

Strong evidence exists for a beneficial role of vitamin D in reducing risk of cardiovascular disease

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The recent review by McGreevy and Williams (1) found strong evidence for a beneficial role of vitamin D in reducing risk of cardiovascular disease (CVD) from clinical studies but stated that until confirmed by randomized controlled trials (RCTs), the evidence was insufficient to conclude that vitamin D reduced the risk of CVD. There are several problems with RCTs: they often use too little vitamin D to produce a large increase in serum 25-hydroxyvitamin D [25(OH)D] concentration; other sources of vitamin D are not always controlled; serum 25(OH)D is generally not measured after supplementation, which is a problem since there is not a consistent relation between oral vitamin D intake and serum 25(OH)D change; and many of the participants have sufficiently high serum 25(OH)D concentrations that vitamin D supplementation may not increase serum 25(OH)D sufficiently to produce a significant result.

The review by Pittas et al. [Ref. 42 in (1)] found that five of nine observational studies reported lower risk of CVD incidence or death with higher serum 25(OH)D concentrations. No meta-analysis was conducted of the nine studies. However, another paper reported a meta-analysis of cohort and cross-sectional studies of risk of CVD with a summary odds ratio of 0.67 (95% confidence interval, 0.56, 0.81) for high vs. low 25(OH)D concentration (2). My meta-analysis of CVD relative hazard ratio based on eight studies in (2) plus an additional one found that the hazard ratio dropped rapidly from 7 ng/ml to 15 ng/ml, then more slowly, reaching a plateau around 40 ng/ml (3).

An observational study published after (1) was submitted found vitamin D deficiency (<30 ng/ml) significantly associated with coronary artery disease, myocardial infarction, heart failure, stroke, heart failure as well as subsequent death from these diseases in a review of 41,497 subjects in Utah with at least one 25(OH)D measurement between 2000 and 2009 (4). Another observational study published after (1) reported vitamin D deficiency significantly associated with several CVD diseases and CVD mortality rate (5).

As to the comment in (1) that it is unlikely that a single hormone could play such an important role, one should consider that skin pigmentation has adapted to solar ultraviolet doses in a manner to ensure adequate vitamin D production but reduce the risk of adverse effects. Also, that every cell in the body has vitamin D receptors, and when activated by 1,25-dihydroxyvitamin D, can affect

the expression of about 1000 different genes.

References

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