

**Table 2.7. Case-control studies of estrogen-only menopausal therapy and ovarian cancer**

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	OR(95% CI)	Adjustment for potential confounders	Comments	
Purdie <i>et al.</i> (1999) New South Wales, Victoria, and Queensland, Australia, 1990-1993	793 histologically confirmed incident cases of ovarian cancer, aged 18-79, diagnosed between 1990-93	855 frequency age (20-year bands)- and geographic-matched controls were selected from the electoral roll. Controls had no history of ovarian cancer or bilateral oophorectomy	Interviewer-administrated questionnaire	Ovary (Epithelial type)	None	662	1.00	age, education, area of residence, BMI, hysterectomy, tubal sterilization, talc use in perineal region, smoking status, duration of OCP use, parity and family history of breast or ovarian cancer		
					Unopposed estrogen	68	1.27 (0.86-1.88)			
					<u>Used unopposed estrogen for</u>					
					<1 year	19	0.95 (0.67-1.36)			
					1-3 years	27	1.28 (0.95-1.72)			
					>3 years	22	1.03 (0.75-1.42)			
					<u>last used unopposed estrogen</u>					
					current user	28	0.93 (0.47-1.85)			
					1-5 years ago	18	1.13 (0.85-1.50)			
					>5 years ago	22	0.92 (0.67-1.25)			
					Ovary (Serous Epithelial type)	Unopposed estrogen	36			1.26 (0.78-2.03)
					Ovary (Endometrioid Epithelial type)	Unopposed estrogen	18			2.56 (1.32-4.94)
					Ovary (Mucinous Epithelial type)	Unopposed estrogen	6			0.85 (0.32-2.23)
Ovary (Undifferentiated)	Unopposed estrogen	4	0.51 (0.14-1.89)							
Ovary (mixed epithelial/mesodermal)	Unopposed estrogen	4	1.15 (0.35-3.80)							
	<u>With hysterectomy</u>	Unopposed estrogen					age, education, area of			

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Purdie <i>et al.</i> (1999) (contd)				Ovary (Epithelial type)	Unopposed estrogen	22	0.65 (0.34-1.24)		
				Ovary (Endometrioid Epithelial type)	Unopposed estrogen	5	1.75 (0.43-7.14)		
				Ovary (others)	Unopposed estrogen	17	0.57 (0.29-1.15)		
				<u>without hysterectomy but with tubal sterilization</u>					
				Ovary (Epithelial type)	Unopposed estrogen	5	1.03 (0.27-3.96)		
				Ovary (Endometrioid Epithelial type)	Unopposed estrogen	2	2.72 (0.27-27.3)		
				Ovary (others)	Unopposed estrogen	3	0.84 (0.17-4.12)		
				<u>without hysterectomy or tubal sterilization</u>					
				Ovary (Epithelial type)	Unopposed estrogen	41	3.00 (1.54-5.85)		
			Ovary (Endometrioid Epithelial type)	Unopposed estrogen	11	4.29 (1.67-11.1)			
			Ovary (others)	Unopposed estrogen	30	2.66 (1.31-5.37)			

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Riman <i>et al.</i> (2001), Sweden, 1993-1995	193 histologically verified incident cases of epithelial ovarian tumours; aged 50-74, cases identified through 6 regional cancer registries	3899 randomly selected controls from a Swedish population registry, without a history of borderline ovarian tumour or invasive ovarian cancer	Telephone interview	Ovary (all)	Medium Potency HRT			age, parity, BMI, age at menopause, ever use of contraceptives, duration of low potency estrogens and the other hormone replacement types	
					<u>Ever use of estrogen</u>				
					No	172	1.0		
					Yes	19	1.63 (0.95-2.79)		
					p value		0.09		
					<u>Duration of use estrogen (year)</u>				
					Never	172	1.0		
					<2	8	1.85 (0.86-3.96)		
					≥2	8	1.42 (0.64-3.15)		
					p value		0.25		
					Ovary (Serous type)				
					<u>Ever use of estrogen</u>				
No	95	1.0							
Yes	13	2.07 (1.08-3.95)							
p value		0.04							
<u>Duration of use estrogen (year)</u>									
Never	95	1.0							
<2	6	2.4 (0.98-5.85)							
≥2	6	1.84 (0.71-4.76)							
p value		0.12							
Ovary (Mucinous type)									
<u>Ever use of estrogen</u>									
No	75	1.0							
Yes	6	1.16 (0.45-2.96)							
p value		0.76							
<u>Duration of use estrogen (year)</u>									
Never	75	1.0							
<2	2	1.21 (0.29-5.11)							
≥2	2	0.96 (0.23-4.05)							
p value		0.97							

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Riman <i>et al.</i> (2002), Sweden, 1993-1995	655 incident cases of ovarian cancer, aged 50-74 and histological verified. Response rate: 76%	3899 controls were frequency matched to the expected age distribution of breast and endometrial and/or ovarian cancers. Response rate: 83%	Mailed questionnaire or telephone interview	Ovary (Epithelial type)	<u>Ever use of ERT</u>			age, parity, BMI, age at menopause, hysterectomy, duration of oral contraceptive use, and ever use of sequential and continuous estrogen-progestin combinations HRT.		
					No	583	1.0			
					Yes	59	1.43 (1.02-2.00)			
					<u>Duration of ERT</u>					
					Never	583	1.0			
					<1 year	17	1.40 (0.79-2.49)			
					1-2 years	5	1.07 (0.40-2.88)			
					2-5 years	8	0.99 (0.45-2.15)			
					5-10 years	11	1.80 (0.86-3.75)			
					≥10 years	12	2.14 (1.03-4.46)			
					Ovary (Serous Epithelial type)	<u>Ever use of ERT</u>				
					No	304	1.0			
					Yes	29	1.33 (0.85-2.09)			
					<u>Duration of ERT</u>					
Never	304	1.0								
<1 year	8	1.34 (0.62-2.89)								
1-2 years	2	0.83 (0.19-3.61)								
2-5 years	3	0.67 (0.20-2.24)								
5-10 years	7	2.01 (0.81-5.01)								
≥10 years	6	1.87 (0.70-4.95)								
Ovary (Mucinous Epithelial type)	<u>Ever use of ERT</u>									
No	52	1.0								
Yes	8	2.40 (1.02-5.65)								
<u>Duration of ERT</u>										
Never	52	1.0								
<1 year	3	3.41 (0.99-11.72)								
1-2 years	0									
2-5 years	3	4.96 (1.40-17.64)								
5-10 years	1	2.14 (0.27-16.86)								
≥10 years	0									

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Riman <i>et al.</i> (2002) (contd)				Ovary (Endometrioid Epithelial type)	<u>Ever use of ERT</u>				
					No	159	1.0		
					Yes	18	1.57 (0.88-2.78)		
					<u>Duration of ERT</u>				
					Never	159	1.0		
					<1 year	4	1.26 (0.44-3.63)		
					1-2 years	2	1.51 (0.34-6.69)		
					2-5 years	2	0.88 (0.21-3.74)		
5-10 years	3	1.96 (0.57-6.77)							
≥10 years	5	3.41 (1.15-10.14)							
Sit <i>et al.</i> (2002) Delaware Valley, USA, 1994-1998	767 incident cases of epithelial ovarian cancer, aged 20–69 years	926 community controls, frequency matched by age and place of residence	Interview		Unopp CEE <sup>a</sup>	50	0.90 (0.61-1.33)	use of OC, number of living births, age at diagnosis, history of tubal ligation, and family history of ovarian cancer	
					Unopp nCEE <sup>b</sup> with hysterectomy	10	0.52 (0.25-1.10)		
					Unopp CEE	22	0.79 (0.40-1.56)		
					Unopp nCEE without hysterectomy	2	0.17 (0.04-0.82)		
					Unopp CEE	28	1.17 (0.69-2.00)		
					Unopp nCEE	8	1.14 (0.44-2.98)		

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Glud <i>et al.</i> (2004), Copenhagen and Frederiksberg, Denmark, 1995-1999	376 incident cases of ovarian cancer aged 35-79 years were recruited from 16 gynecologic in the study area between 1995 and 1999. Histology reviewed by pathologists.	1111 population-based controls were randomly drawn from the Danish Central Population Register. Frequency match in 2 to 3 year age intervals according to the ovary cancer age distribution in the Danish Cancer Registry, 1987-1992. No previous surgery on ovaries or hysterectomy	Interviewer-administrated questionnaire	Ovary	Increase per gram of estrogen intake	338	1.136 (1.008-1.282)	age, ever/never use of oral HT, ever/never pregnant, number of pregnancy, ever/never oral contraceptive use, length of oral contraceptive use, family history of ovarian cancer, menopausap status, infertility, and sterilization	
					Cumulative intake of unopposed estrogen	NG	1.048 (0.966-1.138)		
Moorman <i>et al.</i> (2005) North Carolina, USA, 1999–2003	364 cases of ovarian cancer from North Carolina Central Cancer Registry, postmenopausal, aged 20–74 years, cases histologically confirmed, overall response rate 76%	370 population-based controls selected from the same 48-county area by random digit dialling, frequency matched by age (within 5 years) and race, response rate 71%	In-person interview with questionnaire	Ovary	<u>Duration of ERT</u>			Age, race, parity, tubal ligation, hysterectomy, BMI 1 year before interview, 1st degree family history of breast or ovarian cancer, breastfeeding (yes/no), oral contraceptive use (yes/no), and educational level	Estrogen only
					Never use	129	1.0		
					Ever use	105	1.5 (0.9-2.3)		
					<12 months	5	0.9 (0.3-3.2)		
					12-59 months	23	1.2 (0.6-2.3)		
					60-119 months	17	1.5 (0.6-3.5)		
					≥119	52	2.2 (1.2-4.1)		
					Ever estrogen only by subtype				
					Serous	73	2.0 (1.3-3.1)		
					Endometrioid or clear cell	17	1.0 (0.5-2.0)		
Mucinous	6	0.9 (0.3-2.5)							
Other	9	1.1 (0.5-2.7)							

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Rossing <i>et al.</i> (2007) Washington State, USA, 2002–06	812 women from Cancer Surveillance System (SEER program), diagnosed with a primary invasive or borderline epithelial ovarian tumour, aged 35–74 years; response rate 76.7%	1313 population-based controls selected by random-digit-dialling, matched by age and county; response rate 84.1%	Interviewer-administered standardized questionnaire	Ovarian (153, 154)	Epithelial ovarian cancer associated with exclusive use of ET			Age, county of residence, year of diagnosis/reference date, number of full-term pregnancies, and duration of hormonal contraception	
					Never used	440	1.0		
					Ever	121	1.3 (0.9–1.7)		
					Duration of use				
					<60 mo	38	0.9 (0.6–1.5)		
					60–119 mo	21	1.3 (0.7–2.5)		
					120+ mo	62	1.6 (1.1–2.5)		
					Recency				
					Current users	64	1.3 (0.9–2.0)		
					Former users	57	1.2 (0.8–1.8)		
					Recently quit (6–35 mo ago)	21	1.5 (0.8–2.8)		
					Quit ≥3 y ago (36+ mo)	36	1.1 (0.7–1.7)		
					Duration of use				
					Among current users				
					<60 mo	9	0.7 (0.3–1.5)		
					60+ mo	55	1.6 (1.1–2.5)		
					Among currently quit				
					<60 mo	6	1.2 (0.4–3.4)		
					60+ mo	15	1.8 (0.8–3.7)		
					Among quit ≥3 y ago				
					<60 mo	23	1.1 (0.6–1.9)		
					60+ mo	13	1.2 (0.6–2.7)		

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Rossing <i>et al.</i> (2007) (contd)					Invasive epithelial ovarian cancer associated with exclusive use of ET				
					Never used	299	1.0		
					Ever	94	1.3 (0.9–1.8)		
					Duration of use				
					<60 mo	25	0.8 (0.5–1.4)		
					60–119 mo	17	1.4 (0.7–2.6)		
					120+ mo	52	1.7 (1.1–2.7)		
					Recency of use				
					Current users	49	1.3 (0.9–2.0)		
					Former users	45	1.2 (0.8–1.9)		
					Recently quit (6–35 mo ago)	18	1.7 (0.9–3.2)		
					Quit ≥3 y ago (36+ mo)	27	1.0 (0.6–1.7)		
					Duration of use				
					Among current users				
					<60 mo	6	0.6 (0.2–1.6)		
					60+ mo	43	1.6 (1.0–2.5)		
					Among currently quit				
					<60 mo	19	0.9 (0.5–1.6)		
					60+ mo	26	1.7 (1.0–3.1)		

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Rossing <i>et al.</i> (2007) (contd)					Epithelial ovarian cancer associated with exclusive use of ET				
					BMI<25				
					Never used	191	1.0		
					Ever	59	1.9 (1.2–2.9)		
					Duration of use				
					<60 mo	15	1.3 (0.6–2.6)		
					60–119 mo	9	1.4 (0.6–3.5)		
					120+ mo	35	2.7 (1.5–4.8)		
					Recency of use				
					Current users	36	2.0 (1.2–3.5)		
					Former users	23	1.7 (0.9–3.1)		
					BMI≥25				
					Never used	246	1.0		
					Ever	62	1.0 (0.6–1.4)		
					Duration of use				
					<60 mo	23	0.8 (0.4–1.4)		
					60–119 mo	12	1.3 (0.5–2.9)		
					120+ mo	27	1.1 (0.6–1.9)		
					Recency of use				
					Current users	28	0.9 (0.5–1.6)		
					Former users	34	1.0 (0.6–1.6)		

<sup>a</sup> Unopposed CEE = use of CEE (conjugated equine estrogen) alone

<sup>b</sup> Unopposed nCEE = use of an estrogen formulation other than CEE alone