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### American College of Cardiology (ACC) 59th Annual Scientific Session

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From [Heartwire](#)

## Death, CVD Risk Declines in People Who "Normalize" Vitamin-D Levels



Shelley Wood

[Authors and Disclosures](#)

March 18, 2010 (**Atlanta, Georgia**) — Adding heft to the hypothesis that vitamin-D deficiency is linked to cardiovascular disease, a new study has found that people with low vitamin-D levels who managed to normalize their levels were significantly less likely to develop cardiovascular events over up to six years of follow-up.

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The study was presented as a poster by **Dr Tami L Bair** (Intermountain Medical Center Heart Institute, Murray, UT) earlier this week at the **American College of Cardiology (ACC) 2010 Scientific Sessions**.

According to coauthor **Dr Joseph B Muhlestein** (Intermountain Medical Center Heart Institute), the study looked at baseline and subsequent vitamin-D levels in 9491 subjects with known vitamin-D deficiency, rechecked their vitamin D, then compared subsequent rates of death, coronary artery disease, MI, heart failure, stroke, and renal failure among those who managed to bring up their vitamin-D levels with those who remained vitamin-D deficient. A cut point of  $\leq 30$  ng/mL was used to define vitamin-D deficiency.

"This wasn't a randomized trial, but all of these patients started with low vitamin D, and then the question is, if they treated their vitamin D, did it have an effect? We don't know what they did . . . the presumption is that they were told their vitamin D was low, then started supplementation or got their swimsuit out and went into the sun a lot to treat it."

### Getting to Normal

After a mean of one-year of follow-up, those who had normalized their vitamin-D levels were significantly less likely to have died, developed heart failure, or developed coronary artery disease. A composite end point, looking at all outcomes combined, showed a highly statistically significant reduction among those with normalized vitamin-D levels.

Muhlestein drew particular attention to the 30% reduced risk of death in the normalized vitamin-D group. "A 30% reduction in risk is about the same you could hope to get from taking a statin or treating your blood pressure, so we thought it was certainly promising. It doesn't eliminate the need for a real randomized trial, although I'm trying to figure out a good way to do one."

There are a number of vitamin-D trials under way, most notably [VITAL](#), a **National Institutes of Health (NIH)** study, launched in January.

But Muhlestein is concerned that the NIH trial may come up empty-handed for two reasons. For one, the trial, he says, is not measuring baseline levels or checking whether patients actually reach the optimal vitamin-D range in the intervention arm. "I can see why they aren't [measuring vitamin D at baseline], because if they find

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vitamin D is deficient is it ethical to say, 'I want you to stay vitamin-D deficient'?"

Vitamin-D deficiency is already known to increase the risks of skeletal disease, he notes. But without knowing if participants actually normalize their levels, it will be impossible to link normalization with an effect on events.

His second concern is with the dose chosen in VITAL: 2000 international units (IU) per day. "What I've found is that there are lots of my patients who don't become normalized with 2000 units, so 2000 units may not be enough to treat the really deficient patients."

#### But What's Normal?

In fact, Muhlestein and colleagues conducted a second study, also presented as a poster during the ACC meeting, trying to identify the optimal level of vitamin D by categorizing over 31 000 patients into three levels of vitamin D. When those levels were then linked to rates of 10 adverse outcomes (most of them cardiovascular), the authors demonstrated decreasing risk of adverse outcomes with increasing vitamin-D levels, with a vitamin D level >43 ng/mL to be the cutoff point for optimal.

Currently, they point out, a level of 30 ng/mL is considered "normal"--that cut point may be too low, based on their analysis.

But also of note, "above 43 ng/mL there was no added benefit," Muhlestein observed. "So if your level was 70 ng/mL, you were good, but you weren't any better than if [your level] was 43 ng/mL."

As for whether vitamin D can be too high, Muhlestein noted that there are problems with vitamin-D toxicities typically associated with hypercalcemia, but these tend to arise in people with levels higher than 100 ng/mL, and many people believe the level must be well over 150 ng/mL. "The only way I know of that people can get vitamin D that high is by overdosing on prescription vitamin D, which is supposed to be taken once a week. If someone were to make a mistake and take it once per day, they might get vitamin-D toxicity."

The findings from both studies have convinced Muhlestein that vitamin-D deficiency is worth treating, but he urges physicians to make sure they check to see what a patient's vitamin-D levels are to begin with and to adjust the dose accordingly. Individualization is essential, he noted, which is one reason he's worried about the blanket 2000-IU approach being used in VITAL.

"Effective dose varies from patient to patient, which is one of the problems with the NIH trial. No one is going to become toxic on 2000 IU per day, but there will be lots who are at the highest risk who are not going to become normalized."

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