenuous exercise, menopausal status, stratified by age at baseline;	

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chang *et al*. (2007) (contd)				Interactions **Wine intake (g/day)** *Socioeconomic status: upper 25%* ≥11.1	39	1.96 (1.19–3.24) *p* trend=0.004	(contd) race, total energy intake, parity, oral contraceptive use, strenuous exercise, menopausal status/hormone replacement therapy, stratified by age at baseline	
				Lifetime strenuous physical activity ≤1.4 h None <11.1 ≥11.1	61 58 40	1.00 (reference) 1.07 (0.72–1.59) 1.68 (1.09–2.59) *p* trend=0.01		
				Parity: parous None <11.1 ≥11.1	71 73 48	1.00 (reference) 1.05 (0.73–1.50) 1.57 (1.06–2.34) *p* trend=0.02		
				Median age >50 years None <11.1 ≥11.1	68 72 51	1.00 (reference) 1.10 (0.76–1.57) 1.62 (1.09–2.39) *p* trend=0.01		
				Menopausal status: Peri/ postmenopausal None <11.1 ≥11.1	66 72 51	1.00 (reference) 1.16 (0.80–1.66) 1.72 (1.16–2.55) *p* trend=0.01		

Table 2.71 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Chang *et al*. (2007) (contd)				**Alcohol intake ≥11.1 g/day**				
				Oral contraceptive use				
				Never	29	1.70 (1.02–2.82)		*p* trend=0.03
				Ever	14	1.78 (0.85–3.72)		*p* trend=0.09
				Hormone therapy use				
				None	9	1.20 (0.51–2.78)		*p* trend=0.73
				Estrogen+progestin	16	1.17 (0.58–2.34)		*p* trend=0.45
				Estrogen only	15	2.03 (0.95–4.35)		*p* trend=0.06
				Cigarette smoking				
				Ever	27	1.42 (0.80–2.50)		*p* trend=0.24
				Never	36	1.77 (1.13–2.78)		*p* trend=0.01
				Total folate intake				
				≤473 µg/day	25	1.34 (0.78–2.30)		*p* trend=0.27
				>473 µg/day	37	2.07 (1.29–3.35)		*p* trend=0.002

CI, confidence interval; ICD, International Classification of Diseases

2.13.2 *Case–control studies (Table 2.72)*

Twenty-three case–control studies investigated the relationship between alcoholic beverage consumption and the risk for ovarian cancer in Australia, India, Japan, North America, Scandinavia and western Europe.

Twelve of these were hospital-based (West, 1966; Williams & Horm, 1977; Byers *et al*., 1983; Tzonou *et al*., 1984; Mori *et al*., 1988; Whittemore *et al*., 1988; Hartge *et al*., 1989; La Vecchia *et al*., 1992; Nandakumar *et al*., 1995; Tavani *et al*., 2001a; Yen *et al*., 2003; Pelucchi *et al*., 2005), one was based on cases and controls who were included in a cancer registry database (Kato *et al*., 1989) and 10 were population-based (Gwinn *et al*., 1986; Polychronopoulou *et al*., 1993; Kuper *et al*., 2000b; Goodman & Tung, 2003; McCann *et al*., 2003; Modugno *et al*., 2003; Riman *et al*., 2004; Webb *et al*., 2004; Peterson *et al*., 2006).

Confounding factors were considered in all studies, although adjustment was less extensive in studies published during the 1980s. Overall, the results of case–control studies do not suggest any association between alcoholic beverage consumption and the risk for ovarian cancer, although a few studies indicated either positive or negative associations.

2.13.3 *Evidence for a dose–response*

There was no consistent evidence of a trend of increasing risk for ovarian cancer with increasing alcoholic beverage consumption based on the cohort or case–control studies.

2.13.4 *Types of alcoholic beverage*

In two population-based cohort studies the association between types of alcoholic beverage was investigated (Schouten *et al*., 2004; Chang *et al*., 2007). Intake of wine during the year before baseline was associated with an increased risk for ovarian cancer in one study (Chang *et al*., 2007), but was not confirmed in the other (Schouten *et al*., 2004).

Seven case–control studies evaluated different alcoholic beverages in relation to the risk for ovarian cancer (Gwinn *et al*., 1986; La Vecchia *et al*., 1992; Tavani *et al*., 2001a; Goodman & Tung, 2003; Modugno *et al*., 2003; Webb *et al*., 2004; Peterson *et al*., 2006). Overall, there were no consistent patterns of association between any specific type of alcoholic beverage (beer, wine, spirits) and risk for ovarian cancer.

2.13.5 *Interactions*

Three of the cohort studies (Kelemen *et al*., 2004; Schouten *et al*., 2004; Chang *et al*., 2007) investigated possible interactions between alcoholic beverage intake and

Table 2.72 Case–control studies of ovarian cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
West (1966), Massachusetts, USA, 1959–60 (controlled case–history study)	92 (of 97) patients with primary ovarian malignancy, resident within a 50-mile radius of Boston, MA; aged 25–74 years; from 50 hospitals in Boston and greater Boston area, operated from 1 January 1959 until 31 March, 1960 (date of incidence = date of surgery); exclusions: women aged >75 years, women with co-existent malignancy of another organ, not metastatic from ovary	92 (of 97) hospital patients with benign ovarian tumour; matched for age, residence, day of surgery.	Interview based on the same protocol for cases and controls	Ovary	Use of alcohol	Data not shown p=0.28		No significant difference between alcohol users and non-users

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967–71	7518 cancer patients (all sites, men and women) interviewed; 57% selected randomly	Randomly selected patients with cancer of other, non-related sites	Interview	Ovary	*Wine level*	*Relative odds*	Age, race,	
					1	0.62		
					2	1.00		
					Beer level			
					1	0.54		
					2	0.88		
					Hard liquor level			
					1	0.61		
					2	0.93		
					Total alcohol oz–years level			
					1	0.88		
					2	0.87		
					Wine level		Age, race, smoking	
					1	0.49		
					2	0.85		
					Beer level			
					1	0.51		
					2	0.81		
					Hard liquor level			
					1	0.52		
					2	0.94		
					Total alcohol oz–years level			
					1	0.74		
					2	0.85		

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Byers *et al.* (1983), USA, 1957–65	274 white women patients, diagnosed within 2 years of interview, admitted to Roswell Park Memorial Institute, aged 30–79 years	1034 hospitalized white women admitted to same institute at the same time for non-malignant conditions, not related to the reproductive system or gastrointestinal system, or diagnosed with *diabetes mellitus* or thyroid disease, aged 30–79 years	Mailed questionnaire before admission to hospital, individual interview on the day of admission and second interview at admission by trained interviewer	Ovary	**Drinks per week** *At age 30–49 years* 0 <8 ≥9 *At age 50–79 years* 0 <8 ≥9 *At age 30–79 years* 0 <8 ≥9	 1.0 (reference) 0.84 0.56 1.00 (reference) 0.98 1.09 1.00 (reference) 0.92 0.83	Age	Possible selection bias does not account for the observed risks; possible recall bias; nearly all patients of advanced stage; analysis by stage not possible.
Tzonou *et al.* (1984), Athens, Greece, 1980–81	150 women with common and primary epithelial ovarian cancer, operated in any of 10 large hospitals of the Greater Athens area; 100% histologically confirmed; participation rate, 82.4%	250 women hospitalized at the same time in the Athens hospitals for first-time orthopaedic disorders, randomly chosen; participation rate, 100%	Standard questionnaire at interview by the same physician	Ovary	Non-drinkers Drinkers *Duration (years)* ≤9 10–19 20–29	(reference) 1.5 (0.9–2.5) 0.7 (0.2–2.2) 1.9 (0.7–4.8) 2.9 (1.1–7.6)	Age, parity, age at menopause, use of exogenous estrogens	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Gwinn *et al.* (1986), Atlanta, Detroit, San Francisco, Seattle, the states of Connecticut, Iowa and New Mexico and the four urban counties of Utah, USA, December 1980–December 1982	433 women diagnosed between December 1980 and December 1982, lived in one of the study areas at the time of diagnosis, aged 20–54 years; 100% histologically confirmed; participation rate, 71%	2915 women identified by randomly selecting telephone numbers of households in the geographic areas where the cases lived, aged 20–54 years; matched by age (5-year intervals); no history of bilateral oophorectomy; response rate, 83.4%	Standard questionnaire in participants' homes by trained interviewers; questions about alcohol consumption habits in the last 5 years added to the questionnaire in August 1981	Ovary	*Average weekly consumption* Never drank Ever drank <50 g/week 50–149 g/week 150–249 g/week ≥250 g/week	 1.0 (reference) 0.9 (0.7–1.2) 1.0 (0.7–1.4) 0.8 (0.5–1.1) 1.0 (0.6–1.6) 0.5 (0.2–0.9)	Age, geographic region, religion, education, smoking, oral contraceptive use, parity, infertility, family history of ovarian cancer	Lack of information on drinking status for 13 cases and 50 controls (one drink=12.6 g alcohol)

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Mori *et al.* (1988), Hokkaido, Japan, 1980–81 and 1985–86	110 women with primary epithelial ovarian cancer, hospitalized in any hospital in Hokkaido; participation rate, 100%	220; two series: 110 patients from wards in hospitals in Hokkaido with diseases other than ovarian cancer; 110 identified from outpatients without any malignant gynaecological diseases; matched to cases by year of birth, year of the survey; participation rate, 100%	In-person interview	Ovary	*Consumption of alcoholic beverages* Less than once a week At least once a week	 1 (reference) 1.0 (0.6–1.9)	Unclear (none?)	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Whittemore *et al.* (1988), San Francisco Bay area, USA, 1983–85	188 women from northern California diagnosed between January 1983 and December 1985 in one of the seven hospitals in Santa Clara County or at University of California San Francisco, Medical Center, aged 18–74 years	539; 280 hospitalized in one of the hospitals where cases were admitted, without overt cancer; 259 chosen from the general population by random-digit dialling; matched to cases by age (within 5-year intervals), race (white, black, oriental)	Structured home interviews by trained interviewers	Ovary	*Previous alcohol consumption* Non-drinker Drinker Non-drinker Heavy drinker (>20 drinks/ week)	 1 0.74 p=0.14 1 0.66 p=0.34	Observations not altered by adjustment for cigarette smoking or coffee consumption	No evidence of a trend in risk with increasing duration or amount of alcohol consumption; absence of data on diet may preclude examination of potential confounders.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Hartge *et al.* (1989), Washington DC, USA, August 1978–June 1981	296 women with primary epithelial ovarian cancer, residents of metropolitan area of Washington DC, aged 20–79 years; diagnosis microscopically confirmed after operation; participation rate, 74%	343 women hospitalized at the same time and the same hospitals as cases, identified from hospital discharge lists; matched to cases by hospital, age, race; exclusion criteria: patients with psychiatric diagnosis and with diagnosis related to the major exposures of interest; patients with bilateral oophorectomy; participation rate, 78%	Standardized questionnaire by trained interviewers at participants' home shortly after diagnosis	Ovary	*Average weekly consumption* 0 Occasional drink 1–6 drinks 7–13 drinks ≥14 drinks	 1.0 (reference) 1.1 (0.7–1.9) 1.4 (0.8–2.3) 1.2 (0.7–2.2) 1.5 (0.8–2.8) p=0.14	Age, race	
Kato *et al.* (1989), Japan, 1980–86	417 women registered at Aichi Cancer Registry, diagnosed between 1980 and 1986, aged ≥20 years	8920 cases of cancer of other sites excluding cancers known to be alcohol-related	Records from Aichi Cancer Registry with available data on alcohol drinking habits	Ovary	*Alcohol drinking* Daily versus less	 0.38 (0.15–0.95) p<0.05	Age	Possible bias due to control selection from cancer patients; no information on important risk factors

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
La Vecchia *et al.* (1992), Milan, Italy, January 1983–May 1990 (overlaps with La Vecchia *et al.*, 1986)	801 women with incident ovarian cancer, aged 22–74 years; 100% histologically confirmed	2114 women admitted to a network of teaching or general hospitals in the greater Milan area for acute, non-neoplastic, gynaecological or hormone-related conditions diagnosed within the year before the interview, and not undergone bilateral oophorectomy, aged 24–74 years	In-person interview based on a standardized questionnaire during hospital admission	Ovary	*Alcohol consumption (drinks/day)* 0 <1 1<2 2<3 ≥3	 1.0 1.0 (0.7–1.4) 1.1 (0.9–1.4) 1.2 (1.0–1.5) 1.3 (0.9–1.8) $p \leq 0.05$ $\chi^2=4.29$	Age, education, smoking, menstrual and reproductive factors, oral contraceptive use, indicators of fat and green vegetable consumption	

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Polychronopoulou *et al.* (1993), Greater Athens, Greece, June 1989–March 1991	189 women residents of Greater Athens, operated for epithelial ovarian cancer in two hospitals, aged ≤75 years	200 residents of Greater Athens, visitors of patients hospitalized in the same wards as the cancer patients at the same time, aged <75 years; exclusion criteria: previous cancer diagnosis or at least one ovary removed; not matched by age	In-person interview questionnaire by resident doctor at each of the hospitals	Ovary	*Consumption of alcoholic beverages (glasses/day)* Never ≥1 1 1–2 >2	 1.00 0.85 (0.52–1.39) 1.06 (0.82–1.36) 0.94 (0.49–1.79) 1.62 (0.66–3.96) *p*=0.67	Age (10-year group) Age, years of education, age at menarche, weight before the onset, menopausal status, age at menopause, parity, age at first birth, smoking, coffee drinking	
Nandakumar *et al.* (1995), Bangalore, India, 1982–85	97 ever-married women obtained from the cancer registry in Bangalore; mean age, 48.3 years	194 women from the same area, attending a referral hospital for cancer or suspected cancer, with the diagnosis of no evidence of cancer; no hysterectomy; matched by age, material status, calendar time	Interview	Ovary	*History of alcohol consumption* No Yes	 1.00 (reference) 1.3 (0.2–8.0)	Age, marital status, calendar time, area of residence	Statistical analysis accounted for the matched design of the study

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Kuper *et al.* (2000b), eastern Massachusetts/ New Hampshire, USA, May 1992–March 1997	549 women born and resident in New Hampshire or Massachussetts, without any previous ovarian malignancy or bilateral oophorectomy, aged 50–74 years; reported to the regional Cancer Registries; specimens reviewed by one of authors; histological classification based on original histology of local pathologists; participation rate, 79%	516 identified by combination of random-digit dialling and selection from community lists; matched to cases by community of residence, age within 4 years	In-person interview self-administered food-frequency questionnaire	Ovary	*Drinks/day* 0 0–1 >1–2 >2–3 >3	 1.00 0.91 (0.67–1.23) 1.33 (0.88–2.01) 0.92 (0.50–1.69) 1.35 (0.80–2.26) p=0.20	Age, centre, material status, parity, body mass index, oral contraceptive use, family history of breast, ovarian and prostate cancer, tubal ligation, education, alcohol consumption, pack–years of smoking	Low participation rate for cases and controls, possible selection bias; heavy alcohol drinkers could be under-represented, especially among controls.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Tavani *et al.* (2001a), Milan, Pordenone, Pauda, Gorizia, Latina, Naples, Italy, January 1992–September 1999	1031 women with incidental invasive epithelial ovarian cancer, aged 18–79 years; 100% histologically confirmed	2411 women admitted to the hospital for acute, non-neoplastic, non-hormone-related diseases and unrelated to known and potential risk factors for ovarian cancer, aged 17–79 years	Structured questionnaire, in-person interview at hospitals	Ovary	*Total alcohol (g/day)* Never drinker <12 12–<24 24–<36 ≥36	 1.00 (reference) 1.02 (0.80–1.30) 1.29 (1.00–1.67) 1.04 (0.80–1.36) 1.09 (0.76–1.57) χ^2 for trend=0.68 p=0.409	Study centre, year of interview, age, education, parity, age at menopause, oral contraceptive use, family history of ovarian or breast cancer, body mass index, energy intake	Limitations common to other hospital-based case–control studies

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Goodman & Tung (2003), Hawaii, Los Angeles, CA, USA, 1993–99	558 women resident in Hawaii or Los Angeles County for at least 1 year, no history of ovarian cancer before, identified through the rapid reporting systems of Hawaii Tumor Registry and Los Angeles County Cancer Surveillance Program, aged ≥18 years; 100% histologically confirmed; response rate, 62%;	607 women with no prior history of ovarian cancer and at least one intact ovary; from lists of female Oahu residents/Hawaii; if ≥65 years, supplemented by participants of Health Care Financing Administration in Oahu; in Los Angeles, >95% selected based on a neighbourhood walk procedure; frequency-matched to patients based on ethnicity, 5-year age group, study site; participation rate, 67%	Structured in-person interviews; reference date for cases, year before diagnosis; for controls, interview date	Ovary	*Total alcohol* Never drinker Ever drinker Former drinker Current drinker	 1.00 0.88 (0.67–1.16) 1.16 (0.82–1.64) 0.69 (0.50–0.96)	Age, ethnicity, education, study site, oral contraceptive use, parity, tubal ligation	Possibility of recall bias; participation rates not optimal and may have affected the validity of the findings.

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
McCann *et al.* (2003), western New York, USA, 1986–91	124 women with primary ovarian cancer, aged 40–85 years; 100% histologically confirmed	696; randomly selected from driver's licence lists for women <65 years and from Health Care Financing Administration for women ≥65 years of age; frequency-matched to cases on age (±5 years), county of residence	In-person interview	Ovary	*Alcohol intake (g/day)* <0.2 0.2–1.1 1.1–3.7 3.7–12.9 >12.9	 1.00 0.55 (0.30–1.02) 0.67 (0.36–1.25) 0.97 (0.54–1.73) 0.62 (0.34–1.12) $p<0.05$	Age, education, total months menstruating, difficulty becoming pregnant, oral contraceptive use, menopausal status, total energy	Small number of cases, possible recall and information bias, short time between diagnosis and interview
Modugno *et al.* (2003), Delaware Valley, USA, May 1994–July 1998	761 women from 39 hospitals around Delaware Valley diagnosed within 9 months before interview, aged 20–69 years, 100% confirmed by pathology; response rate, 88%	1352 women ascertained by random-digit dialling (aged ≤ 65 years) or through Health Care Financing Administration lists (aged 65–69 years); frequency-matched to cases by 5-year age groups, three-digit telephone exchanges	Standardized, in-person interview	Ovary	**Ethanol consumption** *Non-mucinous cancers* Never Ever Current Former *Mucinous cancers* Never Ever Current Former	 1.0 (reference) 1.03 (0.84–1.26) 0.96 (0.75–1.23) 1.12 (0.86–1.46) 1.0 (reference) 0.92 (0.61–1.40) 0.97 (0.60–1.57) 0.87 (0.51–1.49)	Age, parity, use of oral contraceptive, education, race, tubal ligation, smoking, family history of ovarian cancer	Possibility of error in the histological classification; possibility for selection bias among controls and under representation of heavy drinkers in the control group

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Yen *et al.* (2003), Taipei, Taiwan, China, 1993–98	86 women with primary epithelial ovarian cancer resident in Taiwan for at least 20 years, aged 20–75 years; hospital pathological records; exclusions: major gynaecological operation, hysterectomy, oophoerectomy	369 women hospitalized for non-malignant, non-gynaecological conditions, unrelated to hormones or digestive tract or to long-term modification of diet; matched by age (5-year range), hospital, admission date	In-person interviews at the hospitals	Ovary	*Alcohol consumption* No Yes	 1.0 (reference) 0.71 (0.20–2.51)	Age, income during marriage, education	Limitation on power of the test due to small sample involved; possible selection bias
Riman *et al.* (2004), Sweden, 1 October 1993–31 December 1995	655 women born and resident in Sweden, with primary, newly diagnosed epithelial ovarian cancer, aged 50–74 years; 100% histologically confirmed; participation rate, 79%	3899 women randomly selected from a national population registry and sampled simultaneously with cases; frequency-matched to the expected age distributions; exclusion: women with previous bilateral oophorectomy	Mailed, self-administered questionnaires and additional telephone interview with cases who failed to respond	Ovary	Alcohol consumption (g/day) Non-users <*5* ≥*5*	 1.0 (reference) 0.94 (0.77–1.14) 0.99 (0.75–1.29) *p*=0.80	Age, parity, body mass index, age at menopause, duration of oral contraceptive use, ever use of hormone replacement therapy; *p*-value for the likelihood ratio test of heterogeneity	Possible recall bias

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Webb *et al.* (2004), Australia (New South Wales, Victoria and Queensland), August 1990–December 1993	696 Australian women treated in the major treatment centres in New South Wales, Victoria and Queensland, aged 18–79 years; 100% histologically confirmed; participation rate, 89%	786 cancer-free women selected at random from the electoral roll; frequency-matched to the cases for age (within 10-year bands), urban/rural district of residence; women with reported history of ovarian cancer or bilateral oophorectomy excluded	Face-to-face interview and food-frequency questionnaire	Ovary	None 1/week 1–6/week 1–1.9/day ≥2/day	*Invasive cancers* 1.0 0.84 (0.62–1.14) 0.73 (0.53–1.02) 0.85 (0.53–1.36) 0.46 (0.27–0.79) p=0.009 p=0.05 (excluding non-drinkers)	Age (in years), age squared, education, body mass index, smoking (newer, past, current), duration of oral contraceptive use, parity, caffeine intake	
Pelucchi *et al.* (2005), Italy (four areas), 1992–99	1031 women admitted to the major teaching and general hospitals; 100% histologically confirmed	2411 women admitted to the same network of hospitals for acute, non-malignant and non-gynaecological conditions, unrelated to hormonal diseases or to long-term modifications of diet	Standard questionnaire during hospital stay by centrally trained interviewers; food-frequency questionnaire	Ovary	Non-drinkers/light alcohol drinkers (<1.8 g/ day) Moderate/heavy alcohol drinkers (≥1.8 g/day)	0.93 (0.76–1.14) χ^2=0.97 p=0.32 1.02 (0.86–1.23) χ^2=0.10 p=0.75	Age, study centre, year of interview, education, parity, body mass index, alcohol consumption, oral contraceptive use, physical activity, non-alcohol energy intake	Ovarian cancer risk for folate intake in alcohol strata (null results in brief)

Table 2.72 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Peterson *et al*. (2006), Massachusetts (excluding Boston) and Wisconsin, USA, 1993–95 and 1998–2001	762 English-speaking women from two case–control studies (new diagnosis reported to the respective state cancer registries with listed telephone numbers and drivers' licences) verified by self report if less than 65 years of age or Medicare beneficiaries if 65 years or older, aged 40–79 (1993–95) or 20–75 years (1998–2001); 63 cases excluded due to unclear pathological diagnosis and 7 due to missing data on alcohol consumption; participation rate, 66%	6271 randomly selected from lists of licensed drivers if less than 65 years and from rosters of Medicare beneficiaries compiled by the Health Care Financing Administration if 65 years or older; all women had publicly available telephone number; frequency-matched to the age distribution of ovarian cancer and breast cancer cases enrolled in a breast cancer study; participation rate, 80.6%	Structured telephone interview with interviewers blinded to case/control status of the subjects	Ovary	*Recent past* None Ever drank <1 drink/week 1–6 drinks/week ≥1 drink/day	 1.00 1.06 (0.87–1.29) 1.05 (0.84–1.32) 1.15 (0.92–1.42) 0.89 (0.70–1.20) p=0.77	Age, state of residence	Possible bias related to control selection and recall bias

CI, confidence interval; ICD, International Classification of Diseases

other variables. Some weak interactions were found by Chang *et al*. (2007) for women who drank more than one glass of wine daily and were over 50 years of age, post-menopausal, used estrogen only hormone therapy, belonged to a higher social class, were never smokers and had higher total folate intake. Among the case–control studies, there was no consistent evidence of interaction between alcoholic beverage consumption and different variables known or suspected to be associated with ovarian cancer, such as reproductive history, education, body size or diet.