

# Timing of HT found key to its risks and benefits

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SAN DIEGO -- The scale that weighs risks and benefits tips more favorably for newly menopausal women who begin hormone therapy at age 50-59 years and who use it for 5 years, compared with women who start the therapy in their 60s, according to a systematic review of several studies and position statements.

Younger women who are newly menopausal and who use hormone therapy have a 30%-40% reduction in total mortality, a phenomenon "that's not seen in older women," said Dr. Richard J. Santen, professor of medicine at the University of Virginia, Charlottesville, who called the findings "very surprising."

"Physicians and their patients need to rethink the use of menopausal hormonal therapy" on the basis of these findings, said Dr. Santen, who chaired the 12-member task force that wrote a scientific statement on behalf of the Endocrine Society suggesting that menopausal hormone therapy may benefit women who start it in their 50s rather than in their 60s.

Importantly the new analysis points to the need to look beyond data from the Women's Health Initiative, in which the average age was 63 years, in order to advise younger women. "The therapy clearly needs to be individualized, primarily based on symptoms. But if a woman has an underlying risk of breast cancer ... you're going to be very cautious about this," Dr. Santen said during a press briefing.

Dr. Santen and his associates used the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system to evaluate the benefits and risks associated with menopausal hormone therapy based on published randomized controlled trials, cohort studies, and case-control studies, as well as position statements related to the topic.

"Hormone therapy has gone through a series of twists and turns," Dr. Santen commented. "The WHI was directed at women starting hormone therapy [more than 10 years] after the menopause. The average age of the women starting the WHI study was 63, and only 3.4% of the women were between the ages of 50 and 55, ... the usual time when women would decide to take hormone therapy"

With the publication of the WHI data in 2002, "there was a huge scare" because hormone therapy was shown to be associated with an increased risk of heart disease, breast cancer, stroke, blood clots in the legs and lungs, and memory loss. As a result, the use of menopausal hormone therapy declined by about 80%.

Dr. Santen explained that the new analysis is more applicable to the typical menopausal patient whom physicians see in practice: the 53-year-old who had her last period a year ago, and is now trying to make a decision about whether to start menopausal hormonal therapy to relieve her symptoms.

Overall, the researchers found that women who start menopausal hormone therapy at age 50-59 years experienced a 30%-40% decrease in mortality no increased risk of heart disease, and a 90% reduction of menopausal symptoms such as hot flashes or overactive bladder.

"Relief of symptoms is really the key issue," Dr. Santen said.

Compared with women who did not take hormone therapy, younger women and those who were newly menopausal experienced 10 fewer diagnoses of diabetes per 1,000 women, 4 fewer cases of heart disease (among those on estrogen only), 5 fewer bone fractures, and 2 fewer cases of colon cancer per 1,000 women (among those on estrogen plus progestin only).

Risks associated with menopausal hormone therapy included gallbladder disease (10 more per 1,000 women), blood clots in the legs and lungs (5 more women), and stroke (2 more women).

Women who were on estrogen therapy alone had no increased risk of developing breast cancer, but there were 7 more cases of breast cancer per 1,000 women among those who took estrogen and progestin for 5 years, compared with non-HT users.

"Our tentative conclusion is that estrogen plus progesterone actually didn't cause tumors; it caused preexisting tumors to grow to a size where they became detectable," Dr. Santen said. "There have been eight studies in women [aged 40-80 years] at autopsy, to find out how many women have breast cancer that's undiagnosed. [Those studies found that] 7% of women at autopsy have breast cancer that's too small to be diagnosed by mammography, MRI, or clinical examination."

"Put simply, estrogen plus progesterone causes preexisting tumors to grow, rather than initiating the onset of de novo tumors," according to the document.

He added that he hopes the scientific statement will lead to a new perspective on menopausal hormone therapy. "This perspective is only in younger women, and we need to consider the risks and benefits for the women who are considering its use," he said.

The statement is published in the July 2010 issue of the Journal of Clinical Endocrinology and Metabolism.

Disclosures: Dr. Santen reported having no conflicts of interest. The statement is available at [www.endo-society.org](http://www.endo-society.org).