2.12   Cancer of the endometrium

2.12.1   *Cohort studies (Tables 2.67 and 2.68)*

Since 1988, three prospective cohort studies have examined the association between alcoholic beverage intake and the risk for endometrial cancer in special populations, namely women hospitalized or being treated for alcohol dependence (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994, Sigvardsson *et al.*, 1996; Weiderpass *et al.*, 2001a; Table 2.67) and three have studied the association in the general population (Gapstur *et al.*, 1993; Terry *et al.*, 1999; Jain *et al.*, 2000b; Folsom *et al.*, 2003; Table 2.68) (see the Tables for overlapping study populations).

These studies were conducted in North America (Gapstur *et al.*, 1993; Jain *et al.*, 2000b; Folsom *et al.*, 2003) and in Scandinavia (Adami *et al.*, 1992a; Tønnesen *et al.*, 1994; Sigvardsson *et al.*, 1996; Terry *et al.*, 1999; Weiderpass *et al.*, 2001a).

Three studies (Gapstur *et al.*, 1993, Terry *et al.*, 1999; Jain *et al.*, 2000b) presented risk estimates adjusted for multiple possible confounders (body size and reproductive factors), while only one (Jain *et al.*, 2000b) adjusted the analysis of alcoholic beverages for smoking (ever/never). Smoking showed a non-significant protective effect in all of these studies.

In one study among alcoholics (Weiderpass *et al.*, 2001a), there was an inverse association between alcoholic beverage consumption and endometrial cancer, but the analytical models did not include important covariates that may have confounded the association, such as cigarette smoking and body size. In the two other studies among alcohol-dependent populations, there was no evidence of an association. There was no evidence of an association between alcoholic beverage intake and the risk for endometrial cancer in the three cohort studies conducted in the general population (Gapstur *et al.*, 1993; Terry *et al.*, 1999; Jain *et al.*, 2000b).

2.12.2   *Case–control studies (Table 2.69)*

Case–control studies that have investigated the relationship between alcoholic beverage consumption and the risk for endometrial cancer were carried out in Japan, North America and Europe.

Seven of these were hospital-based, particularly studies from southern Europe (La Vecchia *et al.*, 1986; Shu *et al.*, 1991; Austin *et al.*, 1993; Levi *et al.*, 1993; Parazzini *et al.*, 1995a; Kalandidi *et al.*, 1996; Petridou *et al.*, 2002), two were based on cases and controls who were included in a cancer survey or registry database (Williams

Table 2.67 Cohort studies of alcoholic beverage consumption and endometrial cancer in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Adami *et al.* (1992a), Sweden, National Board of Health and Welfare/ Study of Alcoholics Women	9353 individuals (1013 women) with a diagnosis of alcoholism in 1965–83; follow-up for 19 years (mean, 7.7 years); all cancers in the first year of follow-up excluded	Registry-based	*Corpus uteri*	Women with diagnosis of alcoholism	3	**SIR** 1.4 (0.3–4.2)		
Tønnesen *et al.* (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 male and female alcohol abusers admitted to an outpatient clinic in Copenhagen during 1954–87; 3093 women observed for 9.4 years	Registry-based	*Corpus uteri*	Alcohol abusers	3	0.4 (0.1–1.3)		

Table 2.67 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson *et al.* (1996), Sweden, Temperance Boards Study	Nested case–control study; records of 15 508 alcoholic women born between 1870 and 1961 obtained from Temperance Boards; controls matched for region and day of birth; incidence data from Swedish Cancer Registry	Registry-based	*Corpus uteri* (ICD-7, 172)	Alcohol abusers	30	0.7 (0.4–1.1)		

Table 2.67 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Weiderpass *et al.* (2001a), Sweden, National Board of Health and Welfare/ Study of Alcoholic Women	36 856 women (mean age, 42.7 years) hospitalized for alcoholism between 1965 and 1994 based on data from Inpatients Register; linkages to nationwide Registers of Causes of Death and Emigration and national Register of Cancer; average follow-up time, 9.6 years; the first year of follow-up was excluded from all analysis	Registry-based; linkages	Endometrium	Women with diagnosis of alcoholism	69	**SIR** 0.76 (0.59–0.96)	Age, calendar period	Enlarged population with longer follow-up than Adami *et al.* (1992a)

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

Table 2.68 Cohort studies of alcoholic beverage consumption and endometrial cancer in general populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Gapstur *et al.* (1993), USA, Iowa Women's Health Study	25 170 women, aged 55–69 years, randomly selected from Iowa's 1985 drivers' licence list; cohort at risk, 24 848 women; questionnaire mailed in 1986; exclusions: prevalent cancer other than skin, prior hysterectomy, menstruation during the last year; 167 incident endometrial cancers	Mailed, self-administered questionnaire	Endometrium; *corpus uteri* (182.0) and *isthmus uteri* (182.1)	*Ethanol (g/ day)* 0 <4.0 ≥4.0	101 27 32	1.0 (reference) 0.7 (0.5–1.1) 1.0 (0.7–1.6)	Age, body mass index, number of live births, age at menopause, non-contraceptive estrogen use	The same population as Folsom *et al.* (2003); Cox proportional hazard regression

Table 2.68 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Terry *et al.* (1999), Sweden, Swedish Twin Registry and Swedish Cancer and Death Registry	11 659 women born 1886–1925; follow-up through to 1992; record linkages to Swedish Cancer and Death Registries; 133 incident cases detected	Questionnaire concerning lifestyle factors, diet, physical activity, 1967	Endometrium	*Drinks/week* 0 <2 2–4 ≥4	78 22 10 7	1.0 (reference) 1.7 (1.0–2.8) 1.2 (0.6–2.4) 1.3 (0.6–2.8)	Age, physical activity, weight at enrolment, parity	
Jain *et al.* (2000b), Canada, National Breast Screening Study, 1980–85	56 837 women, aged 40–59 years, enrolled between 1980 and 1985; subcohort of 10% of randomly selected women from the main study in the dietary cohort; follow-up to 31 December 1993; 221 women diagnosed with incident adenocarcinoma	Self-administered questionnaire	Endometrium	*Alcohol consumption* 1 (low) 2 3 4 (high)	65 62 41 53	1.00 (reference) 1.01 (0.69–1.46) 0.78 (0.52–1.18) 1.00 (0.67–1.50)	Age, total energy intake, body mass index, ever smoked, oral contraceptive use, hormone-replacement therapy use, university education, live births, age at menarche	

Table 2.68 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Folsom *et al.* (2003), USA, Iowa Women's Health Study	23 335 women, aged 55–69 years, randomly selected from Iowa's 1985 drivers' licence list; follow-up from 1986 through 2000; 415 incident endometrial cancers detected	Baseline questionnaire	Endometrium	*Alcohol consumption* Yes No	260 155	1.00 (reference) 0.73 (0.59–0.89)	Age	*p*<0.05; *p* for difference from reference category
Beral *et al.* (2005), United Kingdom, Million Women Study	716 738 post-menopausal women in the UK without previous cancer or hysterectomy recruited into the Million Women Study in 1996–2001	Questionnaire	Endometrium	*Alcohol consumption* ≤10 g/week >10 g/week	69 17	1.77 (1.39–2.18) 1.81 (1.08–3.05)	Time since menopause, parity, oral contraceptive use, body mass index, region of residence, economic status	

CI, confidence interval; ICD, International Classification of Diseases

Table 2.69 Case–control studies of alcoholic beverage consumption and endometrial cancer

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967–71	7518 patients (all sites, men and women) interviewed; 57% selected randomly	Randomly selected patients with cancer of other, non-related sites	Interview	*Corpus uteri*	*Wine level* 1 2 *Beer level* 1 2 *Hard liquor level* 1 2 *Total alcohol oz–years level* 1 2 *Wine level* 1 2 *Beer level* 1 2 *Hard liquor level* 1 2 *Total alcohol oz–years level* 1 2	Relative odds 0.77 0.60 0.23 0.42 0.91 0.79 0.72 0.65 0.78 0.49 0.23 0.31 0.95 0.77 0.69 0.63	Age, race, Age, race, smoking	Consumers of alcohol were divided in categories 1 and 2 with 51 drink x years as level of division (years of alcohol consumption ≥ once per week

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
La Vecchia *et al.* (1986), Milan, Italy, Jan. 1983– Jun. 1984	206 women, aged 75 years and less, admitted to the Obstetrics and Gynecology Clinics of the University, The National Cancer Institute and oncology, gynecology wards of the Ospedale Maggiore, Milan	206 women matched by 5-year range to cases, admitted to the same hospital network for acute conditions; women who undergone hysterectomy excluded	Structured questionnaire	Endometrium	*Alcohol consumption* (drinks/day) 0 <2 ≥2 and <3 ≥3 and <4 ≥4	1.00 (reference) 1.59 (0.80–3.18) 1.57 (0.77–3.21) 3.44 (1.03–11.51) 4.33 (1.02–18.43) χ^2 trend=5.73 *p*=0.02	Various dietary items, interviewer, age, marital status, years of education, body mass index, parity, history of diabetes, hypertension, age at menarche, age at menopause, of oral contraceptives, hormone-replacement therapy use	
Cusimano *et al.* (1989b), Ragusa, Italy, 1 Jan. 1983–30 Jun. 1985	57 women from Ragusa and province (Italy/Sicily) diagnosed between 1 Jan. 1983 and 30. Jun 1985; aged 37–79 years; 100% histologically confirmed; participation rate; 95%	228 women from the same geographical region; aged 36–79. matched to cases by age (2.5-year range), type of health service consulted; women who had undergone hysterectomy excluded	Structured questionnaire; interview	Endometrium	*Alcohol consumption* No Yes	1.00 (reference) 1.31 (0.73–2.34)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Kato *et al.* (1989), Japan, 1980–86	417 women registered at Aichi Cancer Registry, diagnosed between 1980 and 1986; aged ≥20 years	8920 cancers at other sites excluding cancers known to be alcohol-related	Records from Aichi Cancer Registry with available data on alcohol drinking habits	*Corpus uteri*	*Alcohol drinking* Current versus none	0.67 (0.41–1.09)	Age	Possible bias due to control selection from cancer patients and the effect of alcohol consumption diminished; however, status of the controls' illness may have changed their alcohol drinking habit before diagnosis; lack of information on important risk factors.
					Daily versus less	0.46 (0.15–1.41)		
					Occasional versus none	0.74 (0.44–1.26)		
					Daily versus none	0.44 (0.15–1.38)		
					Daily versus less	0.53 (0.16–1.70)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Webster *et al.* (1989), USA, multicentre: Atlanta, Detroit, San Francisco, Seattle, states of Connecticut, Iowa, 1980–82	351 women newly diagnosed with primary epithelial endometrial cancer (from 1 December 1980 to 31 December 1982); aged 20–54 years; 100% histologically confirmed	2247 women selected by random-digit dialling, from same geographical areas as cases, during the same period; aged 20–54 years; frequency-matched by 5-year age groups	Structured questionnaire; interview at participants home.	Endometrium	*Alcohol consumption (g/week)* Non-drinker 1–49 50–149 ≥150	1.83 (1.11–3.10) 1.61 (1.04–2.49) 1.11 (0.68–1.81) 1.00	Age, race, parity, oral contraceptive use, smoking	27% women unable to be interviewed
Shu *et al.* (1991), Shanghai, China, 1988–90	268 Shanghai residents diagnosed between 1 April 1988 and 30 January 1990; aged 18–74 years; data obtained from cancer registry in Shanghai; 98.5% histopathologically confirmed; participation rate, 91.2%	268; matched to cases by age (2-year range) randomly; participation rate, 96.4%	In-person interview at participants' home; questionnaire	Endometrium	*Drinking* No Yes	1.0 1.2 (0.6–2.6)		

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Austin *et al.* (1993), Alabama, USA, 1985–88	168 women identified through University Hospital and private gynaecological–oncological practice in Birmingham between June 1985 and December 1988, aged 40–82 years; 100% histologically confirmed; participation rate, 93%	334 women attending the University optometry clinic, aged 40–82 years; intact uterus; frequency-matched by age, race; participation rate, 77%	Standardized and food-frequency questionnaires	Endometrium	*Alcohol category* Any type	*Relative rate* 0.64 (0.32–1.28) *p*=0.20	Age, race, education, body mass, index of central obesity, cigarette habit, use of replacement estrogens, number of pregnancies	
Levi *et al.* (1993), northern Italy and Switzerland,1988–9	274 patients from local cancer registry, aged 31–75 years; 100% histologically confirmed	572 women admitted to the same hospitals for acute, non-gynaecological, non-hormone-related, metabolic or neoplastic disorders, aged 30–75 years	Structured questionnaire/ interview at hospital	Endometrium	**Frequency of alcohol consumption** *Wine* Low Intermediate High *Beer* Low Intermediate High *Liquor* Low Intermediate High	*Odds ratios* 1.0 1.03 1.70 χ^2=5.67 *p*<0.05 1.0 0.99 2.43 χ^2=0.27 1.0 1.46 5.24 χ^2=4.39 *p*<0.05	Study centre, age	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Swanson *et al.* (1993), USA, 1987–90	400 women newly diagnosed in June 1987 to May 1990 from seven hospitals in Chicago, Hershey, Irwine and Long Beach, Minneapolis, Winston-Salem, aged 20–74 years; inclusion criteria: no previous treatment for the cancer and intact uterus; 100% pathologically confirmed; participation rate, 87.1%	297 women selected by random-digit dialling or Health Care Financing Administration; matched by age (5-year range), race, residence; participation rate, 65.6%	Short telephone interview	Endometrium	*Alcohol intake in adulthood (drinks per week)* None Any <1 1–4 >4	 1.00 0.82 (0.53–1.26) 0.75 (0.47–1.19) 1.04 (0.61–1.76) 0.72 (0.39–1.35)	Age, education, smoking status, age at menarche, use of oral contraceptives, Quetelet index, body fat distribution	13% of eligible cases and 35% of eligible controls not interviewed; bias if non-response associated with alcohol use; possible recall bias among cases due to their condition

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Parazzini *et al.* (1995a), Milan, Italy, 1979–93 [population partially overlapping with La Vecchia *et al.* (1986)]	726 patients admitted to six greatest hospitals and clinics in Milan until 1 year before interview, aged 28–74 years; 100% histologically confirmed	2123 women admitted to the same network of hospitals for acute, non-malignant, non-gynaecological conditions, unrelated to hormonal diseases, aged 25–74 years; exclusion: women with hysterectomy	Standard questionnaire, by trained interviewers	Endometrium	*Total alcoholic beverages (drinks/day)* 0 >0–≤1 >1–≤2 >2	1.0 (reference) 1.1 (0.9–1.4) 1.4 (1.1–1.8) 1.6 (1.2–2.2) χ^2 trend=11.33 $p<0.001$	Age, education, Quetelet index, parity, menopausal status, smoking, oral contraceptive and estrogen replacement therapy use, diabetes, hypertension, alcohol	Data on alcohol consumption may not represent a lifelong pattern; common weaknesses for hospital-based case–control study.
Kalandidi *et al.* (1996), Greater Athens, Greece, 1992–94	145 women diagnosed between 1992 and 1994, operated in two specialized cancer hospitals in Greater Athens; 100% histologically confirmed; participation rate, 83%	298 women, residents of Greater Athens, admitted at the same time to the greater hospitals in Athens for bone fractures or other orthopaedic conditions	Structured questionnaire; hospital interview	Endometrium	*Alcohol intake* No Yes	1.0 (reference) 0.72 (0.44–1.37) $p=0.67$	Age, education, body mass index, occupation, age at menarche, menopausal status, oral contraceptive use, smoking, menopausal estrogens, coffee	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Goodman *et al.* (1997b), Oahu, Hawaii, USA, 1985–93	332 women diagnosed between 1 January 1985 and 1 June 1993, residents of Oahu and of Japanese, Caucasian, native Hawaiian, Filipino, Chinese origin, obtained from Hawaii Tumor Registry, aged 18–84 years; 100% histologically confirmed; participation rate, 66%	511 women selected randomly from lists of Oahu residents; matched to cases on ethnicity, age (range, 2.5 years); intact uteri; exclusions: hysterectomized women, mental incompetence; participation rate, 73%	Interviewer-administered standardized questionnaire	Endometrium	*Alcohol use* No Yes	1.00 (reference) 0.90 (0.6–1.4)	Pregnancy history, oral contraceptive use, unopposed estrogen use, diabetes, body mass index	
					Alcohol type (g ethanol equivalent) Reference 0 0.2 17.8	1 0.8 0.8 0.8 *p* for trend=0.44	Carbohydrate or fat calories, pregnancy history, oral contraceptive use, unopposed estrogen use, diabetes, body mass index	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Newcomb *et al.* (1997), Wisconsin, USA, 1991–94	739 female residents of Wisconsin, diagnosed between 1991 and 1994, aged 40–79 years; identified by a state-wide mandatory cancer registry; limited to cases with listed telephone numbers and drivers' licences; 98% histologically confirmed ; participation rate, 87%	2313 women selected randomly from lists of licensed drivers; matched by age distribution; criteria: listed telephone number, no previous diagnosis of uterine cancer; participation rate, 85.2%	Structured telephone interview	Endometrium	*Recent consumption (drinks/week)* None Any <1 1–2 3–6 7–13 ≥14 *Continuous*	 1.00 1.07 (0.86–1.33) 1.22 (0.96–1.56) 0.86 (0.65–1.14) 1.11 (0.83–1.50) 0.81 (0.55–1.19) 1.27 (0.78–2.07) 1.00 (0.98–1.02) *p*=0.82	Age, smoking status, education, relative weight, hormone replacement therapy use, parity	Any possible information and recall bias unlikely to have an important effect on the results

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Jain *et al.* (2000c), Ontario, Canada, 1994–98	552 women diagnosed in August 1994–June 1998 (adeno-carcinoma, carcinoma, cystadeno-carcinoma or mixed Mullerian carcinoma), aged 30–79 years; data from Ontario Cancer Registry (four areas: Toronto, Peel, Halton, York); 100% histologically confirmed; response rate, 70%	562 randomly selected women from property assessment lists; frequency-matched by age group, geographical areas (Toronto, Peel, Halton, York); selection criteria: intact uterus, no history of hysterectomy and listed with telephone number	Home interview, standardized questionnaire	Endometrium	*Intake (g absolute alcohol)* 0 <1.2 <8.3	*Odds ratio* 1.0 (reference) 0.85 (0.63–1.18) 0.72 (0.52–0.99) *p≤0.05* *p* trend=0.04	Total energy, age, body weight, ever smoked, diabetes, oral contraceptive use, hormone replacement therapy use, university education, live births, age at menarche	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
McCann *et al.* (2000), western New York, USA, 1986–91	232 women, aged 40–85 years; exclusions: women with more than one primary carcinoma and non-adenomatous carcinoma of the endometrium; 100% histologically confirmed; response rate, 51%	639 women randomly selected from the drivers' lists (<65 years) and from Health Care Finance administration (≥65 years); exclusions: hysterectomy and early menopause, before age 37 years; frequency-matched for age, county of residence	Interview: self-reported food-frequency questionnaire (2 years before) and additional telephone interview of controls	Endometrium	*Alcohol intake (g)* Q1 ≤0.5 Q2 0.6–2.1 Q3 2.2–9.0 Q4 >9.0	1.0 (reference) 1.0 (0.6–1.6) 0.8 (0.5–1.3) 1.0 (0.5–1.8) *p*=0.58	Age, education, body mass index, diabetes, hypertension, smoking pack–years, age at menarche, parity, oral contraceptive use, menopausal status, post-menopausal estrogen use, total energy	Limitations due to low response rate among cases and controls

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Weiderpass & Baron (2001), Sweden, 1994–95	709 born in Sweden and residing Sweden in 1 January 1994–31 December 1995 identified through six regional cancer registries, aged 50–74 years; intact uterus and no previous diagnosis of endometrial or breast cancer; 100% histologically confirmed by one pathologist (blinded); participation rate, 75%	3368 randomly selected from population register at the same time as cases; participation rate, 79.9%	Mailed questionnaire, or/and telephone interview	Endometrium	*Alcoholic beverage consumption (g/day)* Non-drinkers Drinkers >0–<1.59 1.6–3.99 ≥4	1.00 (reference) 1.00 (0.83–1.21) 1.16 (0.90–1.49) 0.92 (0.70–1.20) 0.92 (0.70–1.20) *p*=0.44	Smoking, age, body mass index, parity, age at menopause, age at last birth, hormone replacement therapy use, oral contraceptive use, diabetes mellitus (self-reported)	

Table 2.69 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Petridou *et al.* (2002), Greater Athens area, Greece, 1999	84 women with no history of malignancy, resident in Greater Athens area, speaking Greek	84 women admitted at the same time as cases to the same hospital and department for small gynaecological operations; matched to cases for age; no history of malignancy, resident in Greater Athens, speaking Greek	Standardized questionnaire, interview	Endometrium	*Alcohol drinking* No Yes ≥2 glasses/ week	1.00 (reference) 0.57 (0.23–1.42) *p*=0.23	Age, education, height, body mass index, age at menarche, ever pregnant, age at first pregnancy, number of children, abortions, menopausal status, alcohol, coffee, current smoking, appendectomy, cholecystectomy, thyroidectomy	Possible information and selection bias did not influence the validity of the results

CI, confidence interval; ICD, International Classification of Diseases

& Horm, 1977; Kato *et al.*, 1989) and eight were population-based (Cusimano *et al.*, 1989b; Webster *et al.*, 1989; Swanson *et al.*, 1993; Goodman *et al.*, 1997b; Newcomb *et al.*, 1997; Jain *et al.*, 2000c; McCann *et al.*, 2000; Weiderpass & Baron, 2001).

Ten studies (Cusimano *et al.*, 1989b; Kato *et al.*, 1989; Webster *et al.*, 1989; Austin *et al.*, 1993; Swanson *et al.*, 1993; Parazzini *et al.*, 1995a; Kalandidi *et al.*, 1996; Newcomb *et al.*, 1997; Weiderpass & Baron, 2001; Petridou *et al.*, 2002) were designed to examine the association between alcoholic beverage intake, other lifestyle factors such as cigarette smoking, use of hormone-replacement therapy and other risk factors in the etiology of endometrial cancer. Six studies (La Vecchia *et al.*, 1986; Shu *et al.*, 1991; Levi *et al.*, 1993; Goodman *et al.*, 1997b; Jain *et al.*, 2000c; McCann *et al.*, 2000) were designed to evaluate nutritional factors in relation to the risk for endometrial cancer.

Confounding factors were considered in all of the above studies except for one (Cusimano *et al.*, 1989b), although adjustment may have been incomplete in three studies (Williams & Horm, 1977 [age, race and smoking]; Shu *et al.*, 1991 [pregnancies and weight]; Levi *et al.*, 1993 [only adjusted for age and centre]). Interviews were conducted with or questionnaires were completed by the subjects in all studies.

The results of case–control studies were not consistent. Ten reported little or no association between alcoholic beverage consumption and the risk for endometrial cancer (Kato *et al.*, 1989; Webster *et al.*, 1989; Austin *et al.*, 1993; Swanson *et al.*, 1993; Kalandidi *et al.*, 1996; Goodman *et al.*, 1997b; Newcomb *et al.*, 1997; McCann *et al.*, 2000; Weiderpass & Baron, 2001; Petridou *et al.*, 2002). Two found an inverse association (Williams & Horm, 1977; Jain *et al.*, 2000c), which was significant in the latter study. Four studies reported an increased risk for endometrial cancer with higher alcoholic beverage consumption (La Vecchia *et al.*, 1986; Cusimano *et al.*, 1989b; Shu *et al.*, 1991; Levi *et al.*, 1993; Parazzini *et al.*, 1995a); in two of these, the association was non-significant (Cusimano *et al.*, 1989b; Shu *et al.*, 1991), in one it was significant with a positive trend analysis (Parazzini *et al.*, 1995a) and one (Levi *et al.*, 1993) found a positive association relative to wine and liquor, but not to beer.

2.12.3   *Evidence of a dose–response*

There was no evidence of a trend of increasing risk for endometrial cancer with increasing alcoholic beverage consumption in the cohort studies.

In the case–control studies, there was no dose–response association between alcoholic beverage consumption and the risk for endometrial cancer in most studies. One study (Jain *et al.*, 2000c) presented a negative dose–response association and one report showed a clear dose–response trend (Parazzini *et al.*, 1995a). In another study, there was an indication of a dose–response in the association but no formal test for trend was presented (Webster *et al.*, 1989).

2.12.4   *Types of alcoholic beverage*

Only one cohort study investigated the effect of specific types of alcoholic beverage (beer, wine, spirits) on the risk for endometrial cancer (Gapstur *et al.*, 1993) and found no evidence of any association.

Seven case–control studies evaluated different alcoholic beverages in relation to risk for endometrial cancer (Williams & Horm, 1977; Austin *et al.*, 1993; Levi *et al.*, 1993; Swanson *et al.*, 1993; Parazzini *et al.*, 1995a; Goodman *et al.*, 1997b; Weiderpass & Baron, 2001). The studies by Levi *et al.* (1993) and Parazzini *et al.* (1995a) showed an increased risk for endometrial cancer with increasing consumption of wine and hard liquor, but not beer. Overall, there were no consistent patterns of association between any specific type of alcoholic beverage and risk for endometrial cancer.

2.12.5   *Interactions*

Few studies presented information on possible interactions between alcoholic beverage intake and other variables. One cohort study investigated alcohol as an interacting factor with hormone-replacement therapy (Beral *et al.,* 2005). A positive association was found for Tibolone and an inverse association for continuous combined hormone-replacement therapy among women who consumed less than one drink daily.

Among the case–control studies, there was no consistent evidence of an interaction between alcoholic beverage consumption and different variables known or suspected to be associated with endometrial cancer, such as use of hormone-replacement therapy, body size, age, tobacco smoking, parity, education, physical activity, calory intake and other dietary aspects, oral contraceptive use or menopausal status.