

**Table 2.1. Cohort studies of tamoxifen use and endometrial cancer**

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Cook et al. (1995), United States	All women under the age of 85 years registered in the Washington State Cancer Registry with a diagnosis of breast cancer between 1978 and 1990.	Medical records of tamoxifen use (mainly 20 mg/day) The mean duration of use was 14 months for cases and 21 months for controls.	Any tamoxifen use			Nested case-control study. Exposure of cases compared to that of 64 matched controls with an intact uterus. Odds ratio adjusted for cytotoxic chemotherapy and duration of estrogen replacement therapy.
			No	28	1 (ref)	
			Yes	6	0.6 (0.2–1.8)	
Curtis et al. (1996), United States	Cohort of 87 323 women reported to the US SEER Program diagnosed with early-stage (localized or regional) breast cancer between 1980 and 1992, aged at least 50 years at diagnosis who had not been given chemotherapy as an initial treatment, mean follow-up of [4.4] years	The SEER database indicated that they had received hormonal therapy (which for over 90% was tamoxifen treatment).	Received tamoxifen			Expected rates relative to the general SEER population The differences in risk for endometrial cancer between hormone-treated women and women with no/unknown hormone treatment status were greatest in 5-year survivors (SIRs of 3.6 and 1.2, respectively).
			Yes	73	SIR 2.0 (1.6–2.6)	
			No	384	SIR 1.2 (1.1–1.4)	
Katase et al. (1998), Japan	Cohort of 825 patients with primary breast cancer who underwent annual gynaecological examinations and cancer screening; patients aged 20–91 years	Hospital records	Treated with tamoxifen			All tamoxifen treated (at a dosage of 20–30 mg/day) received the drug for at least a year.
			Yes	4	1.00 ( $P = 0.01$ )	
			No	9	1 (ref)	

**Table 2.1. Cohort studies of tamoxifen use and endometrial cancer**

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Newcomb et al. (1999), United States	Cohort of 85 411 women with local or regional breast cancer diagnosed from 1983–90, followed to December 31, 1994	Reported as receiving hormonal therapy at the time of initial registration. 14 984 women received hormonal therapy (nearly all tamoxifen) and 70 427 did not.	Tamoxifen use (yes)			Expected rates from SEER incidence rates The similar stage distribution in the two treatment groups suggests a lack of serious detection bias in this study.
			Overall cancer	859	1.00 (0.93–1.08)	
			Endometrium	101	1.39 (1.09–1.77)	
Curtis et al. (2004), United States	Cohort of 39 451 breast cancer patients diagnosed from 1980 through 2000 registered with the US SEER program	Reported as initially treated with tamoxifen	Tamoxifen use		<i>O/E</i>	Expected rates relative to the general SEER population
			Yes	354	Overall: 2.17 (1.95–2.41)	
				Ad: 306	2.07 (1.85–2.32)	
				MMMT: 34	4.62 (3.20–6.46)	
Bouchardy et al. (2002), Switzerland	Cohort of 3 972 women diagnosed with histologically confirmed invasive and/or in situ breast cancer between 1985 and 1999 registered with the Geneva Cancer Registry	Reported use of tamoxifen (1 664 women) Person-years: 6 446 in the tamoxifen group and 14 581 in the group not treated with tamoxifen.	Tamoxifen use		SIR	Expected rates relative to the general population, observed cases being women who developed corpus uteri cancer at least 1 year after the initial diagnosis of breast cancer.
			Yes	All patients 22	2.0 (1.3–3.0)	
			Yes	Tamoxifen 11	2.8 (1.4–5.0)	
			No	No Tamoxifen 11	1.6 (0.8–2.8)	
					29.0	
				MMMT		
	Yes	With tamoxifen 2	29.0 (3.5–104.9)			
	No	Without Tamoxifen 0	--			

**Table 2.1. Cohort studies of tamoxifen use and endometrial cancer**

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Matsuyama et al. (2000), Japan	Retrospective cohort study of 6 148 women treated for breast cancer during 1982–90 in nine institutions in Japan.	Medical records or a prospectively compiled computer database at each institution. 3 358 women received tamoxifen, mainly for 2 years or less, and were followed for a mean of 7.64 years, 2 560 women did not receive tamoxifen and were followed for 8.10 years.	Yes/No		IRR	
			Tamoxifen group	9	2.37 (0.64–8.77)	
			No tamoxifen	3	1 (ref)	
Ursic Vrscaj et al. (2001), Slovenia	Cohort of 630 women diagnosed with breast cancer from 1987 to 1994 from a population-based registry, and followed for 8.5 years (range 5–12 years)	Reported use of tamoxifen – 440 patients (median treatment duration of 40 months, range 1–97 months); 190 no tamoxifen.	Yes/No			
			Tamoxifen group	11	2.38 (0.53–10.61)	
			No tamoxifen	2	1 (ref)	
Yamazawa et al. (2006), Japan	Retrospective hospital-based cohort study of 674 consecutive patients who underwent surgery for primary breast cancer between January 1989 and December 1998 and followed to December 2003	Hospital records	Tamoxifen use for longer than 5 years	6	Hazard ratio 7.92 (0.69–90.89)	

**Table 2.1. Cohort studies of tamoxifen use and endometrial cancer**

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases	Relative risk (95% CI)	Comments
Lavie et al. (2008), Israel	Cohort of 1 507 breast cancer cases linked to the Israel cancer registry 15 years after the diagnosis of breast cancer	Oncology records	Yes/No			There were four uterine sarcomas among the tamoxifen users, but none among nonusers. Five of the tamoxifen users (0.6%) died of uterine cancer, compared to none among nonusers.
			Tamoxifen	17	OR: 3.1 (1.0–9.1)	
			No tamoxifen	4	1 (ref)	
Beiner et al. (2007) Multicountry	Cohort of 857 women known to carry a <i>BRCA1</i> or <i>BRCA2</i> mutation, aged 45 to 70, identified from an international registry, average follow-up period of 3.3 years.	Subjects completed a baseline questionnaire and one or more follow-up questionnaires.	Yes/No			Expected number of endometrial cancers was calculated using age and country-specific incidence rates derived from IARC's Cancer Incidence in Five Continents [volume not specified by authors].
			Tamoxifen	4	11.6 ( $P = 0.0004$ )	
			No tamoxifen	2	2.7 ( $P = 0.17$ )	
			Overall		5.3 ( $P = 0.0011$ )	

Adc, adenocarcinoma; MMT, mixed malignant mullerian tumour of the uterus