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Reply to the letter to the editor "Vitamin D deficiency and cardiovascular disease" by Ahmed et al.

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We thank Ahmed and colleagues for their kind and interesting comments. The authors pointed out the classical divergence between observational and experimental results. Observational studies are prone to reverse causation and confounding [1]. Associations between vitamin D status and cardiovascular health outcomes in observational studies could merely indicate that vitamin D is a "simple" indicator of health status; compared with healthier subjects, sicker subjects could have lower vitamin D levels or status. The diversity of biological systems with which vitamin D deficiency has been associated (cardiovascular, diabetes, depression, neurodegenerative diseases, cancers, etc.) [2–4] could further suggest that vitamin D is a marker of health status rather than a predictor of health outcomes. Yet, both the wide distribution of vitamin D receptors in the human organism [5] and the influence of vitamin D on more than 3% of the human genome [6] could explain the broad influence of vitamin D on health.

Randomised clinical trials testing the efficacy of vitamin D supplementation in reducing cardiovascular events are ongoing. The Vitamin D and Omega 3 Trial (VITAL, US clinical trial registry number: NCT01169259) is investigating, in 20,000 USA adults, whether taking daily dietary supplements of vitamin D3 (2000 IU) or omega-3 fatty acids for 5 years reduces the risk of developing cancer and cardiovascular disease. The Vitamin D Assessment Study (ViDa, ANZCTR clinical trial registry number: ANZCTR12611000402943) is investigating, in 5,100 adults in New Zealand, whether taking vitamin D3 200,000 IU at baseline and 100,000 IU monthly for 4 years reduces the risk of cardiovascular disease. Both trials are still recruiting participants and first results will not be available before year 2016. Meanwhile, we agree with Ahmed and colleagues that the previously reported associations of vitamin D with cardiovascular disease should not be interpreted as causal.

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Letter to the Editor:
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