

ROBIN K. DORE, MD

Clinical Professor of Medicine, Division of Rheumatology, David Geffen, UCLA School of Medicine, Tustin, CA

Should healthy people take calcium and vitamin D to prevent fractures? What the US Preventive Services Task Force and others say

THE UNITED STATES PREVENTIVE SERVICES TASK FORCE (USPSTF) recently threw cold water on the use of calcium and vitamin D supplements to prevent fractures in adults, either finding inadequate evidence to make a recommendation or recommending against supplementation, depending on the population and the doses used.¹

Complicating this issue, several recent studies have raised concern about the long-term cardiovascular risk of calcium supplementation.

With so many people taking calcium supplements, how do we put this into context for our patients? I believe that we need to consider the whole person when discussing these supplements, as there are data that they also help reduce the risk of falls, cancer, and even overall mortality rates.

■ THE USPSTF'S METHODS

The USPSTF bases its recommendations on explicit criteria² developed by its Evidence-based Practice Center, which is under contract to the US Agency for Healthcare Research and Quality to conduct systematic reviews of the evidence on specific topics in clinical prevention. The USPSTF grades the strength of the evidence for the effectiveness of specific clinical preventive services as:

- A (strongly recommended)
- B (recommended)
- C (no recommendation)
- D (recommended against)
- I (insufficient evidence to make a recommendation for or against).

doi:10.3949/ccjm.80a.13050

USPSTF recommendations consider the evidence of both benefit and harm of the intervention but do not include the cost of the intervention in the assessment.³

■ THE USPSTF'S GRADES ON CALCIUM AND VITAMIN D SUPPLEMENTATION

The USPSTF made the following recommendations in February 2013 about the use of calcium and vitamin D supplementation:

- **For primary prevention of fractures in premenopausal women and men:** grade I (current evidence is insufficient to assess the balance of the benefits and harms)
- **For primary prevention of fractures in noninstitutionalized postmenopausal women, in daily doses greater than 400 IU of vitamin D and greater than 1,000 mg of calcium:** also grade I
- **For primary prevention of fractures in noninstitutionalized postmenopausal women, in daily doses of 400 IU or less of vitamin D and 1,000 mg or less of calcium:** grade D (the USPSTF recommends *against* it, as these doses increase the incidence of renal stones and there is "adequate" evidence that these doses have no effect on the incidence of fractures).

■ WHAT THE USPSTF DID NOT DISCUSS

These recommendations do not apply to everybody. Rather, the document discusses "the effectiveness of specific clinical preventive

Recent findings from the USPSTF need to be put in context

services for patients without related signs or symptoms,”¹ and states that the recommendations do not pertain to patients with osteoporosis or vitamin D deficiency or those who have had fractures.

Also, the document does not discuss the use of calcium supplementation by itself in fracture prevention, nor does it discuss possible benefits of calcium and vitamin D other than fracture prevention, such as reducing the risk of falls, cancer, or death. Further, the document states that “appropriate intake” of vitamin D and calcium is “essential to overall health”¹ but does not state the amount that is considered appropriate.

The document does refer the reader to other USPSTF recommendations concerning screening for osteoporosis in women age 65 and older and in younger women who demonstrate the fracture risk of a 65-year-old woman,⁴ as well as to its recommendation for vitamin D supplementation to prevent falls in community-dwelling adults age 65 and older who are at higher risk of falls.⁵

Not included: A new meta-analysis

The USPSTF document also notes that after their review was completed, another meta-analysis concluded that fracture risk may be reduced by taking vitamin D in doses of 800 IU or higher.⁶

In that study, Bischoff-Ferrari et al⁶ performed a pooled analysis of vitamin D dose requirements for fracture prevention from 11 double-blind, randomized, controlled trials of oral vitamin D supplementation taken either daily or at weekly or 4-month intervals with or without calcium, compared with placebo or calcium alone in people age 65 and older. The primary end points were the incidence of hip fracture and any nonvertebral fracture according to Cox regression analysis, with adjustment for age, sex, community or institutional dwelling, and study. The aim was to evaluate actual vitamin D intake rather than the assigned dosage groups in the trials.

On the basis of actual vitamin D intake, the incidence of hip fracture was significantly (30%) lower in people with the highest actual intake (792–2,000 IU per day) than in controls. There was no reduction in the risk of hip fracture at any actual intake levels lower than

792 IU per day. Using this same analytic technique, the reduction in the incidence of nonvertebral fracture at the highest actual intake level was 16%.

Why were their findings different than those of the USPSTF? The authors hypothesized that some previous high-quality trials of vitamin D supplementation either showed no benefit because the participants were non-compliant and thus took less than the intended dose of vitamin D, or showed an unexpected benefit because the participants actually took more vitamin D than was specified in the study.

The USPSTF recommendations did not include studies of vitamin D without calcium, whereas Bischoff-Ferrari et al did, which could also explain some of the differences in the findings, as not all of the studies included in the two documents were the same. Several previous meta-analyses suggested that the dose of vitamin D was irrelevant when vitamin D was combined with calcium.

The data from Bischoff-Ferrari et al suggested that at the highest actual intake level of vitamin D, a smaller amount of calcium supplementation (< 1,000 mg daily) may be more beneficial in reducing fracture risk than a larger amount (\geq 1,000 mg daily). This is important, given the current level of concern initially raised by Bolland et al⁷ and others about the possible risks of higher doses of calcium supplements increasing cardiovascular risk. (More on this below.)

■ WHAT OTHER ORGANIZATIONS SAY

Both the National Osteoporosis Foundation and the American Society of Bone and Mineral Research suggest following the 2010 recommendations of the Institute of Medicine⁸ on calcium and vitamin D instead of those of the USPSTF, as the former address the overall health benefits of calcium and vitamin D in healthy individuals rather than only fracture prevention.

Neither the Institute of Medicine nor the USPSTF, however, addresses vitamin D requirements of people at high risk, such as those with vitamin D deficiency due to very little sun exposure, dark skin, problems absorbing dietary fat, or medications that interfere with vitamin D absorption, or those with osteoporosis.

The Institute of Medicine suggests that, for healthy adults under age 71, an adequate vitamin D intake is 600 IU daily, and for healthy adults age 71 and older it is 800 IU daily. They state that the safe upper limit for daily intake of vitamin D is 4,000 IU. As for adequate calcium intake, the daily recommendation is 1,200 mg for women ages 50 through 70, and 1,200 mg for all adults age 71 and older. As I have already discussed, the Institute of Medicine recommendations are based on the overall health benefits of calcium and vitamin D rather than solely on fracture prevention. Monitoring of vitamin D levels is not recommended unless the patient has osteoporosis or is at risk for vitamin D deficiency.

Risks of calcium supplementation

Much has been written recently about the risks of calcium supplementation.

This concern was first raised in 2008 by Bolland et al⁷ in a post hoc analysis of data collected to evaluate the effect of calcium supplements on bone density and fracture.⁷ More myocardial infarctions occurred in the calcium supplement group than in the placebo group, but the difference was not statistically significant, and the events occurred only in those who took more than 1,000 mg of calcium daily.

The same group reanalyzed data from the Women's Health Initiative and found a 24% higher risk of myocardial infarction in women who took calcium with or without vitamin D, but only in those women assigned to take calcium supplementation who had not taken calcium supplements before the study began.⁹

More recently, Xiao et al¹⁰ evaluated the effect of both dietary and supplemental calcium on cardiovascular disease mortality rates.¹⁰ This was a prospective study of 388,229 men and women who participated in the National Institutes of Health-American Association of Retired Persons Diet and Heart Study. Supplemental calcium intake was associated with an elevated risk of cardiovascular disease in men, but not in women. Dietary calcium intake was unrelated to cardiovascular death.

The latest study to address this issue was from the Swedish Mammography Cohort, a population-based cohort that included 61,433 women born between 1914 and 1948, with a mean follow-up of 19 years.¹¹ Diet was evalu-

ated by food frequency questionnaires. A daily dietary intake of calcium below 600 mg was associated with higher risks of all-cause mortality, cardiovascular disease, ischemic heart disease, and stroke. However, compared with women whose daily calcium intake was between 600 and 999 mg, a dietary intake of more than 1,400 mg/day was associated with a higher death rate, with a hazard ratio for all-cause mortality of 1.40, cardiovascular disease 1.49, and ischemic heart disease 2.14.

Unfortunately, none of these studies were designed to assess the risk of cardiovascular disease related to calcium supplementation. Like the USPSTF, both the National Osteoporosis Foundation and the American Society of Bone and Mineral Research state that this type of study is needed to clarify both the benefit and risk of calcium supplementation.

Until these data are available, the American Society of Bone and Mineral Research has advised doctors and their patients "to discuss the best strategy for each individual patient, putting supplements as the last resort for healthier adults if they cannot reach recommended levels through the intake of calcium and vitamin rich foods." For adults who cannot tolerate dairy products, calcium can be obtained from calcium-supplemented foods such as orange juice and Jello and from non-dairy sources such as leafy green vegetables, almonds, garbanzo beans, tofu, and eggs.¹²

The National Osteoporosis Foundation suggests following the Institute of Medicine recommendations for adequate calcium and vitamin D rather than the USPSTF recommendations, most likely because the former are based on the overall health benefits of calcium and vitamin D rather than fracture prevention only. However, it reminds us that the Institute of Medicine recommendations do not apply to patients who are at the highest risk of fracture, ie, those with osteoporosis and vitamin D deficiency.

■ TAKE-HOME POINTS

- All medications, including those available over the counter, have benefits and risks.
- Even the USPSTF states that for a healthy lifestyle, the diet should contain adequate calcium and vitamin D intake.

All medications, including those available over the counter, have benefits and risks

- When following guidelines, practitioners should be certain that the guidelines pertain to the population they are treating—for example, not to apply the Institute of Medicine recommendations to a woman with a hip fracture, but that a healthy premenopausal woman who is taking calcium supplements should be advised to stop the supplements and focus on dietary sources of calcium.
- Only if individuals cannot obtain the recommended amount of calcium in their diet is it advisable for them to take a calcium supplement.

My recommendations

Based on the information summarized above, I recommend that my patients ob-

tain as much calcium as possible from their diet—between 600 and 1,200 mg daily—and to take a calcium supplement only if they cannot obtain that amount of calcium in the diet. However, 24-hour calcium excretion is not recommended as a marker of calcium intake.

I also advise my patients to take a vitamin D supplement, per the Institute of Medicine report for overall good health. The USPSTF recommendations concerning vitamin D and calcium address only fracture prevention. As I am responsible for the overall health of my patients, not just fracture prevention, I choose to follow the National Osteoporosis Foundation and Institute of Medicine recommendations, not those of the USPSTF. ■

REFERENCES

1. **Moyer VA, on behalf of the U.S. Preventive Services Task Force.** Vitamin D and calcium supplementation to prevent fractures in adults: US Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2013; E-pub ahead of print. <http://annals.org/article.aspx?articleid=1655858>. Accessed April 23, 2013.
2. **Harris RP, Helfand M, Woolf SH, et al; Methods Work Group, Third US Preventive Services Task Force.** Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med* 2001; 20(suppl 3):21–35.
3. **US Preventive Services Task Force.** Procedure Manual. AHRQ Publication No. 08-05118-EF, July 2008. <http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmannual.htm>. Accessed April 22, 2013.
4. **Nelson HD, Haney EM, Dana T, Bougatsos C, Chou R.** Screening for osteoporosis: an update for the US Preventive Services Task Force. *Ann Intern Med* 2010; 153:99–111.
5. **US Preventive Services Task Force.** Prevention of Falls in Community-Dwelling Older Adults, Topic Page. <http://www.uspreventiveservicestaskforce.org/uspstf/uspfalls.htm>. Accessed April 22, 2013.
6. **Bischoff-Ferrari HA, Willett WC, Orav EJ, et al.** A pooled analysis of vitamin D dose requirements for fracture prevention. *N Engl J Med* 2012; 367:40–49.
7. **Bolland MJ, Barber PA, Doughty RN, et al.** Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. *BMJ* 2008; 336:262–266.
8. **Standing Committee on the Scientific Evaluation of Dietary Reference Intakes.** Food and Nutrition Board. Institute of Medicine. Dietary reference Intakes on Calcium and Vitamin D. Washington, DC: The National Academic Press; 2010.
9. **Bolland MJ, Avenell A, Baron JA, et al.** Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. *BMJ* 2010; 341:c3691.
10. **Xiao Q, Murphy RA, Houston DK, Harris TB, Chow WH, Park Y.** Dietary and Supplemental Calcium Intake and Cardiovascular Disease Mortality: The National Institutes of Health-AARP Diet and Health Study. *JAMA Intern Med* 2013;1–8.
11. **Michaëlsson K, Melhus H, Warensjö Lemming E, Wolk A, Byberg L.** Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. *BMJ* 2013; 346:f228.
12. **National Osteoporosis Foundation (NOF).** A Guide to Calcium-Rich Foods. <http://nof.org/articles/886>. Accessed April 22, 2013.

ADDRESS: Robin K. Dore, MD, Clinical Professor of Medicine, Division of Rheumatology, David Geffen, UCLA School of Medicine, 12791 Newport Avenue, #201, Tustin, CA 92780; e-mail: rkdmail@sbcglobal.net

I am responsible for the overall health of my patients, not just fracture prevention