Still no clear evidence for health benefits of vitamin D

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Despite a huge number of studies into the role of vitamin D on health, there is still no clear evidence that it has a beneficial effect on many conditions, conclude researchers.

They argue that "universal conclusions about its benefits cannot be drawn" and say further studies and better designed trials are needed.

A growing body of evidence indicates that vitamin D may reduce risks of a wide range of diseases, including bone mineral disease, multiple sclerosis, autoimmune disorders, cancer and cardiovascular problems. Yet, despite hundreds of trials, the evidence for vitamin D is still being debated.

Two papers published on in *BMJ* today attempt to make sense of the existing data.

The first, by researchers based in the UK, Europe and USA, examined data from observational studies and clinical trials (an umbrella review) to summarise health outcomes associated with vitamin D levels, both naturally circulating and as a result of taking supplements.

Of a remarkable 137 different health outcomes reportedly linked to vitamin D, they found that only 10 had been thoroughly tested in trials, and only one (birth weight – linked to a mother's vitamin D levels in late pregnancy) had apparently concordant evidence of "benefit."

In other words, the researchers failed to find any convincing evidence of a clear role of vitamin D for any of the outcomes.

Based on this review, they suggest a "probable" association between vitamin D levels and birth weight, dental caries in children, maternal vitamin D levels at term and parathyroid hormone levels in chronic kidney disease patients requiring dialysis, but "further studies and better designed trials are needed to draw further conclusions."

In contrast to previous reports, their results also cast doubt on the effectiveness of vitamin D-only supplementation for osteoporosis and / or prevention of falls. This suggests that vitamin D "might not be as essential as previously thought in maintaining bone mineral density," they write.

Although vitamin D has been extensively studied in relation to a range of outcomes - and there are some indications that low blood vitamin D levels might be linked to several diseases - "firm universal conclusions about its benefits cannot be drawn," say the authors.

In the second paper, an international team led by researchers at the University of Cambridge and the Erasmus Medical Centre, analysed the extent to which vitamin D is associated with death from cardiovascular disease, cancer, or other conditions, under various circumstances.

They analysed the results of observational cohort studies and randomised controlled trials of both naturally circulating vitamin D and supplements (given singly as either vitamin D2 or D3 supplements).

They found that low circulating vitamin D levels in blood were associated with increased mortality risks from cardiovascular disease, cancer, and other causes.

Average follow-up in the randomised controlled trials ranged from about 3 to almost 7 years. Among the people who received vitamin D supplements in the trials, there were 2,527 deaths in total, compared to 2,587 events in the control groups. Further analysis of subgroups in the trials showed that, when given alone (i.e. not co-administered with other supplements), vitamin D2 supplements did not seem to reduce the risk of death during follow up. However, in the 14 trials that evaluated vitamin D3 alone, among people taking these supplements the risk of death during

follow up was cut by 11%.

However, the authors stress that "further clinical investigations will be essential to establish the optimal dose, duration and safety, and whether vitamin D2 or D3 have different effects on mortality risk, since the available trials are based on elderly populations in general (an age group with high competing risk of death often due to multiple co-existing disease conditions) and they do not typically include cause-specific deaths as the primary outcomes."

In an accompanying editorial, Naveed Sattar and Paul Welsh from the British Heart Foundation Research Centre at Glasgow University, say the apparent degree of benefit from D3 "seems remarkable," but warn that "several limitations must be considered" before these results are taken as a green light for widespread D3 supplementation.

They suggest healthcare professionals treat all observational data cautiously, and call for new trial data "with a focus on potential risks as well as benefits." And they urge clinicians to avoid costly measurement of vitamin D in patients without bone disease related conditions.

"Some may argue that supplementing those who are apparently "deficient" is cheap, but patients may gain false reassurance from prescription of a "protective" tablet, they write. "To improve health and prevent chronic disease, we should stick to what is proven: encourage better lifestyles in general and target established risk factors in people at elevated risk," they conclude.

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