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## Vitamin D and effects on Fractures, Falls and Bone Mineral Density

The recent study by Bolland and colleagues published in the Lancet Diabetes Endocrinology (Oct 4, 2018) is an updated meta-analysis that evaluated the effects of vitamin D supplementation on fractures, falls and bone mineral density (BMD) in adults. This study analyzed the pooled findings of 81 randomized control trials, collectively involving more than 50,000 participants.

The majority of the trials included in this analysis were of vitamin D alone, with daily doses of more than 800 IU daily, vs. untreated controls, in community-dwelling women age 65-years or older. Trials of high-dose vs. low-dose vitamin D, as well as co-administration of calcium with vitamin D were also included. Study duration was 1 year or less. The primary outcomes were fractures and falls; and the secondary outcome was change in BMD from baseline at the lumbar spine, total hip, femoral neck, total body, and forearm (1).

This meta-analysis found that vitamin D supplementation did not have an effect on the risk of fractures or falls, and there were no meaningful effects on BMD. The authors also concluded that there were no differences between the effects of higher and lower doses of vitamin D (1).

In more than half of the trials, subjects had a baseline vitamin D level (25OHD) of <50 nmol/L (a cutoff considered by many including the Endocrine Society (2) to indicate vitamin D insufficiency), and almost all had a baseline 25OHD <75 nmol/L. Only four trials (6%) studied people with vitamin D deficiency (25OHD <25 nmol/L), in whom vitamin D supplementation may produce different results. Since there is large variability in how vitamin D levels respond to fixed doses of vitamin D (most studies used 1000 IU per day or less), 25OHD levels may not have reached the target range of interest in these studies.

The finding that vitamin D alone may not prevent fractures, falls or improve BMD is consistent with prior published studies. While studies have shown little impact on outcomes when vitamin D or calcium are used separately, a review of trials of calcium and vitamin D used together in individuals living in long-term care showed benefit (3). The current meta-analysis by Bolland included only 20 trials (25%) of vitamin D taken with calcium vs. calcium alone, and did not include studies that compared vitamin D used together with calcium vs. no treatment.

Although the major strength of the current study lies in the large number of studies included in the analysis, it is important to recognize potential limitations including the heterogeneity of populations, study designs and results of the studies in the meta-analysis. Importantly, this study did not specifically address the vitamin D requirements of individuals with osteoporosis,

those with risk factors for osteoporotic fractures, or those with risk factors for vitamin D deficiency.

It is important to remember that vitamin D is needed for optimal calcium absorption from the gut, and plays an important role in calcium balance and bone mineralization. Inadequate vitamin D can result in poor bone mineralization, as well as bone loss due to a rise in parathyroid hormone levels.

Although this study suggests that routine vitamin D supplementation, in particular, high dose vitamin D, may not be necessary for healthy individuals in the general population, these findings cannot be applied to people with osteoporosis, or to those with risk factors for fractures or vitamin D deficiency.

Osteoporosis Canada recommends that individuals with osteoporosis or with risk factors for fractures receive adequate vitamin D, as recommended at 800-2000 IU per day (4), however vitamin D dosing may require adjustment in order to achieve the adequate 25OHD level needed for optimal calcium homeostasis. Further studies are needed to clarify the optimal 25OHD level for those with osteoporosis or with risk factors for fracture. High dose vitamin D supplementation should be avoided due to potential harms (5). There are large randomized trials currently ongoing to help answer questions about effects of vitamin D supplementation on other aspects of health (6).

Appropriate osteoporosis medication may be required for those at high fracture risk. It is important to note that clinical trials showing the effectiveness of osteoporosis medications all included vitamin D and calcium as part of the treatment regimen.

#### References:

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