

# Soy Matches HT for Menopause Symptoms

BY DAMIAN MCNAMARA

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LAKE BUENA VISTA, FLA. — Soy supplements improved somatic and urogenital symptoms of menopause to the same degree as did low-dose combination hormone therapy, in a small, randomized, double-blind controlled trial.

A total of 60 women who were 1-13 years past menopause were randomized to one of three groups: soy supplements containing isoflavones 90 mg; estradiol 1 mg/norethindrone 0.5 mg; or placebo daily.

After 16 weeks, women in the two treatment groups had significant somatic and urogenital symptom improvements, compared with baseline on the Menopause Rating Scale and compared with scores among women taking placebo.

The findings suggest a role for dietary soy supplementation for improving hot flashes, joint and muscle pain, and vaginal dryness, with results equivalent to

hormone therapy, Dr. Adriana O. Pedro said. "I thought hormone replacement would be better than soy, so I was surprised."

Women taking hormone therapy fared better, however, in terms of cardiovascular health markers. Women on the low-dose combination hormone therapy showed improvement in total cholesterol and low-density lipoprotein levels; these levels were unchanged in those who got soy supplements.

In addition, total cholesterol decreased 12%, compared with baseline, in the hormone treatment group but remained unchanged in the soy supplement and placebo groups. The LDL cholesterol level decreased 18% in the hormone therapy group and did not change in the other groups.

"There was no change with soy—probably because they had normal lipid profiles at baseline," Dr. Pedro of the State University of Campinas (Brazil) said during a poster session at the annual meeting of the North American Menopause Society.



Soy improved hot flashes, joint/muscle pain, and vaginal dryness as much as hormone therapy did.

Psychological symptoms did not change over the treatment period in the soy, hormone replacement, or placebo groups.

The study was funded by the São Paulo (Brazil) Foundation for the Support of Research. Data analysis is ongoing, and they plan to publish additional findings. ■

## Absolute Risks of Hormone Therapy May Reassure Women

BY DAMIAN MCNAMARA

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ORLANDO — When counseling postmenopausal women about hormone therapy, frame the discussion in terms of absolute rather than relative risks, a principal investigator of the Women's Health Initiative said.

"Hormone therapy still has a clinical role in treatment of moderate to severe hot flashes and other menopausal symptoms," Dr. JoAnn E. Manson said. "Recently menopausal women tend to be the best candidates due to low absolute risks and a greater frequency of symptoms. Very often the results of the WHI are discussed in terms of relative risk," she said. For example, the widely publicized findings were that women taking estrogen plus progestin therapy had a 29% increase in coronary heart disease risk, 41% for stroke, 113% for pulmonary embolism, and 26% for breast cancer (JAMA 2002;288:321-33).



From the perspective of absolute risk, stroke occurs in about 1 in 1,000 women aged 50-59 years in the general population. "For a woman struggling with severe vasomotor symptoms and sleep trouble ... telling her the risk will increase from 1 in 1,000 to 1.4 in 1,000 sounds better than telling her the stroke risk will increase 40%," Dr. Manson said at the annual meeting of the North American Menopause Society.

That is not to say that the risk should be dismissed, she qualified. "It is still an important risk and should not be discounted."

WHI researchers also found that adverse effects increased with age. "The number of excess cases of stroke or pulmonary embolism that would be caused by hormone therapy would be much less in younger women," said Dr. Manson, chair of the division of preventive medicine, Brigham and Women's Hospital, and professor of medicine and women's health

at Harvard Medical School, both in Boston.

In 2006, in an estrogen-only trial, "we did see a difference between younger and older women for outcomes of coronary heart disease death or MI," Dr. Manson said (Arch. Intern. Med. 2006;166:357-65). Compared with women not taking estrogen, the relative risk of cardiac death or MI was 0.63 among women aged 50-59 years, 0.94 for women aged 60-69, and 1.11 in women aged 70-79.

In a more recent study, they found the hazard ratio for coronary heart disease among women on hormone therapy was 0.93 for the younger age group, 0.98 for women aged 60-69, and 1.26 for women aged 70-79 (JAMA 2007;297:1465-77). The differences were not significant.

However, Dr. Manson and her associates also found a statistically significant 30% reduction in total mortality in 50- to 59-year-olds. Specifically, younger women taking hormone therapy had a 0.70 hazard ratio for mortality, compared with 1.05 for women aged 60-69 years and 1.14 for women aged 70-79.

Hormone therapy may have a neutral or beneficial effect on the heart if started during early menopause, when the arteries and endothelium are likely to be relatively healthy, Dr. Manson suggested. In contrast, therapy may be associated with a deleterious effect if started in late menopause, when advanced atherosclerosis and unstable plaques may be present.

The implication is not that recently menopausal patients should take hormone therapy to prevent coronary artery disease, Dr. Manson said. Rather, the results could reassure younger women about cardiac risks when they are pondering short-term therapy to ameliorate vasomotor symptoms.

The cardiovascular risks associated with estrogen and progestin may diminish after therapy is stopped, according to another secondary analysis (JAMA 2008;299:1036-45). ■

## Hot Flashes Don't Cause Depression in Menopause

BY ELIZABETH

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SAN FRANCISCO — Hot flashes may not necessarily be a cause of depressive symptoms, according to a study that followed women in the menopausal transition for 10 years.

"We were interested in whether these symptoms were more likely to occur concurrently and which was more likely to come first among women in this transition period," Mary D. Sammel, Sc.D., the study's lead author, said in an interview. The leading hypothesis is that hot flashes cause sleep problems, which lead to depressive symptoms in menopausal women, continued Dr. Sammel of the Center for Clinical Epidemiology and Biostatistics of the University of Pennsylvania, Philadelphia.

The study evaluated 170 women aged 35-47 who were enrolled in the ongoing Penn Ovarian Aging Study. Previous studies of this cohort had looked at these two symptom processes separately; the current study analyzed these symptoms together, she said at the annual meeting of the American Society for Reproductive Medicine.

At baseline, the women had no hot flashes or depressive symptoms, had had regular periods for the previous 3 months, and had premenopausal reproductive hormone levels. Women were then assessed annually via questionnaire. About half were white, and the rest were African American. Over the 10-year period, more than 60% of the women reported experiencing hot flashes and 50% reported depressive symptoms.

About 41% reported that their hot flashes and depressive symptoms started at the same time.

Of the women who reported having both depressive symptoms and hot flashes, nearly 24% experienced depressive symptoms before they had hot flashes, which was a twofold higher rate than would be expected if the two processes were independent, based on statistical probability estimates. Only 8% of the women reported experiencing hot flashes before the development of depressive symptoms, which was less often than would be expected, based on the statistical probability they would occur in this pattern, Dr. Sammel said.

"Both processes have been associated with changes in reproductive hormones, but these patterns of reporting indicate the potential for different underlying mechanisms," she and her coauthors concluded.

Previous studies of these women in the Penn Ovarian Aging Study cohort—which also includes women who already had menopausal symptoms when they were enrolled—have shown that the prevalence of depressive symptoms increases at the earliest stages of the menopausal transition, when women are experiencing small changes in reproductive hormones. This is followed by a decline in depressive symptoms in later stages of the menopausal transition, she said.

These findings suggest "it is the fluctuating hormones, earlier in the transition, which are more likely to influence depressive stages, and not the dramatic changes in estradiol and FSH, exhibited later in the transition," Dr. Sammel noted. ■