

Table 2.19 Case-control studies on cancer of the ovary and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Hartge et al. (1982) USA Not reported Case-control	Cases: 158; Hospital-based Controls: 187; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, parity, smoking	Short report focused on coffee; information from medical records, not linked with registry; no association also in no smokers. Strengths: Interviewer-administered FFQ; elimination of controls admitted for diseases modifying diet Limitations: The use of hospital controls; no information on: the years of study conduction, age of subjects, participation rate, previous cancer among cases and controls, on oophorectomy among controls, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee, no adjustment for menstrual factors and exogenous hormone use
			0	39	1		
			< 2	29	1 (0.5–2.2)		
			2–3	52	1.8 (0.6–3.6)		
			≥ 4	38	1.4 (0.6–3)		
			Trend-test p-value: 0.115				
Byers et al. (1983) USA 1957–1965 Case-control	Cases: 274; Hospital-based Controls: 1034; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, age at first marriage, pregnancy, previous hospitalization for benign breast disease	No information on menopausal status but stratification for age as a proxy; further adjustments for selected risk factors did not change the estimates; Strengths: interviewer-administered FFQ; elimination of controls admitted for diseases modifying diet; a 100% participation rate of cases and controls. Limitations: the use of hospital controls; no information on: previous cancer among cases and controls, on oophorectomy among controls, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee; no adjustment for menstrual factors and exogenous hormone use; CI are missing, but statistical significance of the OR was reported
			0	19	1		
			> 0- 2	129	1.3		
			≥ 3	126	0.97 (p>0.05)		

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Cramer et al. (1984) USA 1978–1981 Case-control	Cases: 215; Population-based Controls: 215; None Exposure assessment method: Questionnaire	Ovary	Coffee (regular use = at least weakly use)			Age, parity	Paper focused on diet; diagnoses reviewed by physicians; no differences in strata of smoking; no significant increase risk for coffee + alcohol, coffee + smoking, coffee + alcohol + smoking. No significant interaction among coffee and smoking. Strengths: Population controls; bilateral oophorectomized women excluded from controls; interviewer-administered FFQ; a high participation rate of cases and controls. Limitations: the no information on: previous cancer among cases and controls, on FFQ validity/reproducibility, time of coffee consumption before the symptoms of the current disease, on intake of caffeinated/decaffeinated coffee; no adjustment for smoking, menstrual factors and exogenous hormone use; CI are missing, but statistical significance of the OR was reported
			No drinkers	10	1		
			Regular users	68	1.66 (0.69–4.01)		
		Ovary	Coffee (regular use = at least weakly use)			Age, parity	
			No drinkers	27	1		
			Regular users	188	1.79 (0.69–4.62)		
La Vecchia et al. (1984) Italy 1979–1983 Case-control	Cases: 247; Hospital-based Controls: 494; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Education, age, parity, age at first birth, OC, age at menopause, body mass index, smoking, alcohol consumption	Focused on coffee; case ascertainment by medical records; increased risk similar for duration of consumption < 20/≥ 20 years, with a p trend = 0,02 for duration. Strengths: high participation rates; exclusion of previous cancer and gastrointestinal diseases among cases and controls and of oophorectomized women from controls; interviewer-administered FFQ; fully adjusted. Limitations: the use of hospital controls; no information on FFQ validity/reproducibility and intake of caffeinated/decaffeinated coffee
			0	47	1		
			1	50	1.5 (0.9–2.5)		
			2–3	111	1.9 (1.2–3)		
			≥ 4	39	2.2 (1.2–3.9)		
			Trend-test p-value: 0.003				

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		Ovary	Duration (years)			Education, age, parity, age at first birth, OC, age at menopause, body mass index, smoking, alcohol consumption	
			0	47	1		
			< 20	NR	1.8 (1–3.1)		
			≥ 20	NR	1.7 (1.1–2.6)		
			Trend-test p-value: 0.02				
Tzonou et al. (1984) Greece 1980–1981 Case-control	Cases: 150; hospital-based, all orthopaedic controls Controls: 250; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, parity, age at menopause, smoking, alcohol consumption, estrogen use	The papers focused on all risk factors. Strengths: interviewer-administered FFQ; no refusal to participation (percent not reported); adjusted for major covariates although not all. Limitations: the use of hospital controls including only orthopaedic disorders; very information in the methods; no information on: mean or range of age of subjects, on previous cancer among cases and controls, on oophorectomy among controls, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee, no adjustment for potential confounders, no CI of OR
			No drinkers	26	1		
			0,5–1	36	0.9		
			1,5–2	60	1.6		
			2,5–3	16	0.9		
			≥ 3,5	11	1.5		
			Trend-test p-value: 0.14				
Miller et al. (1987) USA 1976–1983 Case-control	Cases: 290; hospital-based. 476 controls with melanoma or lymphoma or leukaemia and 580 controls orthopaedic or respiratory diseases or appendicitis. Controls: 1056; None Exposure assessment method: Questionnaire	Ovary	Coffee (cups/day)			Age, race, religion, smoking, alcohol consumption, OC, conjugated estrogen use, body mass index, age at menarche, age at first pregnancy, age at menopause, type of menopause, education, geographical location of hospital, year of interview, number of non obstetric hospital admissions	Papers focused on coffee; similar results considering cancer and non cancer controls for either caffeinated or decaffeinated coffee; ORs were not heterogeneous in strata of age at menarche, age at first pregnancy, parity, menopause, age at menopause, OC, body mass index and age. Strengths: high participation rates; exclusion of previous cancer among cases and controls; nurse interviewer-administered FFQ; fully adjusted. Limitations: the use of hospital controls; no
			0	59	1		
			1	46	1 (0.5–1.7)		
			2	62	0.9 (0.6–1.6)		
			3	54	0.9 (0.6–1.6)		
			4	30	1.6 (0.8–3.1)		
			≥ 5	36	1 (0.5–1.8)		

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		Ovary	Coffee (cups/day)				exclusion of oophorectomized women from controls; no information on FFQ validity/reproducibility and other characteristics
			0	59	1	Age, race, religion, smoking, alcohol consumption, OC, conjugated estrogen use, body mass index, age at menarche, age at first pregnancy, age at menopause, type of menopause, education, geographical location of hospital, year of interview, number of non obstetric hospital admissions	
			1	46	1.6 (0.9–2.7)		
			2	62	1.5 (0.9–2.6)		
			3	54	1.6 (0.9–2.7)		
			4	30	1.7 (0.9–3.3)		
			≥ 5	36	1.1 (0.6–2)		
Mori et al. (1988) Japan 1980–1981, 1985–1986 Case-control	Cases: 110; 110 hospital-based (gynaecological condition, including cervical cancer); 110 population-based (gynaecological conditions excluding cancer and ovarian diseases). Controls: 220; None Exposure assessment method: Questionnaire	Ovary	Coffee (daily consumption)			Age, year of interview, smoking, body mass index, alcohol consumption, milk, meat, fish	Paper focused on various risk factors; similar results for the two groups of controls. Strengths: interviewer-administered FFQ; no refusal to participation. Limitations: the use of hospital controls including gynaecological disorders; no information on: on previous cancer among cases and controls, on oophorectomy among controls, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee, on cups/day of coffee, no specification of variables used for adjustment for potential confounders
			No daily	64	1		
			Daily	46	1.4 (0.8–2.5)		

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Whittemore et al. (1988) USA 1983–1985 Case-control	Cases: 188; 280 hospital controls and 259 population controls. Controls: 539; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)				Paper focused on talcum powder, tobacco, alcohol, coffee; increased risk with no trend with dose, duration, lifetime consumption; consistently lower OR (not always significant) using only population controls. Strengths: interviewer-administered FFQ; high response rate; oophorectomized women were excluded from controls; information on duration and lifetime coffee drinking. Limitations: no information on: previous cancer among cases and controls, on ascertainment of cases, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee, on cups/day of coffee, no adjustment for many potential confounders	
			0	11	1			
			1	50	2.42 (1.15–5.09)			
			2–3	73	2.26 (1.09–4.66)			
			≥ 4	54	2.07 (0.97–4.38)			
			For increment of 1 cup/day among drinkers	177	1.01 (0.99–1.03)			
			Trend-test p-value: 0.91					
		Ovary	Duration (years)					Age, race, year of interview, hospital, smoking
		0	11	1				
		1–14	18	1.45 (0.59–3.57)				
		15–24	32	2.18 (1–4.79)				
		25–39	62	2.26 (1.06–4.85)				
		≥ 40	65	3.41 (1.46–7.96)				
		Increment of 10 years among drinkers	177	1.11 (0.89–1.38)				
Trend-test p-value: 0.37								

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		Ovary	Cumulative lifetime coffee consumption			Age, race, year of interview, hospital, smoking	
			0	11	1		
			1–30	41	2.3 (1.09–4.86)		
			31–60	32	2.64 (1.21–5.75)		
			61–90	27	2.46 (1.1–5.51)		
			> 90	77	2.28 (1.08–4.78)		
			Increment of 10 cups/year among drinkers	177	1.01 (0.99–1.03)		
			Trend-test p-value: 0.56				
Polychronopoulou et al. (1993) Greece 1989–1991 Case-control	Cases: 189; Population-based, controls visitors of the hospital. Controls: 200; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age	Papers focused on various risk factors. Strengths: population controls; exclusion of women with previous cancer or oophorectomy among controls; interviewer-administered FFQ; high participation rate; fully adjusted. Limitations: controls slightly younger than cases; no information on: previous cancer among cases, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee
			Never	18	1		
			≤ 1	32	0.99 (0.42–2.36)		
			1–2	46	1.28 (0.56–2.96)		
			> 2	93	1.09 (0.52–2.27)		
			Increment of 1 cup/day	189	1.04 (0.82–1.3)		

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Kuper et al. (2000) USA 1992–1997 Case-control	Cases: 549; Population-based. Controls: 516; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, centre, parity, body mass index, OC, family history of breast/ovarian/prostate cancer, tubal alligation, education, alcohol consumption, smoking, marital status	Paper focused on coffee, alcohol and tobacco; direct association only in premenopausal women; no heterogeneity among histological subtypes; similar results for coffee and caffeine. Strengths: population-based; cases identified by medical records and cancer registries; FFQ tested for validity/reproducibility, although no validity specific for coffee intake; interviewer-administered FFQ; adjusted for major confounders, although not all. Limitations: no information on: exclusion of previous cancer among cases and controls and no exclusion of oophorectomized women from controls; no age distribution reported; no separate information for caffeinated/decaffeinated coffee
			Never	128	1		
			< 1	100	1.35 (0.9–2)		
			1	90	1.13 (0.76–1.68)		
			2–3	170	1.1 (0.78–1.54)		
			≥ 4	61	1.88 (1.14–3.09)		
Trend-test p-value: 0.17							
Tavani et al. (2001) Italy 1992–1999 Case-control	Cases: 1031; hospital-based. Controls: 2411; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, study centre, year of interview, education, parity, age at menopause, OC, body mass index, total energy intake, family history of ovarian/breast cancer	Paper focused on coffee and alcohol; no association for coffee, cappuccino and slight inverse association for the caffeinated coffee (based on low numbers); no heterogeneity in strata of age, education, parity, OC, body mass index, energy intake, family history. Strengths: very large study; exclusion of previous cancer among cases and controls and of oophorectomized women from controls; FFQ tested for validity/reproducibility; interviewer-administered FFQ; fully adjusted; separate information for caffeinated/decaffeinated coffee and cappuccino. Limitations: hospital controls
			< 1	188	1		
			1- < 2	244	1.12 (0.85–1.48)		
			2- < 3	282	1.13 (0.86–1.47)		
			3- < 4	162	0.86 (0.64–1.16)		
			≥ 4	155	0.93 (0.69–1.27)		
Trend-test p-value: 0.251							

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Goodman et al. (2003) Hawaii 1993–1999 Case-control	Cases: 164; Population-based Controls: 194; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, race, OC, tubal alligation	Paper focused on coffee and caffeine; direct association for regular coffee and caffeine and no association with decaffeinated coffee; direct association only in the variant A/A of the CYP1A2 polymorphism in a subsample in women with intake above median of cruciferous vegetables, women with mucinous and OC; no significant similar increased risk in pre and post-menopausal women. Strengths: population controls, participation rates reported; interviewer-administered FFQ for most participants; fully adjusted; separate information for coffee/decaffeinated coffee/caffeine and in strata of selected covariates. Limitations: no mention on time between diagnosis and interview; no information on exclusion of previous cancer among cases and controls, on no exclusion of oophorectomized women from controls, on FFQ validity/reproducibility and other characteristics	
			No drinkers	32	1			
			< 1	68	1.3 (0.7–2.5)			
			≥ 1	64	1.5 (0.8–2.7)			
		Trend-test p-value: 0.27						
		Ovary	Caffeinated (regular)			Age, race, OC, tubal alligation		
			No drinkers	50	1			
			< 1	62	1.8 (1–3)			
≥ 1	52		1.7 (1–3.1)					
Trend-test p-value: 0.07								
Jordan et al. (2004) Australia 1990–1993 Case-control	Cases: 696; Population-based Controls: 786; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, body mass index, OC, parity, smoking, alcohol consumption, education, energy intake		
			No drinkers	127	1			
			< 1	176	0.98 (0.69–1.39)			
			1	107	0.88 (0.59–1.3)			
			2–3	200	0.9 (0.64–1.28)			
			≥ 4	86	0.62 (0.41–0.95)			
			Trend-test p-value: 0.05					

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Riman et al. (2004) Sweden 1993–1995 Case-control	Cases: 655; Population-based Controls: 3899; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)				rate reported; exclusion of oophorectomized women from controls; FFQ tested for validity/reproducibility (not for the coffee question); fully adjusted. Limitations: no information: on exclusion of previous cancer among cases and controls, and on separate information for caffeinated/decaffeinated coffee; interviewer-administered FFQ among cases and self-administered FFQ among controls
			Never	33	1	Age, parity, body mass index, age at menopause, OC, HRT	
			< 2	71	1.06 (0.66–1.7)		Paper focused on various risk factors; population with high intake of coffee; no association overall and separately for serous, mucinoid, endometrioid and clear cell tumours.
			2- < 4	297	0.93 (0.61–1.41)		Strengths: population controls; exclusion of oophorectomized women among controls; high participation rate; fully adjusted.
			4- < 6	192	0.87 (0.57–1.33)		Limitations: self-administered FFQ, or telephone interview for more controls than cases; no information: on previous cancer among cases and controls, on FFQ validity/reproducibility, on intake of caffeinated/decaffeinated coffee.
			≥ 6	61	0.68 (0.42–1.10)		
			Trend-test p-value: 0.18				
Baker et al. (2007) USA 1982–1998 Case-control	Cases: 414; Hospital-based Controls: 868; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)				Paper focused on coffee and tea; no association with regular coffee and weak inverse relation with decaffeinated; no heterogeneity among anatomical subtypes. Strengths: cases identified by cancer registries; information for caffeinated/decaffeinated coffee. Limitations: hospital controls; self-
			None	139	1	Age, residence, year of interview	
			≤ 1	107	1.15 (0.83–1.59)		
			2–3	102	1.02 (0.74–1.41)		
			≥ 4	66	1.05 (0.73–1.52)		

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							administered FFQ; no clear information on participation rate; no information: on exclusion of previous cancer among cases and controls and no exclusion of oophorectomized women from controls; on FFQ validity/reproducibility, major confounders adjusted for
Hirose et al. (2007) Japan 1990–2000 Case-control	Cases: 166; Hospital-based Controls: 3224; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, year of interview, motivation of consultation, parity, age at first birth, smoking, alcohol consumption, physical activity, body mass index, various dietary items	Coffee consumption in female hormone-related cancer (hospital-based Epidemiological Research Program et Aichi Cancer Center, HERPACC); population with a low prevalence of coffee drinking (33%); the FFQ was self-administered and then checked by an interviewer; caffeine no related with ovarian cancer. Strengths: cases identified through medical records and cancer registries; self-administered FFQ checked by an interviewer. Limitations: hospital controls (although no difference in lifestyle with a sample of general population); no information: on participation rates, on exclusion of previous cancer among cases and controls, on no exclusion of oophorectomized women from controls, on FFQ validity/reproducibility and other characteristics; no adjustment for menstrual factors and exogenous hormones; no separate information for coffee/decaffeinated coffee
			No drinkers	35	1		
			< 1	42	1.25 (0.75–2.09)		
			1–2	66	0.83 (0.51–1.37)		
			≥ 3	20	1.33 (0.68–2.6)		
							Trend-test p-value: 0.88
							Trend-test p-value: 0.6

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Song et al. (2008) USA 2002–2005 Case-control	Cases: 781; Population-based Controls: 1263; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, county, year of diagnosis, race, parity, duration of OC, body mass index, smoking, tubal ligation/hysterectomy, family history of breast/ovarian cancer	Paper focused on coffee, caffeine and tea; it considers the habit for 5 years before; no relation with coffee, decaffeinated and caffeine. Strengths: large study; cases identified by cancer registries as part of the SEER programme; population controls; exclusion of oophorectomized women from controls; information for caffeinated/decaffeinated coffee and caffeine. Limitations: participants with previous cancer (except for EOC) not excluded; self-administered FFQ; no information on FFQ validity/reproducibility; no adjustment for menstrual factors
			No drinkers	216	1		
			< 1	155	1.05 (0.79–1.4)		
			1- < 2	137	1.1 (0.82–1.48)		
			2- < 3	148	0.9 (0.67–1.19)		
			≥ 3	123	0.87 (0.64–1.19)		
			Trend-test p-value: 0.27				
Kotsopoulos et al. (2009) USA 1992–1997 and 1998–2003 Case-control	Cases: 1120; Population-based, Study name New England Case-Control Study (NECC). Controls: 1160; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, parity, OC, HRT, tubal ligation, family history of breast/ovarian cancer, body mass index, smoking	Paper focused on coffee and genes involved in caffeine metabolism; direct association only in premenopausal women; Strengths: large study; population-based; cases identified by medical records and cancer registries; FFQ tested for validity/reproducibility, although no validity specific for coffee intake; interviewer-administered FFQ; fully adjusted. Limitations: no information on: exclusion of previous cancer among cases and controls and no exclusion of oophorectomized women from controls; no age distribution reported; no separate information for caffeinated/decaffeinated coffee
			< 2,5	645	1		
			≥ 2,5	400	1.08 (0.9–1.3)		

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Gosvig et al. (2015) Denmark 1995–1999 Case-control	Cases: 382; Population-based; 30% of the cases (115) were borderline tumours. Controls: 911; None Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, parity, OC	Papers focused on coffee, tea and caffeine; cases include invasive and borderline tumours; most Danish women drinks caffeinated filtered coffee; similar no or weak inverse association (sometimes statistically significant) for all cases (all stages) and for histological subtypes (serous/ mucinous/endometrioid/other) or for total tumours and borderline tumours; results for caffeine were similar overall and in subgroups. Strengths: cases identified by cancer registries; population controls; exclusion of oophorectomized women from controls; fully adjusted. Limitations: self-administered FFQ within a larger questionnaire on other variables; no separate information for caffeinated/decaffeinated coffee; no information: on exclusion of previous cancer among cases and controls; on FFQ validity/reproducibility
			0	27	1		
			> 0- < 1	25	1.13 (0.59–2.15)		
			1–3	106	1.17 (0.7–1.94)		
			≥ 4	109	0.88 (0.53–1.45)		
		Increment of 1 cup/day	381	0.9 (0.84–0.97)			
		Trend-test p-value: 0.001					
		Ovary (others): Borderline ovarian cancer	All coffee (cups/day)		Age, parity, OC		
			0	10		1	
			> 0- < 1	18		1.7 (0.72–3.99)	
1–3	42		1.16 (0.55–2.45)				
≥ 4	45		0.86 (0.41–1.81)				
Increment of 1 cup/day	115	0.92 (0.83–1.01)					
Trend-test p-value: 0.09							

FFQ, food frequency questionnaire; CI, confidence interval; NR, not reported; OC, oral contraceptive; OR, odds ratio

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