



EDUCATIONAL OBJECTIVE: Readers will measure bone mineral density at reasonable intervals in their older postmenopausal patients

KRUPA B. DOSHI, MD, CCD

Department of Endocrinology, Diabetes, and Metabolism, Cleveland Clinic

LEILA Z. KHAN, MD, CCD

Department of Endocrinology, Diabetes, and Metabolism, Cleveland Clinic

SUSAN E. WILLIAMS, MS, MD, CCD

Department of Endocrinology, Diabetes, and Metabolism, Cleveland Clinic

ANGELO A. LICATA, MD, PhD

Director, Endocrine Calcium Clinic, Department of Endocrinology, Diabetes, and Metabolism, and Director, Center for Space Medicine, Department of Biomedical Engineering, Cleveland Clinic; Clinical Assistant Professor, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

Bone mineral density testing: Is a T score enough to determine the screening interval?

ABSTRACT

To find the rational intervals for bone mineral density screening, Gourlay et al (N Engl J Med 2012; 366:225–233) used T scores to calculate the time required for women age 67 and older with normal bone mineral density or osteopenia to progress to osteoporosis. They estimated that the screening interval for women with normal bone mineral density or mild osteopenia (T score -1.49 or higher) could be as long as 15 years. However, the investigators focused mainly on T scores and when these scores reached -2.5 . In our opinion, the testing interval should be guided by an assessment of clinical risk factors and not just baseline T scores.

KEY POINTS

The criteria for who should undergo bone mineral density measurement are well established, but data on repeat testing are scarce.

Gourlay et al concluded that age and T scores are the key predictive factors in determining the bone mineral density testing interval, while clinical risk factors such as fracture after age 50, current smoking, previous or current use of glucocorticoids, and self-reported rheumatoid arthritis are not.

The Fracture Risk Assessment tool (FRAX) is a useful clinical tool that calculates an individual's 10-year risk of fracture. It is available at www.shef.ac.uk/FRAX.

SOME MEMBERS OF THE PUBLIC may have noticed the conclusions of a recent study¹ that said that if an older postmenopausal woman has her bone mineral density measured to screen for osteoporosis and has a normal or only mildly low result, she does not need to come back for another measurement for approximately 15 years.

See related editorial, page 240

We believe this interpretation of the study's findings is overly simplistic and may have the unfortunate result of causing some people to neglect their bone health. Moreover, the study looked mainly at baseline T scores as the determinant of the subsequent screening interval. However, clinicians must carefully consider a variety of clinical risk factors when deciding how often to obtain bone mineral density measurements. The ultimate goal is to not miss the window of opportunity for early detection and treatment when it would matter the most (ie, before fractures develop).

Here, we will review this recent study, its findings, and its implications.

OSTEOPOROSIS POSES AN ENORMOUS PUBLIC HEALTH PROBLEM

If we consider only the hip, an estimated 10 million people in the United States have osteoporosis (T score ≤ -2.5 or a preexisting fragility fracture), and 33.6 million have osteopenia (T score -1.01 to -2.49).² The number of people with osteopenia can be assumed to be much higher if other skeletal sites are considered.

doi:10.3949/ccjm.80a.12069

By increasing the risk of fragility fractures, osteoporosis poses an enormous public health problem. The surgeon general's report points out that one of every two white women over age 50 will experience an osteoporosis-related fracture in her lifetime.³ Of all osteoporosis-related fractures, those of the hip carry the worse clinical outcome. Approximately one in five elderly people who experience an osteoporosis-related hip fracture need long-term nursing home care, and as many as 20% die within 1 year.³

In recognition of the burden of osteoporosis, the US Preventive Services Task Force (USPSTF)⁴ and other scientific bodies^{2,3} recommend an initial bone mineral density test for all women age 65 and older. Dual-energy x-ray absorptiometry (DXA) is considered the gold standard for bone mineral density testing.

Although the patient population that should receive an initial bone mineral density test has been clearly identified (see below), guidelines on the optimal frequency of testing do not exist, as data have been lacking. Recognizing this knowledge gap, Gourlay et al¹ attempted to answer the question of how often elderly postmenopausal women should be retested.

■ WHEN DO 10% OF ELDERLY POSTMENOPAUSAL WOMEN REACH A T SCORE OF -2.5?

Gourlay et al¹ analyzed data from 4,957 women in the Study of Osteoporotic Fractures. These women were predominantly white, were at least 67 years old and ambulatory, and had normal bone mineral density or osteopenia and no history of hip or clinical vertebral fracture at baseline. They had been recruited between 1986 and 1988 at sites in Baltimore, MD, Minneapolis, MN, the Monongahela Valley near Pittsburgh, PA, and Portland, OR.

DXA of the hip had been performed at baseline and at multiple times thereafter. The average follow-up time was 8 years.

The primary outcome measured was how long it took for 10% of the patients to reach a T score of -2.5 or less at the femoral neck or total hip as they progressed from having normal bone mineral density to osteoporosis or from osteopenia to osteoporosis and before

they developed a fracture or needed treatment for osteoporosis.

Clinical risk factors such as age, body mass index, estrogen use at baseline, fracture after age 50, current smoking, current or past use of glucocorticoids, and self-reported rheumatoid arthritis were included as covariates in time-to-event analyses.

■ ANSWER: 16.8 YEARS (IF NORMAL AT BASELINE)

The authors estimated that 10% of women would make the transition to osteoporosis before having a hip or clinical vertebral fracture in the following intervals:

- 16.8 years in women whose bone mineral density was normal at baseline (T score at femoral neck and total hip of -1.00 or higher)
- 17.3 years in women who had mild osteopenia at baseline (T score -1.01 to -1.49)
- 4.7 years in women with moderate osteopenia at baseline (T score -1.5 to -1.99)
- 1.1 years in women with advanced osteopenia at baseline (T score -2.00 to -2.49).

The authors also found that body mass index and current estrogen use were the only clinical risk factors that influenced these intervals; other clinical factors such as a fracture after age 50, current smoking, previous or current use of oral glucocorticoids, and self-reported rheumatoid arthritis did not.

They concluded that osteoporosis would develop in fewer than 10% of women if the re-screening interval was lengthened to 15 years for women with normal density or mild osteopenia, 5 years for women with moderate osteopenia, and 1 year for women with advanced osteopenia.

■ WHAT DOES THIS MEAN FOR THE PRACTICING CLINICIAN?

Who needs an initial DXA test according to current guidelines?

The USPSTF,⁴ the National Osteoporosis Foundation (NOF),⁵ the International Society for Clinical Densitometry (ISCD),⁶ and the American Association of Clinical Endocrinologists (AACE)⁷ propose that the following groups should undergo DXA:

One of every two white women over age 50 will have an osteoporosis-related fracture in her lifetime

- All women age 65 and older
- All postmenopausal women who have had a fragility fracture or who have one or more risk factors for osteoporosis (height loss, body mass index $< 20 \text{ kg/m}^2$, family history of osteoporosis, active smoking, excessive alcohol consumption)
- Adults who have a condition (eg, rheumatoid arthritis) or are taking a medication (eg, glucocorticoids in a daily dose $\geq 5 \text{ mg}$ of prednisone or its equivalent for ≥ 3 months) associated with low bone mass or bone loss
- Anyone being considered for drug therapy for osteoporosis, discontinuing therapy for osteoporosis (including estrogen), or being treated for osteoporosis, to monitor the effect of treatment.

Assessing fracture risk. Although clinicians have traditionally relied on bone mineral density obtained by DXA to estimate fracture risk, the World Health Organization has developed a computer-based algorithm that calculates an individual's 10-year fracture probability from easily obtained clinical risk factors with or without adding femoral-neck bone mineral density. The Fracture Risk Assessment tool, or FRAX, has attracted intense interest since its introduction in 2007 and has been endorsed by the USPSTF⁴ and by other scientific societies, including the NOF⁵ and the ISCD.⁸ In fact, the most recent USPSTF guidelines,⁴ which recommend screening all women age 65 and older, call for using FRAX to identify younger women at higher risk of fracture.

According to FRAX, a 65-year-old white woman who has no risk factors has a 9.3% chance of developing a major osteoporotic fracture in the next 10 years. And if a younger woman (between the ages of 50 and 64) has a fracture risk as high or higher than a 65-year-old white woman who has no risk factors, then she too should be screened by DXA.

The FRAX calculator is available online at www.shef.ac.uk/FRAX.

What are the current recommendations about follow-up DXA testing?

In eligible patients, the Centers for Medicare and Medicaid Services will pay for a DXA scan every 2 years. This interval is based on the concept that in an otherwise healthy person, it takes a minimum of 2 years to see a sig-

nificant change in bone mineral density that can be attributed to a biological change in the bone and not just chance. The USPSTF⁴ and scientific societies such as the NOF⁵ generally agree with the Medicare guidelines of retesting every 2 years but recognize certain clinical situations that may warrant more frequent retesting (see below).

But the real question is how long the DXA screening interval can be extended so that meaningful information can still be obtained to help make management decisions and before a complication such as a fracture occurs. While there is convincing evidence to support the recommendations for an initial DXA test, data to answer the question of how long the resting interval should be are lacking.

Before the study by Gourlay et al,¹ the only data on repeat DXA came from work by Hillier et al.⁹ But those investigators asked a different question. They were interested in how well repeated measurements predicted fractures. They used the same population that Gourlay et al did but evaluated fractures, not T scores. They concluded that in healthy, adult postmenopausal women, repeating the bone mineral density measurement up to 8 years later adds little value to initial measurement for predicting incident fractures.

Clinical factors also count

The T score should not be the only major factor determining the interval for bone mineral density testing in elderly women; clinical risk factors also should be kept in mind.

Gourlay et al concluded that age and T scores are the key predictive factors in determining the bone mineral density testing interval in elderly, postmenopausal women for screening purposes.¹ In their statistical model, clinical risk factors such as fracture after age 50, current smoking, previous or current use of glucocorticoids, and self-reported rheumatoid arthritis did not influence the testing interval. They say that clinicians should not feel compelled to shorten the testing interval when these risk factors are present.

Readers may take this to mean that if these results were strictly applied to a 70-year-old white woman receiving oral glucocorticoids for rheumatoid arthritis and who has a baseline T score of -1.45 , then her next test may

A fracture after age 50, current smoking, use of oral glucocorticoids, and self-reported rheumatoid arthritis did not affect the outcome of this study

At the same T score, fracture risk differs with different risk factors

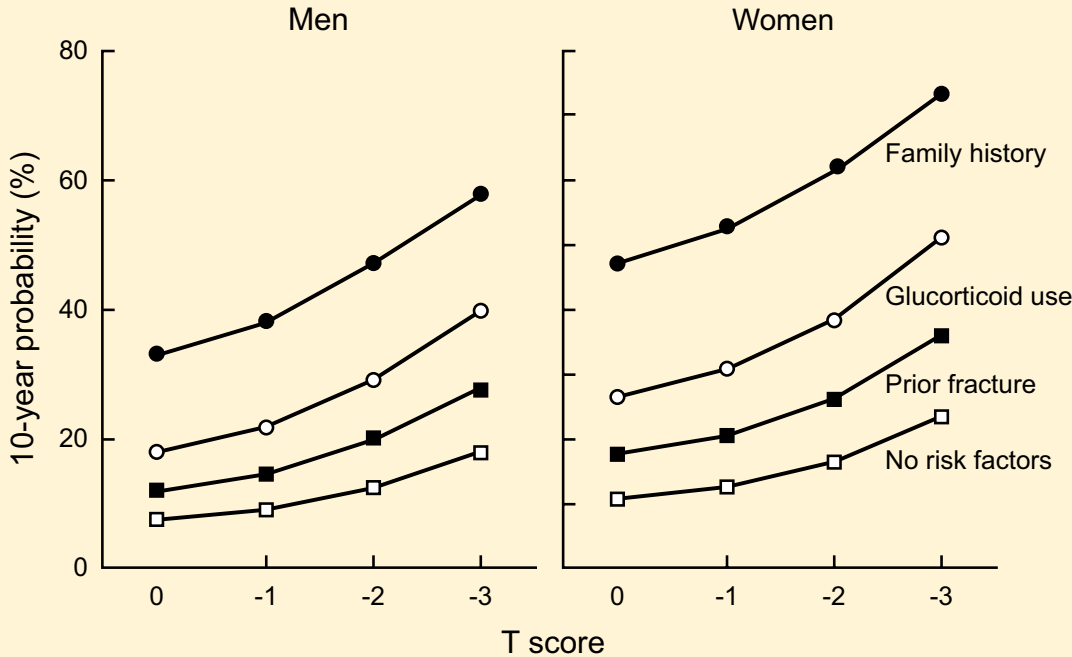


FIGURE 1. The effects of several clinical risk factors on the 10-year probability of a major osteoporotic fracture occurring in 65-year-old white men and women in the United States.

REPRINTED FROM KANIS JA, ODEN A, JOHANSSON H, BORGSTRÖM F, STRÖM O, MCCLOSKEY E. FRAX AND ITS APPLICATIONS TO CLINICAL PRACTICE. BONE 2009; 44:734–743, COPYRIGHT 2009, WITH PERMISSION FROM ELSEVIER. WWW.SCIENCEDIRECT.COM/SCIENCE/JOURNAL/87563282.

be postponed by 15 years (given that both these factors did not influence the testing interval). Readers may also conclude that if this patient's T score were -1.51 , then her screening interval would be 5 years and not 15 years.

However, Gourlay et al say¹ that clinicians can choose to shorten the testing interval if there is evidence of decreased activity or mobility, weight loss, or other risk factors not considered in their analysis.

Soon after this study¹ was published, Lewiecki et al¹⁰ and others^{11–13} published critical commentaries addressing controversial issues surrounding the study. They highlighted the importance of considering clinical risk factors for fracture in addition to the femoral neck and total hip T scores. In response to these comments, Gourlay et al clarified that their results were not generalizable to patients with secondary osteoporosis, such as those taking glucocorticoids or those who have rheumatic diseases.¹⁴

Readers should keep in mind that clinical risk factors make independent contributions to fracture risk (FIGURE 1).¹⁵

Readers should also recognize the following groups in whom the results of the study by Gourlay et al are not applicable since they were not included in their study:

- Men
- Women other than white women
- Women already diagnosed with osteoporosis and on bisphosphonates or any other osteoporosis treatment (except for estrogen). The findings also do not apply to:
- Patients who experience a significant decline in health status or who develop new clinical conditions (such as hyperparathyroidism, paraproteinemias, or type 2 diabetes) or who use medications such as glucocorticoids that cause rapid bone loss. Changes in clinical situations such as these may necessitate more frequent bone mineral density testing in spite of a “good” baseline T score.
- Perimenopausal women or women who received their first bone mineral density test before age 65. Perimenopause and menopause may trigger rapid bone loss, which

The risk is higher in osteoporosis than in osteopenia, but more people have osteopenia

may be as much as one T-score point (ie, 1 standard deviation) at the spine and femoral neck.¹⁶ Therefore, testing done during this time cannot be used as the basis of future monitoring.

The study did not address asymptomatic vertebral fractures and lumbar spine density

Gourlay et al¹ did not take into account asymptomatic spinal fractures; they used only clinical vertebral fractures in their risk estimates of spinal fractures. Ascertainment of morphometric spinal fractures may be methodologically challenging, but if the study had included these fractures, the outcomes and conclusions could have been very different.

Vertebral fractures are present in as many as 14% to 33% of postmenopausal women¹⁷ and indicate osteoporosis (regardless of the bone mineral density). Moreover, most vertebral fractures are clinically silent and escape detection, and approximately only one in three radiographically defined vertebral fractures is reported clinically.^{18,19} Given the prevalence of these fractures, we and others¹⁰ have noted that the results of the Gourlay study may be biased toward longer screening intervals because they did not account for morphometric vertebral fractures.

Gourlay et al used T scores only of the femoral neck and total hip and not those of the lumbar spine. Some studies have found that hip measurements may be superior to spine measurements for overall osteoporotic fracture prediction.^{20,21} However, lumbar spine bone mineral density is predictive of fracture at other skeletal sites,^{22,23} is a widely accepted skeletal site measurement, and is used to diagnose osteoporosis. Moreover, the lumbar spine T score can be -2.5 or higher even if the total hip or femoral neck T score is lower than -2.5 .

More fractures occur in people with osteopenia than with osteoporosis

Osteoporosis imparts a much higher risk of fracture than does osteopenia. However, if one recognizes the much greater prevalence of osteopenia (33.6 million people) compared with osteoporosis (10 million),² it is not hard to appreciate that the number of fractures is higher in the osteopenic group than in those with osteoporosis based on T scores. Siris et

al²⁴ point out that at least half of osteoporotic fractures are in patients with osteopenia, who comprise a larger segment of the population than those with osteoporosis.

Some clinical trials have shown that bisphosphonates are not effective in preventing clinical fractures in women who do not have osteoporosis.^{25,26} However, clinicians must recognize that while bisphosphonates may not be as effective in preventing fractures in the osteopenic group with no other clinical risk factors, the presence of multiple clinical risk factors incrementally increases the fracture risk (which can be assessed via FRAX) and may require starting drug therapy earlier.

Women with vertebral fractures are considered to have clinical osteoporosis even if they have T scores in the osteopenic range, and must be considered for drug therapy.

The public health burden of fractures will not decrease unless individuals with low bone mineral density who are at an increased risk of fracture are identified and treated.²⁴

Is DXA testing overused or underused? Does it decrease the rate of fractures?

The study of Gourlay et al¹ captured a lot of media attention, with many newspapers and blogs claiming that women may be getting tested too often.^{27,28} However, in reality, this test is highly underutilized. The 2011 Healthcare Effectiveness Data and Information Set report noted that 71.0% of women in Medicare health maintenance organizations and 75.0% of women in Medicare preferred provider organizations ever had a bone mineral density test for osteoporosis.²⁹ While these numbers may not appear to be too far from the target, they are a poor gauge of DXA use as they include all types of bone mineral density tests in a woman's lifetime, including even heel tests at health fairs.

Central DXA is used far less than one might expect. King and Fiorentino, in a recent analysis, showed that only about 14% of fee-for-service Medicare beneficiaries 65 years and older had one or more DXA tests in 2010.³⁰ DXA retesting also does not seem to be an issue, with only 1 in 10 elderly women reporting having had a repeat test at 2-year intervals, and fewer than 1 in 100 tested reported testing more frequently.³⁰ ■

**In reality,
DXA testing
is highly
underutilized**

REFERENCES

1. Gourlay ML, Fine JP, Preisser JS, et al; Study of Osteoporotic Fractures Research Group. Bone-density testing interval and transition to osteoporosis in older women. *N Engl J Med* 2012; 366:225–233.
2. National Osteoporosis Foundation (NOF). America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. Washington, DC: National Osteoporosis Foundation; 2002.
3. US Department of Health and Human Services. Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville, MD: US Department of Health and Human Services, Office of the Surgeon General; 2004.
4. US Preventive Services Task Force. Screening for osteoporosis: US preventive services task force recommendation statement. *Ann Intern Med* 2011; 154:356–364.
5. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2010.
6. Baim S, Binkley N, Bilezikian JP, et al. Official Positions of the International Society for Clinical Densitometry and executive summary of the 2007 ISCD Position Development Conference. *J Clin Densitom* 2008; 11:75–91.
7. Watts NB, Bilezikian JP, Camacho PM, et al; AACE Osteoporosis Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract* 2010; 16(suppl 3):1–37.
8. The International Society for Clinical Densitometry (ISCD); the International Osteoporosis Foundation (IOF). 2010 Official Positions on FRAX. www.iscd.org/official-positions. Accessed February 1, 2013.
9. Hillier TA, Stone KL, Bauer DC, et al. Evaluating the value of repeat bone mineral density measurement and prediction of fractures in older women: the study of osteoporotic fractures. *Arch Intern Med* 2007; 167:155–160.
10. Lewiecki EM, Laster AJ, Miller PD, Bilezikian JP. More bone density testing is needed, not less. *J Bone Miner Res* 2012; 27:739–742.
11. Leslie WD, Morin SN, Lix LM. Bone-density testing interval and transition to osteoporosis. *N Engl J Med* 2012; 366:1547.
12. Endocrine Society. The Endocrine Society Recommends Individualization of Bone Mineral Density Testing Frequency in Women Over the Age of 67: February 7, 2012. <http://www.endo-society.org/advocacy/legislative/letters/upload/Endocrine-Society-Response-to-BMD-Testing-Final.pdf>. Accessed January 29, 2013.
13. The International Society for Clinical Densitometry (ISCD). ISCD response to NEJM article: January 20, 2012. http://www.american-bonehealth.org/images/stories/BMD_Testing_Interval_ISCD_Response_to_NEJM_Article.pdf. Accessed January 29, 2013.
14. Gourlay ML, Preisser JS, Lui LY, Cauley JA, Ensrud KE; Study of Osteoporotic Fractures Research Group. BMD screening in older women: initial measurement and testing interval. *J Bone Miner Res* 2012; 27:743–746.
15. Kanis JA, Oden A, Johansson H, Borgström F, Ström O, McCloskey E. FRAX and its applications to clinical practice. *Bone* 2009; 44:734–743.
16. Recker RR. Early postmenopausal bone loss and what to do about it. *Ann NY Acad Sci* 2011; 1240:E26–E30.
17. Genant HK, Jergas M, Palermo L, et al. Comparison of semiquantitative visual and quantitative morphometric assessment of prevalent and incident vertebral fractures in osteoporosis The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res* 1996; 11:984–996.
18. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. *Lancet* 1996; 348:1535–1541.
19. Nevitt MC, Ettinger B, Black DM, et al. The association of radiographically detected vertebral fractures with back pain and function: a prospective study. *Ann Intern Med* 1998; 128:793–800.
20. Leslie WD, Tsang JF, Caetano PA, Lix LM; Manitoba Bone Density Program. Effectiveness of bone density measurement for predicting osteoporotic fractures in clinical practice. *J Clin Endocrinol Metab* 2007; 92:77–81.
21. Leslie WD, Lix LM, Tsang JF, Caetano PA; Manitoba Bone Density Program. Single-site vs multisite bone density measurement for fracture prediction. *Arch Intern Med* 2007; 167:1641–1647.
22. Stone KL, Seeley DG, Lui LY, et al; Osteoporotic Fractures Research Group. BMD at multiple sites and risk of fracture of multiple types: long-term results from the Study of Osteoporotic Fractures. *J Bone Miner Res* 2003; 18:1947–1954.
23. Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 1992; 7:633–638.
24. Siris ES, Baim S, Nattiv A. Primary care use of FRAX: absolute fracture risk assessment in postmenopausal women and older men. *Postgrad Med* 2010; 122:82–90.
25. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA* 1998; 280:2077–2082.
26. McClung MR, Geusens P, Miller PD, et al; Hip Intervention Program Study Group. Effect of risedronate on the risk of hip fracture in elderly women. Hip Intervention Program Study Group. *N Engl J Med* 2001; 344:333–340.
27. Park A. How often do women really need bone density tests? Time: Health & Family. January 19, 2012. <http://healthland.time.com/2012/01/19/most-women-may-be-getting-too-many-bone-density-tests/>. Accessed January 29, 2013.
28. Kolata G. Osteoporosis patients advised to delay bone density retests. The New York Times: Health. January 19, 2012. <http://query.nytimes.com/gst/fullpage.html?res=9B01E1D61230F93AA25752C0A9649D8B63>. Accessed January 29, 2013.
29. National Committee for Quality Assurance. The State of Health Care Quality Report. <http://www.ncqa.org/Portals/0/State%20of%20Health%20Care/2012/SOHC%20Report%20Web.pdf>. Accessed February 1, 2013.
30. King AB, Fiorentino DM. Medicare payment cuts for osteoporosis testing reduced use despite tests' benefit in reducing fractures. *Health Aff (Millwood)* 2011; 30:2362–2370.

ADDRESS: Angelo A. Licata, MD, PhD, Department of Endocrinology, Diabetes, and Metabolism, F20, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail: licataa@ccf.org.