In October 2013, the Women’s Health Initiative (WHI) investigators published a comprehensive overview of findings from their two hormone therapy (HT) trials, including extended follow-up representing 13 years of cumulative data. When I analyzed this latest WHI report, I initially focused almost exclusively on the data presented in figures and tables within the article itself, as well as on supplemental data presented on the Internet. Only then did I read the discussion comments by its authors. I would recommend this approach to anyone who has not yet reviewed this publication.

Overall, the WHI investigators maintain a negative stance toward the preventive and therapeutic benefits of menopausal HT. In my opinion, they also under-emphasize the importance of time since menopause in patient selection. These are the same WHI investigators who initially published un-adjudicated data and who delayed reporting age-stratified data. They also erroneously concluded that HT might increase the risk of ovarian cancer, even though their own data showed otherwise.

The tables and figures contain the most important data point from this extended WHI follow-up: a reduction in all-cause mortality among women who initiated HT within 10 years of menopause, whether they used estrogen-alone (hysterectomized women) or estrogen-progestin therapy (women with an intact uterus), compared with women in the placebo group.

Do the risks of HT really outweigh the benefits?
The dramatic benefits of estrogen-alone HT, in particular, recently were highlighted by Sarrel and colleagues in an analysis that suggests that as many as 90,000 deaths may have occurred after publication of the initial WHI findings, when estrogen therapy was widely withheld. The study by Sarrel and colleagues also was highlighted in a recent issue of this journal.

However, based on a “global index,” which has not been validated, the WHI investigators concluded that the risks of estrogen-progestin therapy outweigh the benefits regardless of age. Yet, the global index does not include all key concerns, omitting several quality-of-life concerns, including sleep disturbance, work productivity, and sexual function, as well as type 2 diabetes mellitus, osteoarthritis, and nonosteoporotic musculoskeletal problems. Nor does the global index provide individual weights.

Although the WHI data show reductions in the incidence of some serious chronic diseases, such as osteoporotic fracture and cardiovascular disease (in women within 10 years of menopause), Manson and colleagues make the blanket statement that HT should not be used for disease prevention, although they admit that it may be a “reasonable option for the management of moderate to severe menopausal symptoms among generally healthy women during early menopause.”

For some time, Wul H. Utian, MD, PhD, a founder of both the
International Menopause Society and the North American Menopause Society, has been calling for an independent commission to reevaluate all of the major WHI reports “to determine whether the data justified the conclusions drawn.” I support his call and suggest that this latest WHI publication be included in that reevaluation. The fact that total mortality is reduced among women using HT—according to the WHI’s own data—is not only impressive, it argues for, not against, the use of HT for chronic disease reduction.

The bottom line

We need to look at the totality of the data on menopausal HT, evaluate our patients individually, treat those who are truly hormonally deficient and suffering, and counsel them that many of the harms linked to HT have been exaggerated.

The pendulum is finally swinging back toward a more balanced assessment of the benefits and risks of HT, indicating that it may be appropriate for primary prevention of cardiovascular disease, osteoporosis, and type 2 diabetes—and thus can potentially expand the lifespan. It’s up to us to communicate this fact to our patients.

References


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