

Nation's Largest Study in Osteoporosis (NORA)

Half of Unassessed Postmenopausal Women at Increased Risk of Breaking a Bone, JAMA Reports

Low bone density linked to higher fracture risk, even within one year of testing

The nation's largest study of osteoporosis, National Osteoporosis Risk Assessment (NORA), found that almost half of the more than 200,000 postmenopausal women assessed in the study had low bone mass, putting them at increased risk of breaking a bone. Seven percent of women in the study were found to have osteoporosis; in addition nearly 40 percent of the women were found to have low bone mass but were not osteoporotic. During the one-year follow-up period, the rate of bone fracture was four times higher for women with osteoporosis and twice as high for women with low bone mass compared to women with normal bone density.

The study tested bone mass and evaluated other osteoporosis risk factors in 200,160 postmenopausal women, aged 50 and older, from 4,236 primary care practices in 34 states over one year. NORA was funded by Merck & Co. Inc. and managed by a steering committee comprised of osteoporosis investigators.

"In our study we found that almost half of the postmenopausal women sitting in their doctors' offices, who have never been assessed for osteoporosis, had low bone mass and were at increased risk of future fractures," said Ethel Siris, M.D., lead author, who is medical director of the NORA research program, and director of the Toni Stabile Center for the Prevention and Treatment of Osteoporosis at the Columbia-Presbyterian Medical Center in New York. "Given the physical and financial toll caused by osteoporotic fractures, these findings underscore the tremendous need for both women and their health care providers to better identify and manage osteoporosis."

Exercise, calcium and Vitamin D can help keep bones healthy but may not be enough if bones are already thinning. Today there are effective once-daily and once-weekly therapies available that can actually reverse bone loss and make bones stronger.

The study also reported that a finding of low bone density at any peripheral skeletal site, such as the heel, forearm or finger, was associated with a near-term risk of fracture even in women with mild to moderate bone loss.

Immediacy of fracture risk significantly increased with low bone mass finding

Despite the availability of simple and painless bone density tests to assess fracture risk and confirm osteoporosis, the disease often remains undiagnosed until a fracture occurs.

"Once a fracture occurs, the risk for subsequent fractures increases dramatically," said Ken Faulkner, PhD, co-author of the article, who is the Chief Scientist at GE Medical Systems Lunar. "Preventing the first fracture is the most important goal in osteoporosis. Bone density measurements are the best way to identify those at risk before fractures can occur."

Bone mineral density (BMD) measurement is the most commonly used method to confirm a diagnosis of osteoporosis and predict fracture risk. In NORA, each study participant had peripheral bone density testing of the forearm, finger or heel. World Health Organization criteria for low bone mineral density, based on BMD measurements at the forearm, were used for this analysis. Test results were calculated as T-scores, which compare an individual's bone density with that of the average healthy young adult woman. A T-score of -1 represents a BMD measurement 1 standard deviation (SD) below this average, and each SD decline in T-score is associated with an approximate doubling of relative risk of fracture. T-scores between 1 and 2.5 SD below the average

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were classified as low BMD (also known as osteopenia). Measurements 2.5 SD or more below the average were classified as osteoporosis.

Study participants included only women who had not been diagnosed with osteoporosis and who had not had a BMD within the preceding year. At study entry, the women also completed baseline questionnaires about personal and family fracture history, lifestyle behaviors and medication use. Eighty-two percent reported their current health as good to excellent and 11 percent reported sustaining a fracture since age 45.

"It's particularly disturbing that 11 percent of these women reported fractures at the study start because these are likely the result of osteoporosis, yet osteoporosis had not been diagnosed or treated," Dr. Siris said. "These findings are a wakeup call for health care professionals and patients that fracture in a postmenopausal woman suggests osteoporosis unless proven otherwise."

Even mild to moderately low bone mass linked to higher risk of fracture

Approximately one year after enrolling in the study, the women were asked to report any new fractures. Information collected from 81.9 percent, or 163,979 study participants, showed:

- Women with osteoporosis had a fracture rate approximately four times that of women with normal BMD. Women with osteopenia had a 1.8-fold higher rate of fracture.
- Women who were osteoporotic and/or had low BMD at any peripheral site were at significantly increased risk of fracturing within 12 months of the finding. When controlling for other risk factors, osteopenia was associated with a 1.7 greater risk of fracture and osteoporosis with a 2.7 greater risk of fracture within one year.

Independent effects of risk factors, lifestyle behaviors reported

Age was the most important risk factor for predicting low bone mass. Number of years since menopause,

poor self-rated health and personal or family history of fracture or smoking were each associated with a significantly higher risk of osteoporosis.

Role of ethnicity identified

NORA enrolled more than 18,000 minority women, making it the largest study of osteoporosis conducted among ethnic minority women.

The study found that compared to Caucasian women, the prevalence of osteoporosis was higher in Asian and Hispanic women, lower in African Americans and similar in Native Americans. The likelihood of fracture was no different for Hispanics and lower for Asians compared to Caucasians.

Although low bone mass was significantly less prevalent among African-Americans, 32 percent of African-American women had low bone mass and 4 percent had osteoporosis, suggesting their absolute risk of fracture may be substantial although less than women of other ethnicities. Future study follow-up will more fully explore the association between BMD and fracture risk among ethnic groups.

What is NORA?

NORA is a health education initiative and patient registry designed to examine the relationship among risk factors, low bone mass and osteoporosis. It was initiated from September 1997 to March 1999, with approximately 12 months of follow-up. Merck & Co., Inc. funded the NORA study, which was managed in collaboration with the International Society for Clinical Densitometry at the time the study started. The study is currently administered by Abt Associates, Inc., a contract research organization. The NORA steering committee, which includes national osteoporosis experts, oversees data collection and analysis and reviews proposals for research utilizing the database.

Reference: Siris E, Miller P, Barrett-Connor E, Faulkner KG, Wehren LE, Abbott T, Berger M, Santora A, Sherwood L: *Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment.* JAMA 286(22):2815-2822, December 2001.



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