Response

Dr Grant suggests that both the Million Women Study and the Women’s Health Initiative (WHI) randomized prospective hormonal therapy clinical trials underestimated breast cancer risk by not using genuine never users of hormones for baseline controls.
and by omitting the effects of total ever hormone use including remote oral contraceptives. However, Dr Grant does not clearly distinguish information regarding combined estrogen–progestin and estrogen-only use, the latter being appropriate only in women with prior hysterectomy.

In the WHI trial evaluating estrogen–progestin hormonal therapy, combined hormonal therapy increased breast cancer incidence (1), interfered with breast cancer detection (2), and was associated with increased breast cancer mortality (3) so that a safe interval for use cannot be reliably determined with respect to breast cancer risk. In addition, both the Million Women Study and the WHI have published subgroup analyses associating a greater breast cancer risk with current use of estrogen–progestin hormonal therapy in women with a longer duration of prior menopausal hormone therapy (4,5).

Dr Grant also suggests that prior use of oral contraceptives should be included in such analyses. However, in my view, the relationship between remote oral contraceptive use and the subsequent influence on the risk of breast cancer after menopause has not been established in women using estrogen–progestin or estrogen-only hormonal therapy. Nonetheless, given the increased breast cancer mortality risk and the increased risk of lung cancer mortality (6) seen in the WHI clinical trial with estrogen–progestin hormonal therapy, our conclusion that use of combined hormonal therapy “other than short-term therapy in women with climacteric symptoms not ameliorated by other therapies seems unwarranted” does not appear to differ substantially from Dr Grant’s position.

Dr Grant seems to consider all menopausal hormone therapy together in her comments. However, the recent update (7) of the WHI prospective randomized clinical trial evaluating estrogen-only hormonal therapy in women with prior hysterectomy (8) emphasizes differences between estrogen–progestin and estrogen-only hormonal therapy and the need to counsel women differently depending on their age and hysterectomy status. In this randomized trial, an overall statistically significant reduction in breast cancer incidence was associated with estrogen use. In addition, there was a suggestion of an overall net benefit in women initiating use of estrogen-only hormonal therapy between the ages of 50 and 59 years compared with either no benefit (for women aged 60–69 years) or potential harm in older women (age ≥70 years) (7). Importantly, only women with prior hysterectomy are candidates for estrogen-only hormonal therapy.

In summary, I am in general agreement with Dr Grant’s position regarding cancer risk being related to combined estrogen–progestin use regardless of age or time from menopause. However, the findings from the WHI randomized trial evaluating estrogen-only hormonal therapy are quite different and require careful consideration in younger women with prior hysterectomy.

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References

Notes
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