

Menopausal hormone therapy and breast cancer mortality

The Collaborative Group on Hormonal Factors in Breast Cancer has brought together the worldwide evidence on menopausal hormone therapy (MHT) and invasive breast cancer.¹ The results showed that all types of MHT examined, except vaginal oestrogens, were associated with a significant excess incidence of breast cancer, with the risks among current users increasing steadily with duration of MHT use. Risks were greater for oestrogen-progestagen than for oestrogen only, and some excess risk persisted for more than a decade after cessation of use. The collaboration collected no information, however, on screening history or on breast cancer mortality. We report such findings from a large population-based prospective study, complementing the collaborative findings for incident breast cancer.

The Million Women Study (which also contributed information on incident breast cancer to the collaboration) recruited 1.3 million UK women from 66 National Health Service (NHS) breast cancer screening centres in 1998 (range 1996-2001). At recruitment, a third of these women were current users of MHT, half were never users, and no material difference was noted between them in the age-standardised proportions who accepted their next screening invitation about 3 years after recruitment (90.9% vs 90.2%).

All study participants were followed up by electronic linkage to NHS cancer records and to death registers up to 1 January 2018, about 20 years after recruitment. Cox regression yielded relative risks and their 95% CIs for breast cancer mortality in current and past versus never-users of MHT, using adjustments similar to those in the collaborative analyses.¹ During 20 years of follow-up of postmenopausal women, 2354 current users, 1249 past users and 3523 never-users of MHT at recruitment died with breast cancer recorded as the underlying cause of death (figure). Where the ER status of the tumour that caused death was known, three quarters had been ER positive.

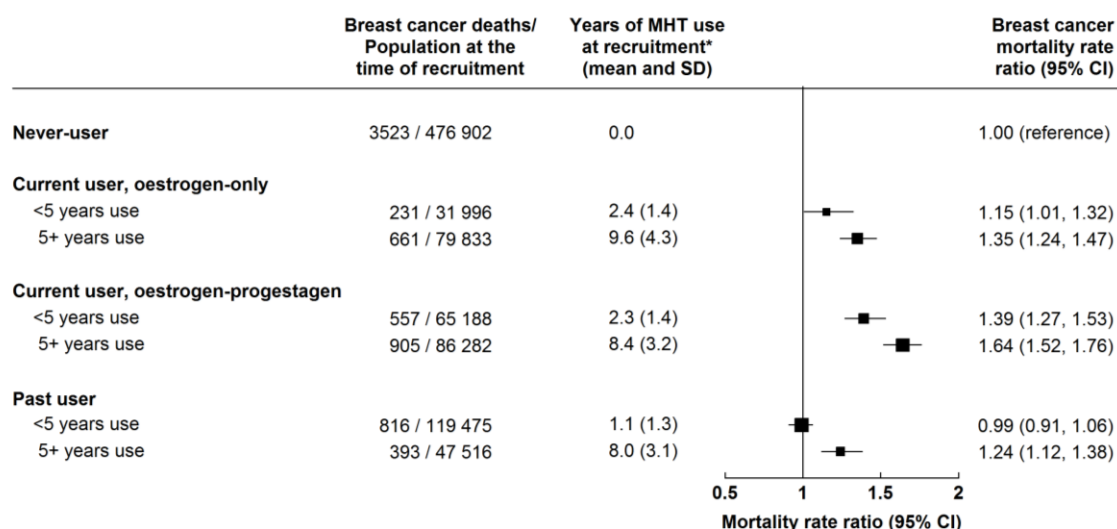
Women who had been current users both of oestrogen-only and of oestrogen-progestagen preparations had significant excess risks. These excess risks were greater the longer the duration of MHT use. After standardising for duration of use, the excesses were greater for oestrogen-progestagen than for oestrogen-only preparations ($p < 0.001$). Past users with 5 or more years of MHT use had a significant excess mortality from breast cancer over about the next 20 years ($p < 0.001$). These results for breast cancer mortality are consistent with the collaborative findings for incident breast cancer.¹

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Figure: 20-year breast cancer mortality risk ratio for current and past use versus never-use of MHT at recruitment in the Million Women Study



* Use would have continued after recruitment in current users, but had stopped in past users. Half were resurveyed about 8 years after recruitment, by which time there had been widespread cessation of MHT use. The mean (SD) years of MHT use reported at resurvey by women in the above 7 categories of use at recruitment (which includes use before and use after recruitment) had become, respectively, 0.1 years for never-users, 7.0 (3.7) and 13.5 (5.5) years for those who had been using oestrogen-only MHT, 6.6 (3.4) and 11.8 (4.3) years for those who had been using oestrogen-progestagen MHT, and 1.2 (2.1) and 7.8 (4.4) years in those who had been past users.

References

- 1 Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet* 2019; published on Aug 29. [http://dx.doi.org/10.1016/S0140-6736\(19\)31709-X](http://dx.doi.org/10.1016/S0140-6736(19)31709-X).
- 2 Green J, Reeves G, Floud S et al. Cohort profile: the Million Women study. *Int J Epi* 2019; **48**: 28–29e [doi10.1093/ije/dyy065](https://doi.org/10.1093/ije/dyy065)