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Review

## Vitamin D status and ill health: a systematic review

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**Summary**

Low serum concentrations of 25-hydroxyvitamin D (25[OH]D) have been associated with many non-skeletal disorders. However, whether low 25(OH)D is the cause or result of ill health is not known. We did a systematic search of prospective and intervention studies that assessed the effect of 25(OH)D concentrations on non-skeletal health outcomes in individuals aged 18 years or older. We identified 290 prospective cohort studies (279 on disease occurrence or mortality, and 11 on cancer characteristics or survival), and 172 randomised trials of major health outcomes and of physiological parameters related to disease risk or inflammatory status. Investigators of most prospective studies reported moderate to strong inverse associations between 25(OH)D concentrations and cardiovascular diseases, serum lipid concentrations, inflammation, glucose metabolism disorders, weight gain, infectious diseases, multiple sclerosis, mood disorders, declining cognitive function, impaired physical functioning, and all-cause mortality. High 25(OH)D concentrations were not associated with a lower risk of cancer, except colorectal cancer. Results from intervention studies did not show an effect of vitamin D supplementation on disease occurrence, including colorectal cancer. In 34 intervention studies including 2805 individuals with mean 25(OH)D concentration lower than 50 nmol/L at baseline supplementation with 50 µg per day or more did not show better results. Supplementation in elderly people (mainly women) with 20 µg vitamin D per day seemed to slightly reduce all-cause mortality. The discrepancy between observational and intervention studies suggests that low 25(OH)D is a marker of ill health. Inflammatory processes involved in disease occurrence and clinical course would reduce 25(OH)D, which would explain why low vitamin D status is reported in a wide range of disorders. In elderly people, restoration of vitamin D deficits due to ageing and lifestyle changes induced by ill health could explain why low-dose supplementation leads

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