NAMS
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FIRST TO KNOW®

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Under the editorship of NAMS Executive Director JoAnn V. Pinkerton MD, NCMP, *First to Know* presents commentary on the latest, breaking scientific articles as suggested by members of The North American Menopause Society (NAMS), the leading nonprofit scientific organization dedicated to improving women's health and quality of life through an understanding of menopause and healthy aging. Opinions expressed in the commentary are not necessarily endorsed by NAMS or by Dr. Pinkerton.

USPSTF seeks comment on draft recommendation regarding hormone therapy for the primary prevention of chronic conditions

Statement concludes there is no net benefit for the use of hormone therapy for the prevention of chronic conditions in most postmenopausal women.

Gartlehner G, Patel SV, Viswanatha M, et al. *Menopausal Hormone Therapy for the Primary Prevention of Chronic Conditions: An Evidence Review for the US Preventive Services Task Force*. AHRQ Publication No. 15-05227-EF-1. May 2017.

Summary. The US Preventive Services Task Force (USPSTF) is seeking comments on a draft recommendation statement and draft evidence review on hormone therapy (HT) for the primary prevention of chronic conditions. Based on its review of the evidence, the Task Force recommends against the use of combined estrogen and progestin for the prevention of chronic conditions in postmenopausal women. This is a D recommendation. The Task Force also recommends against the use of estrogen for the prevention of chronic conditions in postmenopausal women who have had their uteruses removed. This is a D recommendation. The draft recommendation statement and draft evidence review are available for review and public comment from May 16, 2017, to June 12, 2017, at www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/menopausal-hormone-therapy-preventive-medication1.

The recommendation applies to postmenopausal women who are considering HT for the primary prevention of chronic medical conditions. It does not apply to women who are considering HT for the management of menopause symptoms such as hot flashes or vaginal dryness. It also does not apply to women aged younger than 50 years who have had premature menopause or surgical menopause.

Commentary. The USPSTF panel recommends against using HT for prevention of chronic disease, giving HT a D recommendation because "harms far outweighed the benefits." The panel used only randomized, clinical trial (RCT) data, primarily the Women's Health Initiative (WHI) and the 13-year cumulative follow-up data on which to base their recommendations. The panel found "convincing evidence" that "combined therapy was linked with 'moderate benefit' in

reducing the risk of fractures and 'adequate evidence' that it was associated with a 'small benefit' in reducing the risk of diabetes." The panel found "convincing evidence" that combined use of estrogen and progestin was linked with "moderate harms," including an increased risk of invasive breast cancer and venous thromboembolism, with "small to moderate harm" of heightened risk for coronary heart disease.

Persistent vasomotor symptoms

At age 65, women have a life expectancy of more than 20 years, and many continue in the workforce. The most frequent considerations for longer uses of systemic HT are persistent vasomotor symptoms (VMS), prevention of bone loss and fractures, maintenance of quality of life (QOL), and for low-dose vaginal estrogen, to prevent or treat the genitourinary syndrome of menopause (GSM). Vasomotor symptoms persist on average 7.4 years, may last more than 10 or 20 years, and may be associated with cardiovascular or cognitive risks.

In a study of Swedish women aged older than 85 years, 16% reported hot flashes at least several times per week. The WHI selectively excluded women with VMS, and thus decision-making about how to treat women with persistent VMS cannot be made exclusively from trials in which this group is not represented.

Women with early menopause

The WHI data does not apply to women with early menopause, because there were few enrolled. The USPSTF draft recommendation provides limited mention of the increased health risks seen with early menopause, whether natural, induced, or surgical. The benefit of HT to median age of menopause is based on observational evidence of potential prevention of risks related to early estrogen loss on coronary heart disease, osteoporosis, affective disorders, sexual dysfunction, GSM, and lowered cognitive function. Because of exclusion of observational data by the panel, potential health benefits for women with early menopause who take HT to the median age of menopause are not included.

2017 NAMS Hormone Therapy Position Statement

A NAMS panel of 23 experts (clinicians, researchers, and epidemiologists) completed an 18-month review of pertinent literature on HT, including randomized trials, observational literature, and smaller randomized trials and found clear evidence of benefit of the use of HT for symptomatic women and those at elevated risk of bone loss if aged younger than 60 years or within 10 years of menopause onset.

The 2017 Hormone Therapy Position Statement supports

1. The benefit of the use of HT for symptomatic women or who are at elevated risk of bone loss for those aged younger than 60 years or within 10 years of menopause onset.
2. Early initiation of HT and continued use at least until the median age of menopause (52 y) in women with primary ovarian insufficiency or early natural or induced menopause or who have had surgical menopause aged younger than 45 years, and particularly younger than 40 years, and who are otherwise appropriate candidates for HT.
3. The use of HT to prevent osteoporosis. Hormone therapy is approved by FDA to prevent osteoporosis, and numerous RCTs have documented HT's efficacy in preventing osteoporosis and decreasing the incidence of hip and other osteoporotic fractures, recognizing efficacy is lost once HT is discontinued.
4. The recognition that the WHI, the largest RCT to date, used only one formulation (conjugated equine estrogen and synthetic medroxyprogesterone acetate) of HT at a relatively high dose in women aged a median of 63 years and more than 10 years from menopause onset.

5. Determining the most appropriate type, dose, formulation, route of administration, and duration of therapy for an individual woman, recognizing that risk may be minimized by lowering doses, changing type of progestogen, or changing to transdermal therapies. Periodic reassessment is needed of changes in a woman's health and anticipated benefits, risks, and treatment goals over time.
6. Discussions between healthcare providers and women about extended duration of use of HT for persistent VMS, prevention of bone loss, or to improve QOL should include shared determination, based on the best evidence available, that the benefits of HT outweigh the potential risks for the particular woman after an assessment of comorbidities, options to minimize risk with transdermal or lower doses, and the risks of stopping HT, such as bone loss and fracture.
7. For women who initiate HT more than 10 or 20 years from menopause onset or aged 60 years or older, the benefit-risk ratio appears less favorable than for younger women because of greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia.
8. Low-dose vaginal estrogen for GSM symptoms not relieved with over-the-counter or other therapies.

NAMS recommends that the USPSTF include areas in which HT has been shown to be safe and effective and could be considered for extended duration, with specific recommendations to include

1. A statement of benefit for relief of hot flashes and prevention of bone loss and fracture in women aged younger than 60 years and within 10 years of menopause onset.
2. A statement of possible benefit for women with early menopause who take HT to the average age of menopause.
3. A statement of possible health benefits for women without contraindications who, after evaluation and discussion, elect to continue HT for persistent VMS, prevention of bone loss, or for QOL.
4. A statement that the findings of "harm greater than benefit" for HT for chronic diseases were based primarily on a study of women initiating HT aged in their mid-60s (median age), using a higher dose than used today of one type of estrogen combined with a potent synthetic progestin, and that these findings might not hold true for younger users, different formulations, lower doses, or different routes of administration.
5. A statement that estrogen alone in women with a hysterectomy and aged younger than 60 years or within 10 years of menopause onset had fewer breast cancers, less cardiovascular disease, and less mortality.
6. A statement that low-dose vaginal estrogen has been shown to relieve GSM at any age.

We strongly encourage a call to action to comment on this draft recommendation and have your voices heard before women lose their right to shared decision making about the use of HT for relief of menopause symptoms, prevention of bone loss, or QOL as they age.

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