



FIRST TO KNOW[®]

Released December 12, 2017

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.

USPSTF releases statement on hormone therapy for prevention of chronic conditions in postmenopausal women

Task force recommends against use of hormone therapy for prevention of chronic conditions

US Preventive Services Task Force. Hormone therapy for the primary prevention of chronic conditions in postmenopausal women. USPSTF recommendation statement. *JAMA*. 2017;318(22):2224-2233.

Summary. Based on its review of randomized, clinical trials (RCTs), the US Preventive Services Task Force (USPSTF) has published its recommendation against the use of combined estrogen and progestin and of estrogen alone in women with prior hysterectomy for the prevention of chronic conditions in postmenopausal women (a D recommendation).

The task force determined that the small to moderate benefits (prevention of osteoporotic fractures, diabetes, and colorectal cancer) do not outweigh the harms (elevated risk of invasive breast cancer, coronary heart disease [CHD], venous thromboembolism [VTE], stroke, dementia, gallbladder disease, and urinary incontinence) that result from the use of hormone

therapy (HT). Accordingly, the task force concluded that HT has no net benefit for the primary benefit of chronic conditions for most postmenopausal women.

The recommendation against use of HT for preventing chronic conditions applies to estrogen-progestin HT as well as estrogen-only HT used posthysterectomy. It does not apply to symptomatic women who are considering HT for the management of menopause symptoms such as hot flashes or vaginal dryness. It also states that the evidence in women aged younger than 50 years who have had premature menopause or surgical menopause is inconclusive for a recommendation, based on inadequate RCT data.

Commentary. NAMS is concerned by the USPSTF rating of D for the use of HT for prevention of chronic disease. Such a sweeping dismissal of HT does not recognize that the USPSTF has overgeneralized and grouped all postmenopausal women and all hormone therapies together.

We believe that this D rating of “harms outweigh benefits” will have a profound negative effect on postmenopausal women's health and access to important preventive treatment for women who need HT.

The USPSTF recommendations do not address the primary ways that healthcare providers use HT in clinical practice, including initiating HT in symptomatic, younger, menopausal women aged younger than 60 years and within 10 years of menopause onset; using HT in women at high risk for osteoporosis (especially those unresponsive to other treatments or for whom other treatments are contraindicated); using longer-duration HT to treat persistent vasomotor symptoms (VMS) and osteoporosis or to maintain quality of life (QOL) in older women; and using low-dose vaginal estrogen for genitourinary symptoms.

NAMS and the 2017 Hormone Therapy Position Statement of The North American Menopause Society support individualized, evidence-based discussions about benefits and risks of HT on the basis of a woman's symptoms, medical history, risk factors, personal preferences, and QOL concerns, using shared decision-making regarding the use of HT for relief of menopause symptoms, prevention of bone loss, or maintenance of QOL, despite the USPSTF's recommendations.

The task force used only RCT data of 3 years or more, relying heavily on the Women's Health Initiative (WHI) and the 13-year cumulative follow-up data, on which to base their recommendations. The task force did not include observational data or smaller clinical trials, nor did they highlight that the WHI used only one formulation (oral conjugated equine estrogens and synthetic medroxyprogesterone acetate if women had a uterus) of HT at a relatively high dose in women initiating HT at an average age of 63 years and 13 years from the onset of menopause.

The 2017 Hormone Therapy Position Statement used RCT and observational data. Twenty-three experts in the field found clear evidence of benefit for the use of HT in symptomatic women and in those at elevated risk of bone loss who are aged younger than 60 years or are within 10 years

of menopause onset, with reassuring cardiovascular and all-cause mortality data for these women.

In addition, the decreased number of cases of breast cancer and reduced cardiovascular disease, with less all-cause mortality in those women who used estrogen only, has a more favorable benefit-risk ratio than that provided by USPSTF.

NAMS agrees that in women who initiate HT more than 10 or 20 years from menopause onset or who are aged 60 years or older, the benefit-risk ratio appears less favorable than for younger women because of the greater absolute risks of CHD, stroke, VTE, and dementia.

Areas in which NAMS recognizes benefits of HT that are either not addressed or not recommended by the USPSTF are for women with premature or early menopause, which received a USPSTF rating of I or insufficient data because of limited RCT trial data and exclusion of observational data.

However, the use of HT at least until the median age of menopause (52 y) in women with early menopause (whether natural, induced, or surgical) has been demonstrated in observational studies to mitigate the potential risks related to early estrogen deprivation, including CHD, osteoporosis, sexual dysfunction, genitourinary syndrome of menopause (GSM), cognitive impairment, dementia, and even early mortality.

Second, the most frequent considerations for longer use of systemic HT are VMS, which persist on average 7.4 years but can last 10 or 20 years or more; prevention of bone loss and fractures; and maintenance of QOL. The WHI selectively excluded women with bothersome VMS, thus decision-making about how to treat women with persistent VMS cannot be made exclusively from trials in which this group was not represented.

Last, the USPSTF did not address the benefits and minimal risk of using low-dose vaginal estrogen to prevent or treat GSM.

The USPSTF recommendations do not apply to women using HT for

- Early menopause (natural, induced, or surgical)
- Bothersome menopause symptoms (they were excluded from the WHI)
- Prevention of osteoporosis
- Treatment of genitourinary symptoms
- Longer-term management of VMS, prevention of bone loss, or maintenance of QOL

The 2017 Hormone Therapy Position Statement of The North American Menopause society supports

- Use of HT in symptomatic women and those at elevated risk of bone loss who are aged younger than 60 years or are within 10 years of menopause onset
- Use of HT continued at least until the median age of menopause (52 y) in women with premature (aged <40 y) or early (aged <45 y) natural, induced, or surgical menopause and who otherwise have no contraindications to the use of HT.
- Use of HT to prevent osteoporosis. Numerous RCTs have documented HT's efficacy in preventing osteoporosis and decreasing the incidence of hip and other osteoporotic fractures, recognizing that efficacy is lost once HT is discontinued.
- Individualizing the use of HT, recognizing that risks may be influenced by the dose,

formulation, route of administration, type of progestogen, or tissue-selective estrogen compound used, with periodic reassessment in the context of changes in a woman's health and anticipated benefits, risks, and treatment goals over time.

- Discussions between women and their healthcare providers about extended duration of the use of HT for treating persistent VMS, preventing bone loss, or maintaining QOL should include shared decision-making based on the best evidence available, an individualized assessment of the risk-benefit balance, a review of options to minimize risk with lower doses and transdermal preparations, and the potential risks of stopping HT, such as bone loss and fracture.
- Low-dose vaginal estrogen for management of GSM symptoms, which are often progressive, and although over-the-counter therapies may relieve symptoms, they do not treat the underlying pathophysiology of GSM in women at any age.

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