

## Recent Declines in Hormone Therapy Utilization and Breast Cancer Incidence: Clinical and Population-Based Evidence

**TO THE EDITOR:** Long-term use of estrogen- or progestin-containing hormone therapies (HT) is well recognized to be associated with increased risk of breast cancer both in observational studies and the Women's Health Initiative (WHI) randomized trial.<sup>1</sup> After the early termination of the trial in July 2002 and the subsequent media coverage, reports from clinical series indicated immediate declines of 28% to 46% in prevalences of HT and estrogen-only (ET) use.<sup>2,3</sup> The population-level impact of these declines on breast cancer are uncertain given the 2- to 3-year lag time between diagnosis and data availability in cancer registries.

To better understand the possible impact from changes in HT on breast cancer in larger populations, we compared recent secular trends in HT use and breast cancer incidence in available clinical and population-based data resources, including recently released cancer registry data for the year 2004. We calculated the annual prevalence of HT use and the annual incidence of invasive breast cancer for the period from 1994 to 2003 for women ages 50 to 74 years in Kaiser Permanente's (Oakland, CA) Northern California region (KPNC), a large integrated health-delivery system from which computerized pharmacy, membership, and hospital cancer registry data were obtained. Women filling at least two prescriptions (generally constituting 90 days per prescription) of HT or ET in any calendar year were considered users for that year. First primary invasive breast cancer (International Classification of Disease—Oncology, 3rd edition [ICD-O-3]<sup>4</sup> site 50.0-50.9) diagnoses were identified, with histologic subtypes defined as ductal (ICD-O-3 codes 8500), or "with lobular component" (ICD-O-3 codes 8520, 8522, 8524). Yearly denominators included women who were KPNC members for at least 11 months of the year, and excluded those with unknown age or county of residence. Population-based breast cancer incidence rates for the 13-county catchment area for KPNC and for the state of California were obtained from the California Cancer Registry for the same ICD-O-3 specifications and age group, but for the time period including 2004, which was the most recent year for which data were available. All rates were age-adjusted to the 2000 US standard.

Figure 1 illustrates that between 2001 and 2003, the calendar years before and after the WHI announcement, age-adjusted rates of HT and ET use in KPNC members declined 68% and 36%, respectively. For the same time period, breast cancer incidence declined 10%

in KPNC members, 11% in the catchment population, and 11% in the state. For 2004, breast cancer incidence rates in the catchment population and the state were lower than the rates for 2003. Comparable patterns of decline were observed for both the ductal and lobular histologic subtypes (data not shown).

These recent decreases in breast cancer incidence, evident in both clinical and population-based groups, are temporally consistent with substantial changes in HT and ET use. Furthermore, these patterns are consistent with (1) reports from observational studies of sharp reductions in breast cancer risk observed after HT cessation<sup>5</sup> and (2) proposed biologic mechanisms for the role of HT in breast carcinogenesis whereby HT acts as a promoter of already initiated breast tumors.<sup>6</sup> In California, breast cancer incidence rates have been declining since 1999, but more substantial reductions in 2003 and 2004 may reflect declines in the numbers of hormone therapy users and, if so, could provide further evidence of a short latency between HT discontinuance and reduced risk. While the ecologic nature of the KPNC HT and breast cancer data prohibit a causal interpretation of these associations, and the breast cancer incidence rate declines may have other explanations, population-level breast cancer incidence trends should continue to be monitored closely in light of hormone-use patterns.

*Christina A. Clarke and Sally L. Glaser*

Surveillance Research, Northern California Cancer Center, Fremont CA, and Department of Health Research and Policy, Stanford University School of Medicine, Stanford, CA

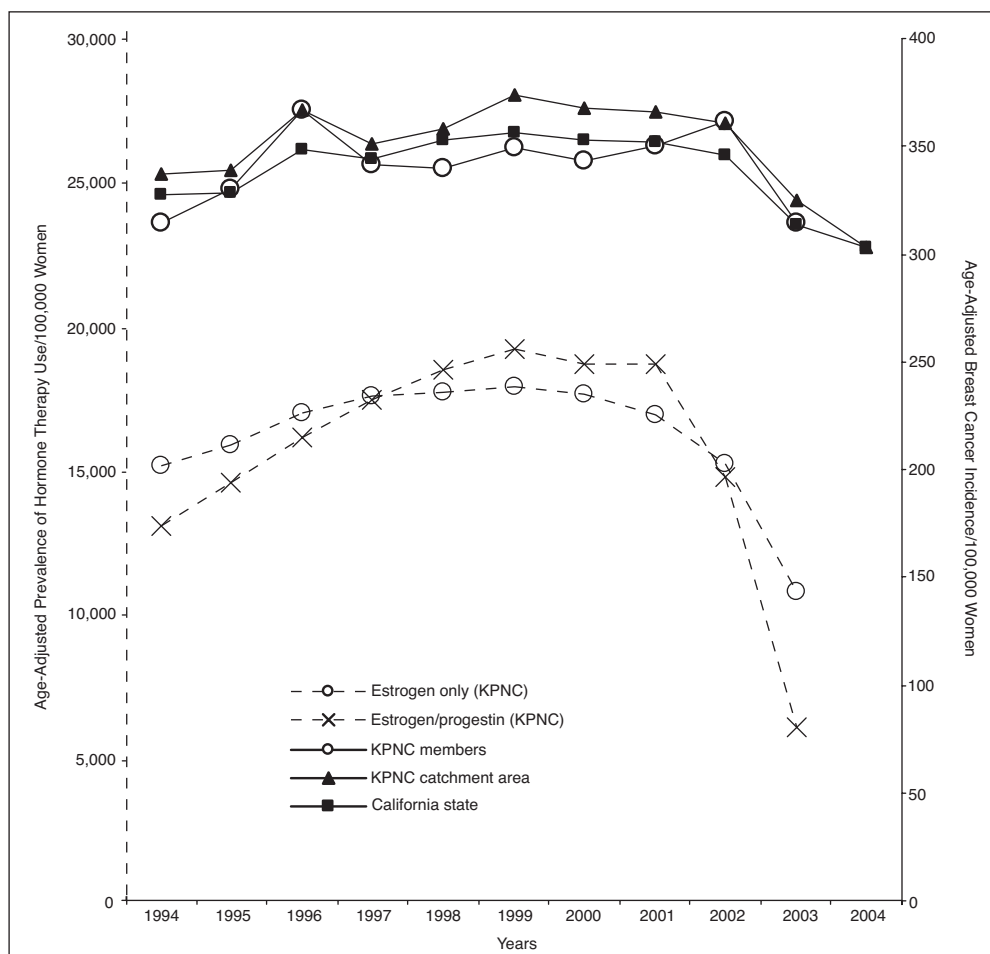
*Connie S. Uratsu, Joseph V. Selby, Larry H. Kushi, and Lisa J. Herrinton*

Division of Research, Kaiser Permanente, Oakland CA

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**Fig 1.** Yearly rates of prevalence of estrogen-only and estrogen/progestin-containing hormone therapy use and incidence of invasive first primary breast cancer in Kaiser Permanente-Northern California (KPNC) members, the 13-county KPNC catchment area, and the state of California, from 1994 to 2004.

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### Authors' Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following author or immediate family members indicated a financial interest. No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Authors	Employment	Leadership	Consultant	Stock	Honoraria	Research Funds	Testimony	Other
Christina A. Clarke							Williams Love O'Leary Craine & Powers, PC	