Does the discontinuation of menopausal hormone therapy affect a woman's cardiovascular risk?

No. Although findings from this large observational study from Finland suggest that women stopping hormone therapy (HT) experienced elevations in cardiac and stroke mortality within the first year after discontinuation, these associations are not likely to be causal and contradict those of the Women's Health Initiative, the largest randomized trial of HT, which found no elevated risks after discontinuation of HT.[1,2]

FAST TRACK

The Women's Health Initiative found no elevated risks after discontinuation of HT

Mikkola TS, Tuomikoski P, Lyytinen H, et al. Increased cardiovascular mortality risk in women discontinuing postmenopausal hormone therapy [published online ahead of print September 28, 2015]. J Clin Endocrinol Metab. jc20151864.

EXPERT COMMENTARY

›› **Andrew M. Kaunitz, MD,** is University of Florida Research Foundation Professor and Associate Chairman, Department of Obstetrics and Gynecology, University of Florida College of Medicine–Jacksonville. Dr. Kaunitz directs Menopause and Gynecologic Ultrasound Services, UF Women's Health Specialists–Emerson. He serves on the OBG MANAGEMENT Board of Editors.

›› **JoAnn E. Manson, MD, DrPH,** is Chief of the Division of Preventive Medicine at Brigham and Women's Hospital in Boston and Professor of Medicine at Harvard Medical School. Dr. Manson is a Past President of the North American Menopause Society (NAMS) and one of the principal investigators of the Women's Health Initiative.

›› **Cynthia A. Stuenkel, MD,** is Clinical Professor of Medicine, University of California, San Diego, School of Medicine, and Past President of NAMS.

Dr. Kaunitz reports that he is a consultant (contraception) to Actavis, Bayer, and Pfizer. The University of Florida receives clinical trial support from Bayer and TherapeuticsMD. Drs. Manson and Stuenkel report no financial relationships relevant to this article.

This recently published study from Finland generated headlines when its authors concluded that stopping HT elevates the risk of mortality from cardiovascular disease (CVD), including cardiac and cerebrovascular events. Using nationwide data, investigators compared the CVD mortality rate among women who discontinued HT during the years 1994 through 2009 (n = 332,202) with expected (not actual) CVD mortality rates in the background population.

Within the first year after HT discontinuation, elevations in death rates from cardiac events and stroke were noted (standardized mortality ratio, 1.26 and 1.63, respectively), while in the subsequent year, reductions in such mortality were observed ($P<.05$ for all comparisons).

The absolute increased risk of death from cardiac events reported within the first year after discontinuation of HT was 4 deaths per 10,000 woman-years of exposure. The absolute risk of death from stroke was 5 additional events per 10,000 woman-years. This level of risk is considered to be rare.

CONTINUED ON PAGE 51

CONTINUED FROM PAGE 52

How these data compare to those of other studies

In contrast with these Finnish data, findings from the Women's Health Initiative—the largest randomized trial of menopausal HT—do not indicate an increase in mortality or an increase in coronary heart or stroke events among women stopping HT.[1,2]

It seems likely that limitations associated with the Finnish observational data account for this discordance. For example, Mikkola and colleagues did not know why women discontinued HT, raising the possibility that women with symptoms suggestive of CVD or development of new risk factors preferentially stopped HT, potentially introducing important bias into the Finnish analysis.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Women and their clinicians should make decisions regarding whether to continue, reduce the dose, or discontinue HT through shared decision making, focusing on individual patient quality of life parameters as well as changing risk concerns related to such entities as cancer, CVD, and osteoporosis.[3] Dramatic as they are, findings from this Finnish report should not impact how we counsel women regarding use or discontinuation of HT.

››ANDREW M. KAUNITZ, MD; JOANN E. MANSON, MD, DRPH; AND CYNTHIA A. STUENKEL, MD

References

1. Heiss G, Wallace R, Anderson GL, et al; WHI investigators. Health risks and benefits 3 years after stopping randomized treatment with estrogen and progestin. JAMA. 2008;299(9):1036–1045.
2. LaCroix AZ, Chlebowski RT, Manson JE, et al; WHI investigators. Health outcomes after stopping conjugated equine estrogens among postmenopausal women with prior hysterectomy. JAMA. 2011;305(13):1305–1314.
3. Kaunitz AM. Extended duration use of menopausal hormone therapy. Menopause. 2014;21(6):679–681.

Do your patients have difficulty filling some of their HT prescriptions?

In his Editorial, "Does hormone therapy reduce mortality in recently menopausal women?" which appeared in the October 2015 issue of OBG MANAGEMENT, Editor in Chief Robert L. Barbieri, MD, expressed:

> Many health insurers use pharmacy benefit managers to control the cost of prescription medicines. These managers often develop formulary algorithms that favor the use of oral estrogen and medroxyprogesterone acetate over transdermal estradiol and micronized progesterone.

He then posed this question to readers:

> When you prescribe transdermal estradiol and micronized progesterone, have your patients had difficulty filling the prescription?

READERS WEIGH IN:

Yes!

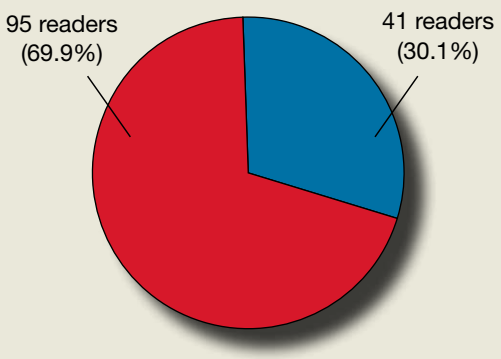
The pharmacies push "cheaper" substitutions. I do a lot of education, but it is exhausting!

Julie Fryman, MD
Cumming, Georgia

Quick poll results

More than 130 readers weighed in, with:

- **69.9% (95 readers)** indicating that their patients have had difficulty filling the prescriptions
- **30.1% (41 readers)** indicating that their patients have not had difficulty filling the prescriptions



To participate in the latest Quick Poll, visit **obgmanagement.com**