Are Current Calcium Recommendations for Adolescents Higher than Needed to Achieve Optimal Peak Bone Mass? The Controversy

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Introduction

The current dietary reference intakes (DRI)7 for calcium for North America were set by the Food and Nutrition Board a decade ago. As pediatric calcium researchers, we considered the need for revising the recommended intakes for calcium in children in light of issues and evidence that have emerged since the mid-1990s. We approached the question of whether or not calcium requirements are unnecessarily high in the form of a debate. In this commentary, our goal is not to systematically review the evidence base for considering revision of calcium intakes, but rather to discuss the pros and cons of changing calcium requirements for building peak bone mass in light of recent evidence. A particular emphasis is given to statistical issues that arise in long-term intervention studies and how these issues influence the impact of the findings.

Current calcium intake recommendations for North America were published by the Institute of Medicine in 1997 (1). The panel considered calcium recommendations from several points of view, including published randomized, controlled trials (RCT), applying the factorial approach that accounted for daily calcium losses plus growth needs, adjusted for fractional calcium absorption, and the intake to achieve maximal calcium retention. The latter approach was prioritized because reports of calcium retention over a range of calcium intakes were available in adolescents, whereas dose-response RCT with bone outcome measures were not. The intake for maximal calcium retention was determined to be 1300 mg/d, using a nonlinear regression model (2), which became the adequate intake (AI) for ages 9–18 y for North America (1). Calcium retention largely reflects bone mass, because 99% of the body’s calcium is in the skeleton and exists as a constant percentage of bone mineral. Bone mass is an important component of bone strength (3). Thus, the panel reasoned that achieving maximal calcium retention would remove dietary calcium as a limiting factor for maximizing peak bone mass within one’s genetic potential to offer the greatest protection against fracture later in life.

Because the DRI for calcium for adolescents was set as an AI and not an estimated average requirement (EAR) with a derived recommended dietary allowance (RDA), this value should be flagged for reconsideration. The criteria for triggers to stimulate a revision of DRI values were outlined as follows at an Institute of Medicine workshop (4): presence of an AI value, that the nutrient for the age group was identified as a research priority, that substantive new research has emerged, or that the nutrient for the age group would affect important public health policy. For the DRI value for calcium for adolescents, all of these criteria apply. The key considerations for setting recommended intakes for any nutrient are the choice of indicator of nutritional adequacy and the strength of the evidence for that chosen indicator. For calcium recommendations for adolescents, the quality of the evidence should be assessed on the following criteria: availability of dose response data, that a period of adaptation to different intakes of calcium has been included in the study design, that response has been measured for both dietary sources of calcium and calcium supplements, and that data from more than 1 laboratory are available, with adequate representation of males and females and ethnic groups. The debate outlined in this article addresses whether or not sufficient new evidence exists to revise the calcium recommendations for adolescents for North America. The debate is broadly relevant beyond North America because average calcium intakes for females are frequently low, but they range from 800 to 1500 mg/d (5). The percentage of adolescents in 20 countries meeting or exceeding country-specific calcium recommendations was 65% for males and 50% for females (6).

Posing the question

Long-term study of calcium supplementation. Since the mid-1990s, when the current calcium DRI were developed, many new published bone health and calcium kinetic studies in adolescents have become available (7,8). In longitudinal studies of bone, ideal outcome measures are bone mass and bone geometry, which are 2 important components of bone strength. Most...
of the RCT of calcium have used bone densitometry, which measures bone mineral content (BMC) and bone mineral density (BMD) from 2-dimensional images. BMC reflects the amount of mineral in a particular skeletal site and is a better reflection of nutrition-related changes in bone than BMD, which attempts to adjust for size by dividing BMC by the area of the region scanned. This can partially mask any important effects of a nutrient on bone size. Yet, BMD is often reported because it has been shown to predict bone fracture in children (9) and it has better precision in longitudinal studies (10). Studies using either outcome measure should be considered until we have better measures of bone strength.

There is only a single RCT that compares a calcium-supplemented group with a placebo-controlled group from pre-puberty to development of peak bone mass (11). The intervention of 1 g/d in 354 Caucasian girls began at 10 y of age at Tanner stage 2, initially as a 4-y intervention, and then continued for another 3 y until subjects were 18 y old. At the 4 y endpoint, BMD at all primary bone sites, i.e., distal and proximal radius, total body, and metacarpal cortical indices, was reported to be significantly higher in the calcium supplemented group when adjusted for baseline values. At the 7 y endpoint, when the demand for calcium had declined, the advantage of calcium supplementation had disappeared for total body and distal radius BMD. This early acceleration of bone accrual with supplementation, followed by a period where the treatment and control groups become equivalent upon achievement of peak bone mass is called the “catch-up phenomenon.” If true, the important question becomes, “Does recommending higher calcium intakes during puberty matter for bone health if bone mass ends up the same in adulthood?” One possible explanation that may have contributed to the observed convergence of the supplement and placebo groups is an increase over time of the correlation between dietary calcium intake and compliance. In other words, subjects who were most likely to benefit from the supplement, i.e., those with low dietary intake, were less likely to be compliant over time than those for whom the benefit would be marginal, i.e., those whose dietary intake was adequate. We tested this using summary statistics in the paper. Pill-taking compliance was similar for the supplement and placebo groups for the first 4-y period (70 vs. 71%). For the entire 7-y period, compliance declined over time but remained similar between groups (65 vs. 66%). The standard deviations ranged from 20 to 22%, suggesting that the distributions are skewed to the left with a relatively long tail corresponding to low compliance. Mean supplementary intake (difference between the total calcium intake and the dietary calcium intake) declined from 778 mg/d at age 12 to a low of 472 mg/d at age 18, a value less than half of the protocol value of 1000 mg/d. The dietary calcium intakes of both the supplemented and placebo groups were roughly constant at ~850 mg/d with standard deviations of ~330 mg/d.

An unexpected result was that, along with the decline in mean total intakes and sample size, there was a corresponding substantial increase in the standard deviations of total calcium intake, which went from ~350 mg/d at age 12 y to 570 at age 18 y. To explore this consequence of the increase in standard deviations, we used the standard deviation of the total intake and the standard deviation of the dietary intake, along with an assumed standard deviation of the supplementary intake based on the pill compliance (22% of 1000 mg is 220 mg). At age 12 y, or early in the study, the estimated correlation was essentially 0 (-0.04); it rose to 0.10 at age 15 y, and to 0.68 at age 16.5 y. In summary, the observed lack of statistical significance for distal radius BMD and total body BMD at y 7 vs. a positive supplement benefit at y 4 can be explained, at least in part, by a change in compliance over time.

Also relevant may be the unequal completion rates, i.e., 69 and 58% at y 4 and 58 and 48% at y 7 for the placebo and calcium supplement groups, respectively.

**Pro Position: It is prudent to maintain the current AI for calcium during adolescence**

**Further evidence to support current requirements.** Current calcium recommendations for adolescents using the intake for maximal retention were based on white girls (1). Since then, maximal retention has been observed over a range of calcium intakes for white boys (12) and black girls (13). The intake for maximal retention was not significantly different from the 1300 mg/d determined for white girls. Thus, general relevance of the current recommended intakes has been demonstrated for adolescents.

A consistent benefit of calcium supplements on bone in children and adolescents has been observed in the >15 RCT in children (14). Most of these studies intervened for 1–2 y and typical increases in bone mineral mass were ~1% per year, despite considerable variability in characteristics such as age, baseline calcium intake, and the type and amount of calcium supplemented. In a recent report (15), benefits of an early 1-y supplementation trial at mean age 7.9 y persisted until mean age 16.4 y in girls who had below-median age of onset of menarche. In the long-term calcium supplementation trial by Matkovic et al. (11), longitudinal patterns of BMD at all primary bone sites, i.e., distal and proximal radius, total body, and metacarpal cortical indices, were significantly higher in the calcium supplemented group than in the placebo group.

**Potential risks of lowering calcium requirements.** When making dietary calcium recommendations for bone health, it is important to remember that there is no cure for skeletal fragility fractures, only treatments. Therefore, prevention is the best strategy, according to the 2004 Surgeon General’s report (16).

Calcium has 2 major functions in bone health. One is structural; calcium constitutes the largest portion of mineral content. Increasing mass is one parameter of increasing bone strength. Pubertal girls only partially adapt to low calcium intakes and suffer from negative calcium balance (17). The second function is to reduce bone resorption. For every milligram of additional calcium absorbed in adolescents, bone resorption was decreased by a similar amount, resulting in more positive bone balance (18). Reduced bone turnover by increased dietary calcium has been proposed to reduce skeletal fragility by a separate mechanism from change in bone mass (19). The advantage to bone occurs long before differences in bone mineral density measures can be distinguished.

Current calcium recommendations are questioned as being impractically high and not of sufficient benefit to warrant the effort to achieve them. Further, it is argued that inadequate intakes will merely slow skeletal accretion and peak bone mass will ultimately be equivalent. The argument was intensified by a metaanalysis that concluded that the role of calcium supplementation in improving BMD in children is modest (8). It would be useful to have this type of analysis for BMC, bone geometry, and fracture risk for dietary calcium, rather than from calcium from supplements. Food sources of calcium may increase bone accretion more than calcium supplementation, possibly from coexisting nutrients or from better compliance. RCT suffer from lack of control of calcium intake. Methods and pitfalls for
assessing calcium intake have been discussed (20). Even if assessment of compliance of supplement intake is good, knowledge of calcium intake from self-selected diets is extremely poor. Animal studies, which have the benefits of controlled calcium intakes and good long-term bone outcome measures, show that the "catch-up phenomenon" does not happen for all bone measures, but that it does for others, when animals are given inadequate calcium intakes during growth followed by adequate calcium intakes later (21). Catch-up growth was not observed in the Matkovic et al. study in girls for taller girls (11) or at the hip in the whole cohort (22). Unfortunately, the measure was not taken at baseline, which calls into question the assumption of equal groups. Even if catch-up growth were possible, fracture risk is higher during the lag years when BMD is already relatively low before consolidation of bone mineral (23).

**Summary Pro position:** Current calcium AI for adolescents should be maintained to optimize calcium retention and reduce bone turnover. Additional evidence supports the current requirements and general relevance. Evidence for "catch-up" growth is equivocal for taller individuals and some skeletal sites. Lowering calcium requirements has the potential for long-term increased risk of fracture and has no known benefit. Thus, the best strategy is to do no harm.

**Con Position: Current DRI values for calcium may be excessive**

**Controlled trials have not clearly shown a benefit to calcium supplementation.** Current calcium intakes are higher than necessary because short-term RCT show only modest skeletal benefits, benefits to supplementation during the intervention do not persist after stopping treatment, and temporary acceleration in bone mineral accretion with supplementation does not result in increased peak bone mass. A Cochrane review of calcium supplementation on BMD in children concluded that benefits of calcium supplementation were small and only for total body bone mineral and upper limb BMD, not hip or spine, that benefits may apply to those on initial low calcium intakes, and that there was a lack of persistent benefit in bone mass following supplementation (8,24).

The absence of a sustained benefit to calcium supplementation after stopping supplementation, relative to placebo, in adolescents is supported by several studies (25,26). In Swiss adolescents, a benefit of a milk-based supplement for 1 y to bone mineral outcomes was sustained at 3.5 y (27) but not at 7.5 y (15). Lack of sustained benefit might have been related to sample-size issues, variability in usual calcium intake, compliance over a long time period, and failure to completely account for the bone-remodeling transient (28).

Despite continuous supplementation in the Matkovic et al. study (11) discussed earlier, there were few, if any, persistent advantages for the supplement group in the primary outcomes at 7 y. A post hoc analysis of the Matkovic et al. study (11) indicated that supplementation was beneficial throughout the course of the study for "tall" girls (those whose height at the end of the study was greater than the median) but not for "short" girls. This finding suggests genetic regulation of calcium utilization, consistent with the identified relationship in both children and adults between height and calcium absorption (29,30). Taken as a whole, this study does not resolve the question or provide evidence in favor of maintaining a dietary recommendation above usual intakes.

Further questions about the benefits of high calcium intakes during adolescence have come from a longitudinal study of calcium intake, exercise, and bone mass (and strength) from Pennsylvania State University (31). In this study in females, gains in bone mineral mass associated with supplementation over 4 y during early puberty were not maintained after supplementation was stopped. Furthermore, overall variations of calcium intakes between ~600 and 1400 mg/d of calcium from ages 12 y to 20–22 y were not reflected in variations in total body bone mass increment. There were few subjects with calcium intakes below <800 mg/d, making it impossible to determine a lower level of intake that provided adequate bone outcomes.

**Calcium intakes have not achieved targets despite considerable effort: Is it time to refocus the effort?** Although DRI values do not need to reflect population intake, when there is a large discrepancy it is prudent to evaluate the causes and implications of this discrepancy and consider the role of the DRI values in public policy. This problem is particularly acute for calcium, in which there are no EAR or RDA values, only an AI. Therefore, the additional guidance provided by the new DRI approach is not available and only a single target number exists.

Despite considerable and widespread public health campaigns of all forms, calcium intake in adolescents, especially girls, remains far below the target AI set by the Food and Nutrition Board. Consistent with data over the past 20 y, current mean calcium intakes are ~800–900 mg/d in girls and 950–1050 mg/d in boys during puberty, with median intakes as much as 100 mg lower than the means and with as many as 20–30% of girls with extremely low intakes (<500 mg/d) (1,32). Calcium intakes are generally lower for non-Caucasians than for Caucasians, largely due to less dairy intake among non-Caucasians (33). There is no evidence that messaging, such as the widespread publicity of a "calcium crisis," the extensive use of media advertising, or policy statements by groups such as the American Academy of Pediatrics (34) and the National Institutes of Child Health and Disease have had any substantial effect on the behavior of adolescents in increasing their calcium intake. Excluding an unlikely mandatory fortification of staple products such as flour, it seems unreasonable to expect a large change in the near future in calcium intake, and, therefore, the implications of current dietary practices and guidelines should be reconsidered. Calcium requirements may be lower for children who are physically active, vitamin D replete, and have lower salt intakes. These are other lifestyle changes that could be targeted in bone health education.

**Summary Con position.** Data from controlled trials with follow-up studies provide strong evidence that the modest benefits of calcium supplementation on bone mineralization seen in prepubertal or early pubertal children are followed by partial, if not nearly complete, catch up. A recent Cochrane review of this topic also supported the lack of any significant persistent benefit in bone mass following supplementation. Rather than focus on meeting the current AI, efforts should be placed on emphasizing the prevention of extremely low calcium intakes and focusing on other crucial modifiable aspects of bone health.

**Future recommendations and areas for research**

Several key gaps in knowledge remain when assessing calcium intake requirements in children and adolescents. Published studies

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**References:**

1. Atkinson et al. (1986)...

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5. **Future recommendations and areas for research**

Several key gaps in knowledge remain when assessing calcium intake requirements in children and adolescents. Published studies...
in humans that address the role of dietary calcium in developing peak bone mass suffer from inaccuracies in the independent and/or the dependent variables. Short-term metabolic balance studies used to determine calcium intake for optimal retention have good control of calcium intake, but rely on highly variable, short-term outcome measures that may not predict long-term fracture risk. RCT in children have bone measures as an outcome, but none use a range of controlled calcium intakes. The primary research gap is an adequately powered long-term RCT of a range of calcium intakes that spans prepuberty to achievement of peak bone mass, with outcome measures that include not only bone mass acquisition, but also bone geometry, to better assess fracture. Fracture outcomes may be desired, but measures of bone strength are more practical in children.

Determining requirements for a single nutrient in the context of bone health outcome is too simplistic. Other factors that influence bone health include nutrients other than calcium, such as vitamin D, vitamin K, salt, homocysteine, vitamin B-12, protein, and fatty acids, as well as fruit and vegetable intake. More mechanistic and descriptive research is needed to elucidate how variability in overall dietary quality and composition of the diet might influence calcium intake requirements, bone acquisition, bone composition, and bone quality among children. Mechanical loading can also modify the mass, geometry, and structural strength of the developing skeleton. Limited information is currently available on interactions between diet and exercise. Multiple genetic loci are integral to bone accrual, and combinations of genotypes at several loci may be as important as a single genotype for determining BMD and BMC among children (35). In children, polymorphisms of the vitamin D receptor Fok1 gene have been associated with variations in calcium absorption and rates of bone mineralization, and these effects may be dependent on usual calcium intake but have not been measured in calcium supplementation trials (36).

Are there vulnerable pediatric populations? Pediatric calcium intervention studies to date have primarily focused on Caucasian populations typically consuming habitual calcium intakes >700 mg/d (8). Although homeostatic mechanisms exist to increase fractional calcium absorption and limit urinary calcium losses when calcium in the diet is limited (<400 mg/d), net deficits are at least 200 mg/d when compared with intakes of 1200 mg/d (17).

The current DRI guidelines do not advocate an increase in calcium intake during pregnancy and lactation, irrespective of age (1). Relationships between calcium intake and retention may differ when the physiological challenges of pregnancy are superimposed on the adolescent need of calcium for bone acquisition. Based on recent investigations, pregnant adolescents may benefit from higher calcium intakes during pregnancy (37).

Over the past decade, important advances relevant to calcium requirements have been made, and new information is available for many of the areas of needed research that have been previously identified. Although an AI is not the same as RDA, its use for calcium has been very similar in practice.

Although longer-term studies on a range of calcium intakes to determine intakes for maximizing peak bone mass are desirable, there is now a wealth of shorter-term studies with outcomes that indicate skeletal acquisition in adolescents and younger children and affirm current calcium recommendations. Data are certainly now available that would support development of EAR for calcium for all ages. Crucial uses of this information include: 1) guidance for the development of food labels and similar indicators of mineral content; 2) reformulation of tables and graphs to indicate intake frequencies below the EAR and RDA to more accurately reflect population deficiencies; 3) consideration of factors that might alter the EAR for specific populations, based on genetic or environmental factors; and 4) guidance for future research into the interaction of various dietary intakes and noncalcium factors involved in bone health.

### Literature Cited


