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Letter to the Editor: In Response

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We agree with the author of the letter addressing our manuscript (1) that HT is efficacious in controlling some menopausal symptoms and that a discussion of the “big picture” is important. This discussion would need to include side effects (breast tenderness) and symptom occurrence after stopping HT. The complex issue of health related quality of life, the components of which extend beyond vasomotor symptoms in menopausal and postmenopausal women, has been the subject of other papers (2,3). It is important in decision making to know what might be expected with therapy including that HT may not be a permanent cure for symptoms and may not improve overall quality of life. However, another “take-home” message is that WHI analyses do not cover the full story with respect to clinical circumstances when CEE might be appropriate and this manuscript cannot address “other options” which were not studied in WHI and indeed may not have been studied in a randomized trial design.

It is not agreed that “the WHI was not designed to investigate the scenario of postmenopausal women who start HT near menopause and continue it for a long time”. We are careful to limit our conclusions to the population and HT preparation studied while noting the population did include women 50–59 as well as 60+ and that it was long-term. Moreover, other analyses provide little support for the hypothesis of favorable health effects among women who initiate postmenopausal estrogen use soon after menopause, either for coronary heart disease or for the health benefits versus risk indices considered (4).

The writer’s characterization of adverse events as having a very small risk is not supported by WHI results. In this estrogen-alone study, ischemic stroke, deep vein thrombosis and pulmonary embolism each increased by about 40–50%. Because of the risks, the FDA cautions in the boxed warning label to prescribe at the lowest effective dose and for the shortest duration consistent with treatment goals and risks for the individual woman.

There are several papers that address the point made in the letter that benefit-risk calculations in the clinical setting cannot be extrapolated from the WHI data, but can be from observational studies such as the Nurse’s Health Study. Re-analysis of the Nurses’ Health Study (NHS) observational data using a methodology similar to that of a clinical trial, and which (unlike all previous analyses) includes coronary heart disease events in the first two years after starting HT gave results very similar to those of the WHI trial of estrogen plus progestin (5,6).

The WHI hormone trial results raised provocative scientific, public health and clinical issues several of which were touched upon here. That the results continue to spark debate clearly

demonstrates the importance of large, carefully designed randomized trials to assess the most widely applied treatments in medicine.

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