THE ENDOCRINE SOCIETY

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Society Supports USPSTF Recommendations on HRT; Clarifies Misconceptions

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The United States Preventive Services Task Force (USPSTF) released recommendations on October 22, 2012 related to the use of menopausal hormone therapy for the primary prevention of chronic disease. In its final report, the USPSTF recommends against the use of postmenopausal hormone therapy for the prevention of chronic conditions, consistent with their 2005 report. The recommendation includes combined estrogen and progestin therapy in postmenopausal women with a uterus as well as estrogen-alone therapy in postmenopausal women who have had a hysterectomy.

The USPSTF reports states clearly, however, that "this recommendation applies only to postmenopausal women who are considering hormone therapy for the primary prevention of chronic medical conditions. It does not apply to women who are considering hormone therapy for the management of menopausal symptoms, such as hot flashes or vaginal dryness. It also does not apply to women younger than 50 years who have had surgical menopause".

The USPSTF further justifies the conclusions, "No randomized trials have prospectively evaluated the effect of the timing of initiation of hormone therapy relative to menopause onset on associated benefits and harms. Post hoc subgroup analyses suggest an increased probability of harm with increasing age at initiation and longer duration of use, but these findings are not consistent across all trials and generally do not reach statistical significance (6, 7)."

The USPSTF makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms, and bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The Endocrine Society provided expert opinion to the USPSTF in June 2012 through their Topic Groups for Stakeholders (TOPS) Process, which aims to increase involvement of experts in the field during different stages of the process. The Society's comments included points of clarification that would provide additional insight to help physicians and their patients in deciding whether to use hormone therapy. These comments focused on the lack of data regarding the safety and efficacy of compounded bioidentical hormones, the inclusion of specific information related to ages of participants and specific hormone therapies utilized in studies included in the analysis, and the addition of information about the resolution or persistence of risks (or benefits) found in the Women's Health Initiative (WHI) when hormonal therapy was stopped.

Overall, the Society agrees with the final recommendations of the USPSTF but is concerned that both patients and their physicians may not look beyond the headlines that emphasized the negative aspects of postmenopausal hormone therapy when considered in light of preventive

benefits and therefore, inappropriately apply the USPSTF recommendations to women considering hormone therapy for relief of menopausal symptoms.

Further confusion may arise from two new studies. Recently released results from the long-awaited 4-year, randomized, double-blind, placebo-controlled KEEPS study (Kronos Early Estrogen Prevention Study) report that when combined with cyclical monthly oral progesterone, oral conjugated estrogen (0.45 mg daily) or transdermal estrogen (50 mcg daily) reduce symptoms of menopause, including hot flashes and night sweats, and provide favorable effects on bone mineral density. Improvements in lubrication and decreased pain with intercourse were also reported. The primary outcomes of the study, surrogate markers of atherosclerosis progression including carotid intima-medial thickness and coronary artery calcium, however, did not differ significantly between treatment and placebo groups. While hormone therapy did not increase the risk of breast cancer or cardiovascular events in KEEPS participants who started hormone therapy within 3 years of menopause (1), investigators note that the small sample size (727 women enrolled) limits definitive conclusions about these important clinical outcomes (www.menopause.org/annual-meetings/2012-meetings/keeps-report; accessed 10/18/12).

Similarly, a post-hoc analysis from the Danish Osteoporosis Prevention Study reported reduced mortality, cardiovascular events and cancer in over 500 early menopausal women treated for 10 years with triphasic estradiol and norethistrone acetate compared to those receiving no treatment, albeit these were non-prespecified outcomes (2). A number of methodologic concerns, however, may limit interpretation of these results (http://www.bmj.com/content/345/bmj.e6409?tab=responses; accessed 10 26 12).

In summary, the Endocrine Society recognizes and agrees with the USPSTF recommendations regarding postmenopausal hormone therapy and prevention of chronic diseases, but maintains a commitment to hormone therapy as an effective and relatively safe treatment for healthy women close in time to menopause seeking relief of symptoms of menopause (Stuenkel CA, JCEM, 2012; menopause map).

For questions, please contact Stephanie Kutler, Director of Government Affairs at skutler@endo-society.org.

See references added to text:
1. www.keepstudy.org/news/pr_100312.cfm
2. Schierbeck LL et al. Brit Med J 2012;345:e6409 doi: 10.1136/bmj.e6409 (Published 9 October 2012).