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Table 2.18 Cohort 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
Larsson & Wolk (2005) Sweden Enrolment 1987–1990; FU 15,1 years Cohort	61 057; women (age 40–76 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, body mass index, education, parity, OC, total energy intake, fruits, intake of vegetables, milk, tea	Women recruited for mammography screening; lack of association for coffee consumption at baseline and long-term; lack of association for serous ovarian cancer (135 cases). Strengths: population-based cohort; linkage with population registers; previous malignancies and oophorectomy excluded; FFQ tested for validity; full adjustment for confounding Limitations: no information on response rate; no information of type of coffee (caffeinated/decaffeinated)
			< 1	24	1		
			1	51	1.13 (0.69–1.86)		
			2–3	177	0.97 (0.62–1.51)		
			≥ 4	49	1.07 (0.64–1.79)		
			For an increment of 1 cup/day	301	0.99 (0.88–1.09)		
			Trend-test p-value: 0.85				
Silvera et al. (2007) Canada Enrolment 1980–1985; FU average 16,4 years Cohort	48 776; women (age 40–59 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, smoking, alcohol consumption, education, body mass index, parity, physical activity, menopause, OC, total energy intake, lactose, study centre, randomization group	Women recruited for breast cancer screening; Strengths: linkage with registries; FFQ tested for validity/reliability; exclusion of women with previous ovarian cancer and oophorectomy; full adjustment for confounding. Limitations: no exclusion of other type of cancer; no information on type of coffee (regular/decaffeinated)
			0	34	1		
			≤ 1	110	1.18 (0.76–1.83)		
			2–3	79	1.36 (0.86–2.15)		
			≥ 4	41	1.62 (0.95–2.75)		
			Trend-test p-value: 0.06				

Table 2.18 Cohort 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
Steevens et al. (2007) the Netherlands Enrolment 1986–1999; FU 13,3 years Cohort	2083; postmenopausal women (age 55–69 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, OC, parity, smoking, tea	Strengths: linkage with Cancer Registry; FFQ tested for validity/reproducibility (no value reported); complete follow-up; women with oophorectomy, previous cancer and borderline invasive epithelial tumours have been excluded; fully adjusted. Limitations: no information on participation rate; no information of type of coffee (caffeinated/decaffeinated)
			< 1	15	0.73 (0.41–1.31)		
			1- < 3	87	1		
			3- < 5	119	1 (0.74–1.35)		
			≥ 5	59	1.08 (0.75–1.57)		
			For an increment of 1 cup/day	280	1.04 (0.97–1.12)		
			Trend-test p-value: 0.35				
Lueth et al. (2008) USA Enrolment 1986, FU about 16 years Cohort	29 060; post-menopausal women (age 55–69 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, smoking, body mass index, age at menopause, parity, OC, education, physical activity, total energy intake	No association for total and decaffeinated coffee and total caffeine; direct association with ≥ 5 cups/day of caffeinated coffee, with no trend in risk; HRs were similar in women with unilateral oophorectomy. Strengths: women with previous cancer and oophorectomy have been excluded; information on validity/reproducibility (ml for validity 0.95); response rate (42.3%); linkage with health registry, fully adjusted. Limitations: based on baseline FFQ although 5 FFQ are available
			0	24	1		
			< 1	30	1.06 (0.62–1.82)		
			1–2	122	1.05 (0.68–1.64)		
			3–4	50	0.96 (0.58–1.59)		
			≥ 5	40	1.28 (0.76–2.16)		
			Trend-test p-value: 0.51				

Table 2.18 Cohort 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
Tworoger et al. (2008) USA Enrolment 1976–1980, FU about 24 years Cohort	80 253; women aged 30–55 years. Exposure assessment method: Questionnaire	Ovary	Caffeinated (cups/day)			Age, parity, OC, HRT, tubal ligation, smoking, body mass index	Cumulative average and updating each questionnaire; similar results for caffeinated, decaffeinated coffee and total caffeine; further adjustments for many other variables did not change the HRs; stratification for caffeine intake did not vary by age, parity, tubal ligation, BMI, HRT; inverse association for coffee and caffeine in never OC users and for caffeine among never HRT users; inverse association of caffeine in postmenopausal women and positive association in premenopausal women, although not statistically significant. Strengths: women with previous cancer and oophorectomy have been excluded; FFQ validated (Person ml 0.78); diagnoses confirmed by medical records; repeated measures of coffee intake (every 2 years); low loss to follow-up (2.2%); fully adjusted. Limitations: no information on participation rate
			0	78	1		
			< 1	93	0.84 (0.62–1.14)		
			1	115	1.01 (0.75–1.36)		
			2	124	0.87 (0.65–1.16)		
			≥ 3	97	0.75 (0.55–1.02)		
			Trend-test p-value: 0.03				
		Ovary	Decaffeinated (cups/day)			Age, parity, OC, HRT, tubal ligation, smoking, body mass index	
			0	140	1		
			< 1	147	0.81 (0.64–1.03)		
			1	71	1 (0.75–1.34)		
			2	36	0.9 (0.62–1.3)		
			≥ 3	14	0.86 (0.49–1.49)		
			Trend-test p-value: 0.97				

Table 2.18 Cohort 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
Kotsopoulos et al. (2009) USA 1976–2004 Nested case-control	Cases: 232; population-based; Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII). Controls: 687; none Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day) < 2,5 ≥ 2,5 Trend-test p-value: 0.68	151 66	1 0.82 (0.57– 1.19)	Age, parity, OC, HRT, tubal ligation, smoking, body mass index, family history of breast/ovarian cancer	Cumulative average and updating each questionnaire; similar results in pre and postmenopausal women. Strengths: women with previous cancer and oophorectomy have been excluded; FFQ validated (Person ml 0.78); diagnoses confirmed by medical records; repeated measures of coffee intake (every 2 years); fully adjusted. Limitations: no information on participation rate
Kotsopoulos et al. (2009) USA 1976–2004 Nested case-control	Cases: 1352; population-based; combined studies: New England Case-Control Study (NECC) and Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII). Controls: 1847; none Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day) < 2,5 ≥ 2,5 Trend-test p-value: 0.34	796 466	1 0.99 (0.77–1.28)	Age, parity, OC, HRT, tubal ligation, smoking, body mass index, family history of breast/ovarian cancer	Paper focused on coffee and genes involved in caffeine metabolism; no association in strata of menopause; no association for caffeine, decaffeinated coffee; no clear gene-environment interaction between caffeine metabolism genes EOC. Strengths: large study; population-based; cases identified by medical records and cancer registries; FFQ tested for validity/reproducibility, although no validity specific

Table 2.18 Cohort 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
							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
Nilsson et al. (2010) Sweden enrolment 1985–1994, FU median 6 years Cohort	32 178; Women (age > 30 years) Exposure assessment method: Questionnaire	Ovary	Occasions/day			Age, body mass index, education, physical activity, smoking	Similar results for filtered and boiled coffee. Strengths: Linkage with Cancer Registry; participation rate (57–67%) Limitations: no mention of FFQ testing; adjustment for main confounders, except for menstrual factors; no information previous malignancy, oophorectomy; exposure mentioned as occasion/day rather than cups/d (occasion may be different from 1 cup); very short follow-up for some subjects
			< 1	5	1		
			1–3	41	1.28 (0.5–3.27)		
			≥ 4	25	1.41 (0.53–3.74)		

Table 2.18 Cohort 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
Braem et al. (2012) European countries enrolment 1992–2000, FU median 11,7 years Cohort	330 849; women (age 25–70 years) Exposure assessment method: Questionnaire	Ovary	Country specific quintiles (ml)			Age, parity, OC, body mass index, smoking, alcohol consumption, total energy intake, breastfeeding, menopause, height, education	No differences in strata of caffeinated and decaffeinated coffee; no effect modification by menopause, HRT and smoking; similar results for serous ovarian cancer (not shown). Strengths: women with previous cancer and oophorectomy have been excluded; FFQ tested for validity; fully adjusted; Limitations: no information on reproducibility; no information on participation rate
			0	84	1		
			1	159	0.91 (0.63–1.31)		
			2	189	0.98 (0.7–1.39)		
			3	286	1.07 (0.77–1.48)		
			4	237	1.02 (0.73–1.44)		
			5	189	1.05 (0.75–1.46)		
			Trend-test p-value: 0.43				
Hashibe et al. (2015) USA enrolment 1992–2001, FU range 10–13 years Cohort	50 563; postmenopausal women (age 55–74 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, race, education, smoking, alcohol consumption	Women recruited for large-scale clinical trial to detect if screening reduces death from selected cancers; coffee intake at baseline; similar results for total caffeine intake. Strengths: women with previous cancers have been excluded; linkage with registry; FFQ tested for validity (no value reported); participation rate (72%). Limitations: no information on reproducibility of FFQ; no information on
			< 1	50	1		
			1–1,9	30	1.21 (0.77–1.91)		
			≥ 2	82	1.17 (0.82–1.67)		
			Increment of 1 cup/day	162	1.04 (0.95–1.14)		
			Trend-test p-value: 0.3982				

Table 2.18 Cohort 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
							oophorectomy; no adjustments for menstrual and reproductive factors; no information separately for caffeinated and decaffeinated
Lukic et al. (2016) Norway enrolment 1991–2004, FU 1996–2013 Cohort	98 405; women (aged 30–70 years) Exposure assessment method: Questionnaire	Ovary	All coffee (cups/day)			Age, menopause, smoking, education, parity, OC, HRT, maternal history of breast cancer	Population-based cohort study. Strengths: women with previous cancers have been excluded; linkage with registry; FFQ tested for validity (RR = 0.82); participation rate (48.4%); fully adjusted. Limitations: no information on oophorectomy; no information separately for caffeinated and decaffeinated
			≤ 1	NR	1		
			1–3	NR	1.07 (0.81–1.42)		
			> 3–7	NR	1.06 (0.79–1.41)		
			> 7	NR	0.87 (0.5–1.51)		
			Trend-test p-value: 0.89				

CI, confidence interval; FFQ, food frequency questionnaire; FU, follow-up; HRT, hormone replacement therapy; NR, not reported; OC, oral contraceptive; RR, relative risk

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