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Breast cancer and hormonal therapy in postmenopausal women

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Chlebowski et al. recently reported from the Women's Health Initiative (WHI) that the risk of breast cancer associated with the use of combined menopausal hormone therapy (HT) markedly decreased after treatment discontinuation.¹ With a similar approach to that used in the WHI observational-study cohort, we investigated whether that decrease was also seen in the French E3N cohort, in which HT use was biennially self-reported.² Among postmenopausal respondents to the 1997-1998 questionnaire, those who were using combined HT or had never used HT at completion of the questionnaire were followed from January 1999 up to the date of diagnosis of any malignancy, last completed questionnaire, or July 2005, whichever occurred first. Hazard ratios of breast cancer for combined HT users vs. HT never-users (in 1997-1998) dramatically dropped towards unity after 2002, in parallel with an important reduction in HT use (Table 1). Our results in a French population therefore corroborate those from the North-American WHI setting and strengthen suggestions of a marked and rapid decline of breast cancer risk after discontinuation of combined HT.³

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Table 1. Year-to-year hazard ratios of invasive breast cancer for users of combined HT in 1997-1998 compared with HT never-users in 1997-1998; year-to-year percentage of HT current users. E3N study

	1999		2000		2001		2002		2003		2004		2005*	
	HT users in 97-98	Never- users in 97-98												
No. at risk	25,689	18,107	25,430	17,965	24,683	17,285	24,233	16,987	21,939	14,836	21,106	14,155	20,805	13,953
Mean follow-up (mo)	11.9	11.9	11.9	11.9	11.9	11.9	11.6	11.5	11.8	11.7	11.9	11.9	5.9	5.9
No. of cases	147	54	133	49	147	59	160	62	125	68	110	70	54	30
Annualized incidence (%)	0.58	0.30	0.53	0.28	0.60	0.35	0.68	0.38	0.58	0.47	0.52	0.50	0.53	0.43
Hazard ratio (95% CI) †	1.87 (1.33-2.62)		2.31 (1.61-3.30)		1.81 (1.30-2.52)		1.92 (1.39-2.64)		1.22 (0.89-1.68)		1.10 (0.80-1.53)		1.22 (0.75-1.98)	
Hazard ratio (95% CI) with adjustment for prior mammograms‡	1.87 (1.32-2.64)		2.41 (1.66-3.48)		1.82 (1.30-2.55)		1.93 (1.39-2.67)		1.19 (0.87-1.64)		1.08 (0.78-1.51)		1.17 (0.72-1.91)	
% current HT users§	84	17	77	18	75	18	58	15	45	12	32	8	30	7

Abbreviations: CI, confidence interval; HT, menopausal hormone therapy

* Data were included until July 2005

† Cox proportional-hazards model adjusted for: age (time scale), age at menopause (continuous), type of menopause (artificial / natural or unknown), parity and age at first full-term pregnancy (nulliparous / first full-term pregnancy at age <30, 1 or 2 children / first full-term pregnancy at age <30, 3 or more children / first full-term pregnancy at age ≥30), personal history of benign breast disease before menopause (yes / no), family history of breast cancer in first-degree relatives (yes / no), family history of breast cancer in other relatives (yes / no), body mass index before menopause (≤20 /]20-25] /]25-30] / >30 kg/m²), physical activity in 1990 (<27 /]27-39[/]39-57[/ ≥ 57 metabolic equivalent task-hour/week), use of oral progestagens before menopause (never / in the past 5 years / more than 5 years ago / ever, but unknown recency), use of oral contraceptives (never / in the past 5 years / more than 5 years ago / ever, but unknown recency). Further stratified on year of birth ([1925-1930]/[1930-1935]/[1935-1940]/[1940-1945]/[1945-1950])

‡ Cox proportional-hazards model adjusted for the same variables as in footnote (†), with further adjustment on mammography during the previous follow-up period (yes / no, time-dependant variable)

§ At the end of the year (or July 2005 for year 2005)