Table 2.2. Case-control studies of tamoxifen use and endometrial cancer

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
van Leeuwen et al. (1994), the Netherlands 1972–1990	98 women with endometrial cancer diagnosed at least 3 months following breast cancer (23 received tamoxifen).	285 controls matched by age and date of diagnosis of breast cancer who survived with an intact uterus at least up to the time of diagnosis of the cases (58 received tamoxifen).	From medical records. 59% users received 40 mg/day, 17% 30 mg/day and 23%, ≤ 20 mg/day	Tamoxifen:			Registry-based study The duration–response trends were similar with daily doses of 40 mg or 30 mg and less. No difference in stage or histology between the exposed and unexposed cases was found.
				Any use	23	1.3 (0.7–2.4)	
				For more than 2 years	10	2.3 (0.9–5.9)	
Sasco et al. (1996), France 1976–1992	43 women with endometrial cancer occurring at least one year after the diagnosis of breast cancer	177 controls matched by age, region, year of diagnosis of breast cancer and survival with breast cancer, with an intact uterus.	From medical records. Median dose of tamoxifen used was 20 mg/day	Tamoxifen			The median duration of treatment was greater in cases (63 months) than in controls (37 months). Information on duration of use was missing for 21% of exposed cases and 45% of exposed controls.
				Any use	29	1.4 (0.6–3.5)	
				< 2 yrs	6	1.5 (0.4–4.9)	
				2–5 yrs	5	1.5 (0.4–5.5)	
				5 yrs of use	12	3.5 (0.9–12.7)	
Mignotte et al. (1998), France 1976–1995	135 women with endometrial cancer diagnosed after breast cancer (91 received tamoxifen)	467 controls matched for age, year of diagnosis of breast cancer and hospital and survival time with an intact uterus (191 received tamoxifen)	From medical records	Tamoxifen			Hospital-based study. The risk increased with the length of treatment or the cumulative dose of tamoxifen received
				No	44	1.0 (ref)	
				Yes	91	4.9 (3.4–7.1)	
				Never	44	1.0 (ref)	
				Current use	49	5.4 (3.5–8.4)	
				Past use	40	4.4 (2.8–6.9)	
				Yes* (adjusted)	91	3.1 (1.1–8.7)	

Table 2.2. Case-control studies of tamoxifen use and endometrial cancer

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Bergman et al. (2000), the Netherlands 1987–1997	299 women with endometrial cancer after breast cancer	860 matched controls with breast cancer but without endometrial cancer, 3:1 matched on date of birth (± 3 years) and year of diagnosis (± 3 years)	From medical records	Tamoxifen use			Case and control selection was based on the records of population-based cancer registries and hospital-based cancer registries. Endometrial cancers of stage III and IV occurred more frequently in long-term tamoxifen users (2 years or more) than in non-users (17.4% versus 5.4%, *P* = 0.006). 3-year endometrial cancer-specific survival was significantly worse for long-term tamoxifen users than for non-users (76% for 5 or more years, 85% for 2–5 years versus 94% for non-users, *P* = 0.02).
				No	191	1.0 (ref)	
				Yes	108	1.5 (1.1–2.0)	
				2–5 yrs	38	2.0 (1.2–3.2)	
				5 or more years	14	6.9 (2.4–19.4)	

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Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Swerdlow & Jones (2005), United Kingdom 1976–1996	813 patients who had endometrial cancer after their diagnosis for breast cancer	1067 control patients who had breast cancer but not subsequent endometrial cancer, matched to case patients on date and age of diagnosis of the primary breast cancer within 6 months; registry region of residence at the date of diagnosis of primary breast cancer; and survival without second cancer, other than non-melanoma skin cancer or breast cancer, for at least as long after the diagnosis of breast cancer as the index duration	Hospital case notes	Tamoxifen			Case and control selection was based on the records of population-based cancer registries
				No	148	1 (reference)	
				Yes	665	2.4 (1.8–3.0)	
				Duration of treatment			
				< 2 yrs	155	1.3 (1.0–1.9)	
				2–4	196	1.9 (1.4–2.7)	
				5–7	160	2.8 (2.0–4.0)	
				8–9	62	4.7 (2.8–7.8)	
				10–17	47	7.2 (3.6–14.6)	
Chu et al. (2007), Canada 1977–2000	566 endometrial cancer cases who had been treated in a large cancer hospital	964 ethnically matched controls who were volunteer participants in a research programme	Hospital records	Women who carried the *CYP3A4*1B* allele:			The variant *CYP3A4* allele was present in 6% of the controls and 9% of the endometrial cancer patients (OR: 1.6; 95% CI: 1.1–2.3). The allele was more common in women with endometrial cancer who had been treated with tamoxifen for breast cancer (16%).
				Use of tamoxifen	63	2.8 (1.4–5.8) (P = 0.004)	