# First-Ever Depression Spikes in Perimenopause

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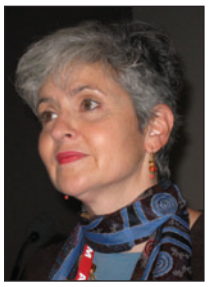
DENVER – Women with no history of depression are at sharply increased risk of first-ever, clinically significant depressive symptoms during the menopausal transition, three major prospective longitudinal studies have shown.

It's a situation that requires clinicians to have their depression-detection radar fully powered up, according to Dr. Nanette F. Santoro.

"A very important thing to remember is that this type of depression is new to these women. This is their first episode. They may come into our offices clearly in distress, but they don't have the vocabulary to tell you they're depressed because they don't know what that feels like," she said in a plenary lecture at the meeting.



**'That late perimenopause is just a bummer. It almost doubles the risk' of new depression.**

DR. SANTORO

Dr. Santoro presented highlights from the ongoing observational Study of Women's Health Across the Nation (SWAN), in which 3,302 African American, white, Hispanic, Japanese, and Chinese women at seven sites in the United States have been evaluated annually since their enrollment during 1996-1997 at age 42-52.

"We're now in our 14th year of SWAN, and we're still cranking out data," noted Dr. Santoro, professor and chair of the department of obstetrics and gynecology at the University of Colorado, Denver.

At baseline, when the women were premenopausal, 23% had clinically relevant depressive symptoms, as defined by a score of 16 or more on the Center for Epidemiologic Studies Depression Scale (CES-D).

The other 77% of women, those with low baseline CES-D scores and no lifetime history of depression, were hit particularly hard by depressed mood symptoms in the menopausal transition. In a multivariate analysis, a woman with a CES-D of less than 16 at baseline had a 30% higher odds of having a CES-D score of 16 or greater when she was in the early perimenopausal period, which is marked by increased menstrual irregularity but at least one menses within the past 3 months.

Women in the late perimenopausal period, as defined by 3-11 months of amenorrhea, had an adjusted 73% increased odds of significant depressive symptoms, compared with those who were still premenopausal.

The risk was elevated even more in women with significant vasomotor symptoms (J. Affect. Disord. 2007; 103:267-72).

"That late perimenopause is just a bummer. It almost doubles the risk," Dr. Santoro observed.

The risk declines slightly to a 63% increased odds of significant depressive symptoms during the postmenopausal period.

Hormone therapy, which was used by 20% of the SWAN women, may have conferred modest relief from depressive symptoms, as hormone therapy users had a peak 64% increase in the odds of a CES-D of 16 or more during the menopausal transition.

The risk of new-onset depressive symptoms during menopause was independent of demographic, psychosocial, and behavioral factors, as well as comorbid conditions, all of which were factored into the multivariate regression analysis.

Chinese women had half the risk of depressive symptoms compared with white women, but the risk in the other ethnic groups didn't vary significantly from that in the white women.

Similar results have been reported from the Harvard Study of Moods and Cycles, in which Dr. Lee S. Cohen and his coworkers studied a cohort of pre-

menopausal women with no lifetime history of major depression. The investigators found that for these women, who were less racially diverse than the SWAN women, entry into perimenopause was associated with a doubled likelihood of developing significant depressive symptoms, compared with similar-age women who remained premenopausal.

As in SWAN, the risk of depression was even greater in women with self-reported significant hot flashes and night sweats. In the Harvard longitudinal study, the use of hormone therapy did not affect the risk of developing depressive symptoms; there was a suggestion that it might have lessened the risk of severe depression arising during the menopausal transition, although the patient numbers were too small to draw firm conclusions (Arch. Gen. Psychiatry 2006;63:385-90).

Investigators at the University of Pennsylvania, Philadelphia, reported that women with no history of depression at enrollment in their longitudinal study were 4.3-fold more likely to post high CES-D scores during the menopausal transition than when they were premenopausal. Formal diagnosis of a depressive disorder was 2.5 times more likely to occur in the menopausal transition (Arch. Gen. Psychiatry 2006; 63:375-82 ).

The Harvard group speculated that the increased risk for developing a first episode of depression when entering the perimenopause could be due in part to the marked sleep disruption caused by hot flashes, and/or to sensitivity to abrupt changes in the reproductive hormone milieu.

In keeping with that hypothesis, the SWAN investigators recently reported that higher testosterone levels appear to contribute to depressive symptoms arising during the menopausal transition. No other hormones were associated with a CES-D score of 16 or more (Arch. Gen. Psychiatry 2010;67:598-607).

The SWAN study is cosponsored by the National Institute on Aging, the National Institute of Nursing Research, the National Institutes of Health Office of Research on Women's Health, and the National Center for Complementary and Alternative Medicine. Dr. Santoro said she had no relevant financial conflicts of interest. ■