

# For adult bone health, low on Vitamin D and generous on Calcium

Comment on the IOM recommendations released on November 30<sup>th</sup> 2010(1)

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*Most evidence on vitamin D and calcium is available for bone health. Thus the recommendations of the IOM panel are largely based on bone health and call for 600 IUs vitamin D daily for all ages up to age 70 and 800 IUs after age 71. This assumes that most people get little sun exposure. The panel raised the safe upper limit of 2000 IU daily to 4000 IUs for adults, and declares a safe upper limit of 1000 to 3000 IU per day in children depending on their age. According to the IOM, serum concentrations of 50 nmol/l is sufficient for 97% of the population, including bone health as the main endpoint.*



While the IOM recommendation of an increase in vitamin D intake is supported by the available data from double-blind RCTs of fracture risk, a threshold of 50 nmol/l for its 25(OH)D blood level is not. In two 2009 meta-analyses of double-blind RCTs, a threshold of 50 nmol/l was insufficient for fracture or fall reduction based on achieved 25(OH)D levels in the treatment groups (2, 3). Also, in the very large population-based NHANES analysis, bone density increased with higher 25(OH)D levels far beyond 50 nmol/l in younger and older adults suggesting that the IOM threshold recommendation is too low for optimal bone health in adults (4). In contrast to the IOM report, the IOF recommended in their 2010 position paper on vitamin D a threshold of 75 nmol/l for optimal fall and fracture reduction and recommended 800 to 1000 IU vitamin D per day for seniors age 60 years and older (5).

With the IOM recommendation of 600 to 800 IU vitamin D, most healthy adults will reach 50 nmol/l 25(OH)D but not optimal bone health with respect to hip bone density or fracture reduction. Despite evi-

dence from several double-blind RCTs and a meta-analysis summarizing these data (3), the IOM report concluded that there is inconsistent evidence on vitamin D and fall prevention. In contrast to the IOM report, the evidence of the effect of vitamin D supplementation at a dose of 700 to 1000 IU vitamin D per day on fall reduction was acknowledged by the 2010 IOF position paper on vitamin D (5).

Although benefits of serum concentrations of 25(OH)D higher than 50 nmol/l on endpoints other than bone health have not been documented by randomized trials, the evidence for benefit is quite strong for some, especially colorectal cancer (6). The IOM conclusion that intakes of vitamin D are adequate for most of the US population assumes that lack of randomized trials means lack of benefit, which seems illogical. At a minimum, the conclusion should indicate uncertainty about benefit of higher intakes and blood levels. In support of a greater safety margin in research and supplementation strategies, the IOM doubled the safe upper limit from 2000 IU to 4000 IU vitamin D per day, which is appropriate.

*The new recommendations of the IOM call for a calcium intake from all sources ranging from 700 milligrams for children aged 1 to 3 up to 1200 milligrams for women 51 and older. Compared to the last IOM report, calcium recommendations remained largely the same with a small reduction for men age 50 to 70 to 1000 from 1200 milligrams per day. The panel confirms a safe upper limit of 2000 to 3000 mg calcium per day for adults.*

The calcium recommendations in different age groups are largely based on calcium balance studies lasting only 7 to 12 days, which is likely to be misleading with respect to long term calcium needs. Less data is available to substantiate recommendations with respect to clinical endpoints including bone density and fracture reduction. Notably, in the large population-based NHANES study, there was no overall relation between intake of calcium and hip bone density. Only at 25(OH)D levels below 50 nmol/l, a greater calcium intake was associated with hip bone density among women (7). Further, in two meta-analyses of randomized trials of calcium supplements alone compared

with placebo there was no significant effect on fracture risk (8, 9). Notably, however, in one meta-analysis of 4 double-blind RCTs an adverse effect of calcium supplementation at a dose between 1000 and 1200 mg per day on hip fracture risk could not be excluded and no dose-response relation between dietary calcium intake and risk of hip fractures was documented in a meta-analysis of large cohort studies (9).

Further, the apparent lack of benefit for high calcium intake on bone density increase or fracture reduction together with recent data on the possible adverse effects of calcium supplements on cardiovascular health (10) and nephrolithiasis (11), may make the IOM safe upper limit for calcium intake appear too high. We note that the WHO has suggested that 500 mg of calcium per day is an adequate intake.

*Finally, the IOM states that more data regarding the interaction of vitamin D and calcium on bone health are needed and no recommendation was provided on their combination.*

Notably, several data suggest that vitamin D increases calcium absorption (12) and that a higher intake of calcium beyond 800 mg per day may not contribute to PTH suppression (13) and hip bone density (7) if 25(OH)D levels are above 40 to 50 nmol/l. In the trials that tested vitamin D plus calcium for fracture reduction confounding by calcium intake cannot be completely eliminated, but two observations are important:

- in one 2009 meta-analysis of double-blind RCTs, fracture reduction was the

same for the main effect of vitamin D and trials that combined vitamin D with calcium if the adherence-adjusted vitamin D dose was more than 480 IU per day (2);

- calcium supplementation by itself did not reduce risk of fractures (9). As noted in the IOM review, in the analysis of NHANES data with more than 9000 subjects, calcium intake was associated with hip bone density only among women with low 25(OH)D levels; in all other groups there was no relation between calcium intake and bone density. In contrast, 25(OH)D levels were consistently and positively associated with hip bone density (7). Thus, with adequate 25(OH)D levels or sufficient vitamin D intake, higher calcium intakes may not be correlated with bone health. Thus, calcium recommendations could be downward adjusted with vitamin D supplementation – possibly also for safety reasons. This has not been considered by the IOM report.

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