The verdict is in: there’s not enough evidence to support screening of asymptomatic individuals for low vitamin D. Here: a look behind the curtain.

Now that the vitamin D research fires have begun to die down, I wanted to look into this apparent health fad to see what, if any, evidence came from the intense focus on this particular supplement. In 2012 alone, there were more than 3600 publications in PubMed on vitamin D: opinion articles, small studies, large studies, evidence reviews, and meta-analyses. Then a review of the meta-analyses with a little “expert opinion” to top things off.

In the end, I think an overwhelming lack of definitive evidence was, in and of itself, the conclusion. We did, however, learn a few things about screening for hypovitaminosis D, potential outcomes associated with it, and potential benefits from treatment.

**Screening**

Just this week, the US Preventive Services Task Force (USPSTF) said there was not enough evidence to support screening asymptomatic individuals for low vitamin D. The main harm associated with testing for hypovitaminosis D is cost. Even though testing may hover around the $100 range, repeat non–evidence-based testing among several groups on an already strained health care system could redirect valuable health care dollars away from patients with other illnesses.

**Causes of Hypovitaminosis D**

Some of the most common causes of vitamin D deficiency are believed to be:

- Inadequate exposure to sunlight (sunscreen or dark skin)
- Obesity
- Fat malabsorption syndrome (eg, celiac disease)
- Bariatric surgery
- Nephrotic syndrome (vitamin D bound to albumin)
- Drug catabolism (HIV medications and anticonvulsants)
- Granuloma-forming disorders, lymphomas, and primary hyperparathyroidism

**Levels**

According to the Institute of Medicine (IOM), a vitamin D level >50 nmol/L is normal for adults. Insufficiency is tracked at <50 nmol/L, and <25 nmol/L is considered deficiency. The American Association of Clinical Endocrinologists (AACE) recommends for postmenopausal women to maintain vitamin D intake, and take supplement vitamin D if needed, to maintain serum levels of 25-hydroxyvitamin D [25(OH)D] in the 30 to 60 ng/mL range (Grade A; BEL 1).

In patients younger than 18, less than 20 ng/mL is considered deficient, and 20 ng/mL or greater is optimal (Wagner et al).

A more mainstream theory is that levels below 50 nmol/L lead to increased bone turnover and/or parathyroid hormone (PTH). There is a possibility that levels above 75 nmol/L may contribute to fewer falls and fractures.

Bischoff-Ferrari et al show a 37% relative risk reduction in hip fracture (HR = 0.63; 95% CI, 0.46-0.87), and 31% relative risk reduction of any nonvertebral fracture (HR = 0.69; 95% CI, 0.57-0.84) when baseline serum 25(OH)D was >61 nmol/L versus <30 nmol/L.

However, this study could be making one of the subtle mistakes that we find with the “retrospect-o-scope.” The elevated baseline level correlates with reduced bad outcomes; therefore, if we artificially elevate this level they will have a benefit like those that are naturally elevated.

**Treatment for Fracture Risk Reduction**

The USPSTF acknowledged the recommendations of WHO and IOM for the daily intake of calcium and vitamin D for overall health, but not for fracture prevention. Rather, they summarized the evidence for treatment as follows: “Except for postmenopausal women,
there is inadequate evidence to estimate the benefits of vitamin D or calcium supplementation to prevent fractures in noninstitutionalized adults. Due to the lack of effect on fracture incidence and the increased incidence of nephrolithiasis in the intervention group of the WHI [Women’s Health Initiative] trial, the USPSTF concludes with moderate certainty that daily supplementation with 400 IU of vitamin D₃ and 1000 mg of calcium has no net benefit for the primary prevention of fractures in noninstitutionalized, postmenopausal women.”

The USPSTF actually recommends against vitamin D and calcium supplementation for fracture prevention in one of the most common outpatient candidates: noninstitutionalized postmenopausal women!

Harms of supplementation in the WHI trial show the absolute risk of nephrolithiasis in individuals having supplementation with calcium and vitamin D at 2.5% in the intervention group and 2.1% in the placebo group. The number needed to harm was 273.

In a 2010 study by Sanders et al, a double-blind, randomized controlled trial with over 2000 women in Australia, aged 70 and older, showed that with an annual dose of 500,000 vitamin D there was a 10% absolute risk increase in this already high-risk group, which went as high as 72.7% to 83.4% when they had supplementation.

David Newman, MD, at NNT.com states that by review of the evidence, the number needed to harm (NNH) with regard to nephrolithiasis or kidney injury from vitamin D supplementation was 36.

**ACTION POINTS**

- The US Preventive Services Task Force (USPSTF) said there was insufficient evidence to support screening asymptomatic individuals for low vitamin D.

- Note that the author recommends efforts to prevent low vitamin levels in our patients by treating the underlying disease process and by educating them about food, reasonable sunlight exposure, and other interventions to allow their bodies to have “naturally” elevated levels of vitamin D.

**Treatment Levels**
The World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Disease found that supplementation of vitamin D had to reach >800 IU daily to differ from placebo.

The Vitamin D Council has a great approach to finding the optimal dose of vitamin D supplementation. The group recommends a dose of 5000 IU/d and gives the following reasons for it:

- Is easy to obtain at most pharmacies
- Will get at least 97% of people above 30 ng/mL
- Will get most people above 40 ng/mL, and close to around 50 ng/mL
- Will not cause anyone to get toxic levels

These are excellent boundaries if one is going to supplement for general health. But, some of the questions yet to be answered by this 2012 generation of studies are:

- If we supplement low vitamin D with a mid-priced supplement, will this improve a patient’s outcome? Or is the theory of supplemental vitamin D based on the ideal levels that exist in people with naturally elevated levels of vitamin D?
- Is it even possible to reach the same quality outcomes in the supplemental group and the naturally elevated group?
- Will dietary intake of vitamin D lead to a better outcome than supplement intake in patients?
- Is the lab value of vitamin D of >90 nmol/L in a patient that only has dietary and sunlight exposure as their source of vitamin D the only way to get the health benefit?

These are the questions that the Vitamin D Council, USPSTF, WHI, NHANES III, Cochrane Collaboration, DIPART group and others have been unable to answer.

**Risk Factor Reduction**
We should strive to prevent low vitamin levels in our patients by treating the underlying disease process. Educating our patients about food, reasonable sunlight exposure, and other interventions to allow their bodies to have “naturally” elevated levels of vitamin D will empower them to take part in their health.

As we support a healthy weight and lifestyle in each patient, especially in the obese, discuss the
risks/benefits of bariatric surgery, and attempt to control the various disease processes that may contribute to malabsorption, we are standing on the best available evidence.

Bottom line: Sunlight exposure of 10 minutes during the peak UVB exposure time, which occurs from 10 a.m. to 3 p.m. for most of the US, in a nonobese individual, with a T-shirt and shorts on, will yield 3000 IU of vitamin D for the majority of people.
That, plus a balanced diet, and maintaining a BMI under 30, are the most likely recommendations to yield endpoints that are desirable without significant negative side effects.

The Questioning Medicine PodCast on Vitamin D can be found here, and here. Thank you for reading. Your thoughts are welcome. We are always available on Twitter @MedQuestioning and @AndrewBuelt. You can also email us at questioningmedicine@gmail.com.

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