Re: Declines in Invasive Breast Cancer and Use of Postmenopausal Hormone Therapy in a Screening Mammography Population

We reported a recent drop in breast cancer incidence rates in US women (1), and others have observed this as well (2–4). Because of the marked decrease in breast cancer incidence around the time of the first report from the Women’s Health Initiative (WHI) announcement, and we generated semiannual screening mammography rates for three of these groups (Figure 1) by linkage with our diagnostic imaging database. The remaining group not presented in Figure 1 are women whose pattern of hormone use did not fit into any of the three groups, such as women who used hormone therapy before July 2002 but did not use it regularly for at least 2 years or women who continued use after December 2002 but again not on a regular basis.

This study was approved by the KPNC Institutional Review Board. In our population, mammography rates (6-month intervals) and breast cancer incidence rates are associated, and both decreased in 2003 (Figure 1). The greatest decrease in mammography rates was seen in women who were regularly using hormones before 2002 but stopped by December 2002, within 6 months after the WHI announcement. These stoppers had a slight increase in the mammography screening rate in the latter half of 2002 and then a substantial decrease in 2003 (>20%). These data suggest that the decline in cancer incidence after 2002 in our population may in part reflect a drop in mammography screening among women who were regular hormone users but who stopped around the time of the announcement of WHI findings. However, studies with individual data on...
hormone use, mammography, and breast cancer incidence are needed to further elucidate the contribution of hormone use and mammography, or other factors, to the recent drop in breast cancer rates.

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References


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A recent article in the Journal (1) indicates that reduced screening mammography is unlikely to explain the recent reduction in breast cancer incidence in the United States, which has been attributed to the general reduction in use of hormone replacement therapy (HRT) (2,3). However, in the United States, both screening mammography and HRT use are individual choice–driven activities, and there could be several confounding factors that influence these analyses.

In Scotland, by contrast, population screening mammography is a state-administered activity and continues to be a part of the routine life of every woman older than 50 years (82% of the eligible population receives screening mammography every 3 years; www.isdscotland.org). Also, almost all the HRT taken by women is through prescriptions issued by the National Health Service. Furthermore, Scotland also has a generally stable population, thus reducing any confounding by population migration. To investigate the relationship between HRT use and breast cancer rates, I obtained information on the yearly number of HRT prescriptions dispensed and breast cancer diagnoses in Scotland from 1997 to 2006 (Figure 1). The number of HRT prescriptions dispensed dropped substantially over this time, from 143,096 to 30,533 (estrogen + progesterone combination) and from 82,708 to 33,416 (estrogen only). However, the number of breast cancer cases has not followed this trend, thus challenging the idea that reduction in HRT use was responsible for the observed reduction of breast cancer in the United States.

A problem with the previous studies (1–3) is the lack of universal coverage by screening mammography and the fact that HRT data were collected by self-reporting (1). One possible explanation for the findings in the most recent US study (1) could be the following: The women who chose to continue having screening mammography may well have adopted other lifestyle changes that reduced their risk, such as increasing physical exercise (4). The association with physical exercise is evident whether it is done at a young age or in the referent year and is especially evident in those women who are recently exposed to HRT (4)—thus benefiting the very women who were risk averse and likely to have started exercise recently. Exercise has dramatic effects on estrogen metabolism (5), and it is possible that endogenous estrogens have a stronger influence on estrogen receptor–positive breast cancer than exogenous estrogens provided by HRT. The full explanation is likely to be much more complex, however.

The findings in Scotland could mean that HRT stimulates the growth of only the clinically significant breast cancer. HRT also increases breast density and reduces the sensitivity of screening mammography (6). In a population that continues to undergo screening mammography, one would therefore expect that a reduction in HRT would move the spectrum of the disease stage to the left, with a higher proportion being detected mammographically, at an earlier stage (albeit some of which may never have crossed the clinical threshold), without a perceptible reduction in the overall number of cancers.

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References


2. Ravdin PM, Cronin KA, Howlader N, et al. The decrease in breast-cancer incidence in

Figure 1. Number of hormone replacement therapy (HRT) prescriptions and breast cancer cases in Scotland from 1997 to 2006.
Notes
I wish to thank Victoria Hepworth and Susan Jensen of Information Services Division Scotland for providing the raw data for the analysis.

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Response
In our recent response (1) to correspondences about our report on declines in invasive breast cancer in a screening mammography population, we outlined potential mechanisms that may contribute to a decline in breast cancer, including a decrease in postmenopausal hormone therapy (HT) use, a decline in screening mammography use, an increase in chemoprevention, the increased detection of ductal carcinoma in situ and saturation of mammography screening.

Vaidya suggests an alternative explanation for the decline in invasive breast cancer that we observed in our study, such as lifestyle changes. It is possible that an unmeasured confounder, such as increases in physical activity, could explain some of the decline we observed in invasive breast cancer. However, a large prevalence of women would need to increase their physical activity to influence breast cancer rates because the reduction in breast cancer risk among women who exercise regularly is modest (2).

Vaidya also suggests that an increase in the sensitivity of mammography among former HT users could have influenced breast cancer rates in our population. However, such an explanation is unlikely, given that previous studies have reported mammographic breast density increases in only about 16%–20% of HT users (3,4) and that missed cancers increased from 0.8 to only 1.7 per 1000 screening examinations among long-term HT users (5). As a result, we would expect a very small increase in detection of breast cancers that were formerly obscured by high mammographic breast density associated with HT use.

Vaidya presents data from Scotland showing a precipitous decline in HT use (similar to observations in the United States) without a comparable decline in breast cancer incidence in women older than 50 years routinely undergoing screening mammography. It is possible that no decline in breast cancer incidence was observed in Scotland because the decline in estrogen and progesterone use occurred predominantly among women who had used estrogen and progesterone for less than 5 years and so were not at increased risk of breast cancer and/or because most formulations of estrogen–progesterone included progesterone or dydrogesterone, hormones that are less likely to increase breast cancer risk (6).

Caan et al. suggest that declines in mammography use among former postmenopausal HT users may have contributed to recent declines in breast cancer incidence in Kaiser women aged 45 years and older. Their figure 1 shows comparable absolute declines in mammography use of about 10% from 2002 to 2003 in women who used HT before 2002 and stopped and in women who continued use after 2002, with both declines starting after the beginning of a decline in breast cancer incidence. Notably, women who were regular HT users before 2002 and who stopped or continued use account for only 6.5% and 5.6%, respectively, of the Kaiser population. Thus, it is unlikely that a small absolute, short-term decline in mammography use among a small population of former and continuous HT users would contribute greatly to a 10% annual decline in breast cancer incidence. Caan et al. show stable to increasing mammography rates among never users of HT (59% of Kaiser women), which explains the minimal change in their overall mammography rates. Because declines in mammography use would need to be large to greatly contribute to a decline in breast cancer incidence, we would not expect the stable overall mammography rates presented by Caan et al. to account for the decline they observed in breast cancer incidence.

References

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