



## CLINICAL REPORT

## Optimizing Bone Health in Children and Adolescents

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COMMITTEE ON NUTRITION**KEY WORDS**calcium, dual-energy x-ray absorptiometry, DXA, osteoporosis,  
pediatrics, vitamin D**ABBREVIATIONS**1,25-OH<sub>2</sub>-D—1,25 dihydroxyvitamin D  
25-OH-D—25-hydroxyvitamin D  
AAP—Academy of Pediatrics  
BMC—bone mineral content  
BMD—bone mineral density  
DMPA—depot medroxyprogesterone acetate  
DXA—dual-energy x-ray absorptiometry  
IGF-1—insulin-like growth factor 1  
IOM—Institute of Medicine  
PTH—parathyroid hormone  
RDA—recommended dietary allowance

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The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

This clinical report has been endorsed by American Bone Health, a national, community-based organization that provides education programs, tools, and resources to help the public understand bone disease and bone health.

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## abstract

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The pediatrician plays a major role in helping optimize bone health in children and adolescents. This clinical report reviews normal bone acquisition in infants, children, and adolescents and discusses factors affecting bone health in this age group. Previous recommended daily allowances for calcium and vitamin D are updated, and clinical guidance is provided regarding weight-bearing activities and recommendations for calcium and vitamin D intake and supplementation. Routine calcium supplementation is not recommended for healthy children and adolescents, but increased dietary intake to meet daily requirements is encouraged. The American Academy of Pediatrics endorses the higher recommended dietary allowances for vitamin D advised by the Institute of Medicine and supports testing for vitamin D deficiency in children and adolescents with conditions associated with increased bone fragility. Universal screening for vitamin D deficiency is not routinely recommended in healthy children or in children with dark skin or obesity because there is insufficient evidence of the cost-benefit of such a practice in reducing fracture risk. The preferred test to assess bone health is dual-energy x-ray absorptiometry, but caution is advised when interpreting results in children and adolescents who may not yet have achieved peak bone mass. For analyses, z scores should be used instead of T scores, and corrections should be made for size. Office-based strategies for the pediatrician to optimize bone health are provided. This clinical report has been endorsed by American Bone Health. *Pediatrics* 2014;134:e1229–e1243

The antecedents of osteoporosis are established in childhood and adolescence, and the pediatrician plays a major role in helping optimize bone health in the pediatric age group. Osteoporosis, a disease of increased bone fragility, is a major cause of morbidity and economic burden worldwide. It is estimated that by the year 2020, one-half of Americans older than 50 years will be at risk for osteoporotic fractures.<sup>1</sup> Once thought to be an inevitable part of aging, osteoporosis is now considered to have its roots in childhood, when preliminary preventative efforts can be initiated. In fact, bone mass attained in early life is thought to be the most important modifiable determinant of lifelong skeletal health.<sup>2</sup> Osteoporosis is not restricted to adults; it can occur in children and adolescents. The aim of the present clinical report was to review bone acquisition during infancy, childhood, and adolescence; discuss assessment of bone health, particularly as it applies to children and adolescents; and update pediatricians on strategies to improve bone health in the pediatric age group. Bone

health needs of pregnant women, lactating mothers, and preterm infants are discussed elsewhere.<sup>3,4</sup> This clinical report has been endorsed by American Bone Health, a national, community-based organization that provides education programs, tools, and resources to help the public understand bone disease and bone health.

## BONE ACQUISITION DURING CHILDHOOD AND ADOLESCENCE

Bone is a living structure comprising a matrix of collagen, hydroxyapatite crystals, and noncollagenous proteins. The matrix becomes mineralized with deposits of calcium and phosphate, which confers strength to the structure. Bone mineral deposition begins during pregnancy, with two-thirds of in utero accrual occurring during the third trimester.<sup>5</sup> Bone mineral content (BMC) increases 40-fold from birth until adulthood, and peak bone mass is achieved toward the end of the second decade of life, although there may still be some net bone deposition into the third decade.<sup>6–11</sup> Approximately 40% to 60% of adult bone mass is accrued during the adolescent years, with 25% of peak bone mass acquired during the 2-year period around peak height velocity. After infancy, peak bone mineral accretion rates occur, on average, at 12.5 years for girls and 14.0 years for boys.<sup>12</sup> At age 18 years, approximately 90% of peak bone mass has been accrued.<sup>13</sup> Childhood and adolescence, therefore, are critical periods for skeletal mineralization. Age of peak bone mass accrual lags behind age of peak height velocity by approximately 6 to 12 months in both boys and girls.<sup>12</sup> This dissociation between linear growth and bone mineral accrual may confer increased vulnerability to bone fragility and may explain, to some degree, the increased rate of forearm fractures in boys 10 through 14 years of age and

in girls 8 through 12 years of age.<sup>14,15</sup> After peak bone mass is achieved, there is a slow but progressive decline in bone mass until a theoretical fracture threshold is reached. Any condition interfering with optimal peak bone mass accrual can, therefore, increase fracture risk later in life.

The skeleton is an active organ, constantly undergoing remodeling, even after linear growth has been completed. During remodeling, bone formation, mediated via osteoblasts, and bone resorption, mediated by osteoclasts, occur concurrently. Remodeling is regulated by local cytokines as well as by circulating hormones, including parathyroid hormone (PTH), 1,25-dihydroxyvitamin D (1,25-OH<sub>2</sub>-D), insulin-like growth factor 1 (IGF-1), and calcitonin. In young children, the rate of cortical bone remodeling is as high as 50% per year. Net bone mass depends on the balance between bone resorption and bone formation. If formation exceeds resorption, as it should during childhood and adolescence, net bone mass increases. If resorption exceeds formation, net bone mass is reduced.

### PRIMARY PREVENTION: OPTIMIZING BONE HEALTH IN HEALTHY CHILDREN

Factors affecting bone health are shown in Table 1. Genetic factors account for approximately 70% of the variance in bone mass,<sup>16</sup> although no specific responsible genes have been identified. Male subjects have higher bone mass than female subjects, and black women have higher bone mass than white non-Hispanic women or Asian women. Mexican-American women have bone densities between those of white non-Hispanic and black women. Modifiable determinants of bone mass include nutritional intake of calcium, vitamin D, protein, sodium, and carbonated beverages (ie, soda); exercise and lifestyle;

**TABLE 1** Factors Affecting Bone Mass

Nonmodifiable
Genetics
Gender
Ethnicity
Modifiable
Nutrition
Calcium
Vitamin D
Sodium
Protein
Soda
Exercise and lifestyle
Body weight and composition
Hormonal status

maintenance of a healthy body weight; and hormonal status. Nutrition and physical activity are each necessary and function synergistically to improve bone acquisition and maintenance.

### CALCIUM

Calcium is necessary for bone accretion, and dietary calcium intake during infancy, childhood, and adolescence affects bone mass acquisition. Approximately 99% of total body calcium is found in the skeleton, and calcium is absorbed by both passive and active transport, the latter mediated by vitamin D. Milk intake during childhood and adolescence is associated with higher BMC and reduced fracture risk in adulthood.<sup>17</sup> The Institute of Medicine (IOM) has published updated dietary reference intakes for calcium and vitamin D, and the American Academy of Pediatrics (AAP) endorses these recommendations for infants, children, and adolescents (Table 2).<sup>18</sup> The recommended dietary allowance (RDA) is the dietary intake that meets the requirements of almost all (97.5%) of the population. Adequate intake is a single value likely to meet the needs of most children and is used for infants younger than 12 months, for whom RDAs have not been established. The upper limit represents the highest average total daily intake likely to pose no risk

of adverse health effects for most people in that age group.

## Sources of Calcium

### Term Infants and Children

The primary source of nutrition for healthy term infants in the first year of life is human milk or, alternatively, infant formula if human milk is not available. Although the BMC may be higher in formula-fed infants than in breastfed infants in the first year of life, the breastfed infant does not demonstrate any evidence of clinical mineral deficiency, and there is no evidence that the breastfed infant should not be the standard for bone mineral accretion. No data support high mineral intake or supplementation with calcium for healthy breastfed infants.<sup>19</sup> After the first year of life, the major source of dietary calcium is milk and other dairy products, which together account for 70% to 80% of dietary calcium intake. Each 8-oz (240-mL) serving of milk provides approximately 300 mg of calcium, and the calcium content of low-fat or flavored milk is similar to that of whole milk (Table 3).<sup>20</sup> However, low-fat chocolate milk contains added sugar and more calories than does low-fat plain milk. One cup of yogurt or 1.5 oz of natural cheese each provides approximately 300 mg of calcium. Other dietary sources of calcium include green leafy vegetables, legumes, nuts, and calcium-fortified breakfast

cereals and fruit juices. Vegetables contributed approximately 7% of the calcium in the food supply between 2000 and 2006.<sup>21</sup> Bioavailability of calcium from vegetables is generally high but is reduced by binding with oxalates in spinach, collard greens, rhubarb, and beans. Although vegetables are a good source of bioavailable calcium, the quantity of vegetables required to meet daily requirements is substantial, making it difficult to attain dietary calcium requirements with vegetables alone. Certain cereals (eg, whole bran cereals) contain phytates, which also reduce bioavailability.

### Preadolescents and Adolescents

The calcium RDA for preadolescents and adolescents aged 9 through 18 years is 1300 mg/d. In the United States, the average dietary calcium intake of adolescent girls is 876 mg/d (67% of the RDA), and less than 15% meet the RDA.<sup>22</sup> In 2011, only 14.9% of high school students drank three or more 8-oz servings of milk per day, with only 9.3% of girls doing so.<sup>23</sup> Milk consumption by adolescents has declined at the same time that soda consumption has increased.<sup>24</sup> Some adolescent girls avoid milk products because they consider them to be “fattening.” Such myths should be dispelled. For example, one 8-oz serving of skim milk contains no fat and only approximately 80 kcal, approximately the same caloric content

as an apple. In contrast, a can of soda contains 140 kcal. Furthermore, milk provides protein and a number of important nutrients other than calcium, including vitamin D, phosphorus, and magnesium, which are important in bone health. Milk alternatives, such as soy- or almond-based beverages, may have a reduced amount of bioavailable calcium per glass, even when fortified with calcium.<sup>25</sup> Further research is needed regarding the mineral levels and bioavailability of these beverages. Lactose intolerance occurs in children and adolescents and is more common in black, Hispanic, and Asian subjects. Some of these children and adolescents will be able to tolerate small amounts of dairy products other than milk. Others may benefit from lactose-reduced or lactose-free milks and cheeses and/or lactase enzymes.<sup>26</sup>

## Calcium Supplementation

Although a number of studies have demonstrated a positive effect of calcium supplementation on BMC in healthy children and adolescents,<sup>27,28</sup> a recent meta-analysis of randomized controlled trials examining the effectiveness of calcium supplementation in increasing BMD in healthy children found that there was no effect of calcium supplementation on BMD of the lumbar spine or femoral neck; a small effect was noted on upper-limb BMD and total body BMC equivalent to approximately

**TABLE 2** Calcium and Vitamin D Dietary Reference Intakes

Age	Calcium		Vitamin D	
	RDA (mg/d) (Intake That Meets Needs of $\geq 97.5\%$ of Population)	UL (mg/d) <sup>a</sup>	RDA (IU/d) (Intake That Meets Needs of $\geq 97.5\%$ of Population)	UL (IU/d) <sup>a</sup>
Infants				
0–6 mo	200 <sup>b</sup>	1000	400 <sup>b</sup>	1000
6–12 mo	260 <sup>b</sup>	1500	400 <sup>b</sup>	1500
1–3 y	700	2500	600	2500
4–8 y	1000	2500	600	3000
9–13 y	1300	3000	600	4000
14–18 y	1300	3000	600	4000

<sup>a</sup> Upper limit (UL) indicates level above which there is risk of adverse events. The UL is not intended as a target intake (no consistent evidence of greater benefit at intake levels above the RDA).

<sup>b</sup> Reflects adequate intake reference value rather than RDA. RDAs have not been established for infants.

**TABLE 3** Dietary Sources of Calcium

Food	Serving Size	Calories per Portion	Calcium Content (mg)
<b>Dairy foods</b>			
<b>Milk</b>			
Whole milk	8 oz	149	276
Reduced fat milk (2%)	8 oz	122	293
Low-fat milk (1%)	8 oz	102	305
Skim milk (nonfat)	8 oz	83	299
Reduced-fat chocolate milk (2%)	8 oz	190	275
Low-fat chocolate milk (1%)	8 oz	158	290
<b>Yogurt</b>			
Plain yogurt, low-fat	8 oz	143	415
Fruit yogurt, low-fat	8 oz	232	345
Plain yogurt, nonfat	8 oz	127	452
<b>Cheese</b>			
Romano cheese	1.5 oz	165	452
Swiss cheese	1.5 oz	162	336
Pasteurized processed American cheese	2 oz	187	323
Mozzarella cheese, part skim	1.5 oz	128	311
Cheddar cheese	1.5 oz	171	307
Muenster cheese	1.5 oz	156	305
<b>Nondairy foods</b>			
Salmon	3 oz	76	32
Sardines, canned	3 oz	177	325
White beans, cooked	1 cup	307	191
Broccoli, cooked	1 cup	44	72
Broccoli, raw	1 cup	25	42
Collards, cooked	1 cup	49	226
Spinach, cooked	1 cup	41	249
Spinach, raw	1 cup	7	30
Baked beans, canned	1 cup	680	120
Tomatoes, canned	1 cup	71	84
<b>Calcium-fortified food</b>			
Orange juice	8 oz	117	500
Breakfast cereals	1 cup	100–210	250–1000
Tofu, made with calcium	0.5 cup	94	434
Soy milk, calcium fortified <sup>a</sup>	8 oz	104	299

Data source: Dietary Guidelines for Americans, 2010. Available at: [www.ndb.usda.gov](http://www.ndb.usda.gov).

<sup>a</sup> Not all soy beverages are fortified to this level.

a 1.7% increase in bone mass.<sup>29</sup> The investigators concluded that, from a public health perspective, calcium supplementation of healthy children is unlikely to result in a clinically significant reduction in fracture risk. For most children and adolescents, the emphasis should be on establishing healthy dietary behaviors with a well-balanced diet that includes calcium intake at or near the recommended levels throughout childhood and adolescence. Dietary sources of calcium should be recommended in preference to calcium supplements, not only because of the improved bioavailability of dietary sources of calcium, but also primarily to encourage lifelong healthy dietary habits.

## VITAMIN D

Vitamin D (calciferol) is a fat-soluble hormone necessary for calcium absorption and utilization. Without vitamin D, only 10% to 15% of dietary calcium is absorbed.<sup>30</sup> Vitamin D includes endogenous conversion of vitamin D<sub>2</sub>, ingested animal-derived cholecalciferol (vitamin D<sub>3</sub>), and plant-derived ergocalciferol (vitamin D<sub>2</sub>). Although there is increasing evidence that vitamin D may also have potential benefits on cardiometabolic risk factors, immunity, and cancer prevention, the focus of the present report is on bone health.

In 2011, the IOM revised the RDAs for vitamin D intake to be higher than previous recommendations (Table 2), and

the AAP endorsed these recommendations.<sup>31</sup> Vitamin D deficiency results in rickets in young children (peak incidence: 3–18 months of age) and increased fracture risk in older children, adolescents, and adults. Deficiency is particularly common in those living in northern climates, those with dark skin, and those with inadequate exposure to sunlight, but deficiency also occurs in sunny climates.<sup>32,33</sup> National US data reveal higher rates of vitamin D deficiency in adolescents compared with younger children<sup>34</sup> and increasing prevalence from the 1988–1994 to 2001–2004 data collections.<sup>35</sup> Cross-sectional studies of vitamin D status in adolescents have found deficiency in 17% to 47% of adolescents,<sup>32,33,36,37</sup> with increased risk in black and Hispanic teenagers<sup>33,37,38</sup> and lower vitamin D concentrations in the winter.<sup>36–38</sup> Children and adolescents who are obese are at increased risk,<sup>33,39,40</sup> possibly because of sequestration of vitamin D in body fat. Certain medications, such as anticonvulsant, glucocorticoid, antifungal, and antiretroviral medications, increase requirements and predispose subjects to deficiency. Severe vitamin D deficiency is associated with reduced bone mass in adolescents.<sup>41,42</sup> On the basis of results of a longitudinal prospective study of 6712 physically active girls aged 9 through 15 years, vitamin D intake—not calcium or dairy intake—during childhood is associated with reduced risk of stress fractures.<sup>43</sup>

Vitamin D<sub>3</sub> is synthesized in the skin from 7-dehydrocholesterol on exposure to sunlight, binds to vitamin D-binding protein, and is transported to the liver where it undergoes hydroxylation to form 25-hydroxyvitamin D (25-OH-D). The half-life of 25-OH-D is 2 to 3 weeks, and serum 25-OH-D is a good indicator of vitamin D stores. Circulating 25-OH-D undergoes a second round of hydroxylation in the kidney to form 1,25-OH<sub>2</sub>-D, the active form of the hormone. In



contrast to 25-OH-D, 1,25-OH<sub>2</sub>-D has a half-life of 4 hours.<sup>44</sup> Under control of PTH, 1,25-OH<sub>2</sub>-D promotes intestinal absorption of calcium and phosphorus, increases renal reabsorption of filtered calcium, and mobilizes calcium from skeletal stores.

## Sources of Vitamin D

### Sunlight

Exposure to UV B radiation in the range of 290 to 315 nm from sunlight is the major source of vitamin D. Synthesis of vitamin D depends on latitude, skin pigmentation, sunscreen use, and time of day of exposure. Synthesis of vitamin D is minimal during winter months north of 33° latitude in the northern hemisphere and south of 33° latitude in the southern hemisphere. Exposure of arms and legs to 0.5 minimal erythemal dose of sunlight for 5 to 15 minutes, 2 to 3 times a week, produces approximately 3000 IU of vitamin D.<sup>31</sup> Subjects with dark skin require exposure 3 to 5 times longer. Sunscreen with a sun protection factor 8 or higher effectively prevents transmission of UV B radiation through the skin and blocks the synthesis of vitamin D<sub>3</sub>. Maximal synthesis occurs between the hours of 10:00 AM and 3:00 PM in the spring, summer, and fall.<sup>45</sup> Children and adolescents are spending more time indoors and, because of concerns regarding skin cancer later in life, when they do go outside, they often wear sun protection, which limits the skin's ability to synthesize vitamin D. With decreased synthesis of vitamin D from reduced sun exposure, dietary sources of vitamin D become more important.

### Dietary Sources

Natural dietary sources of vitamin D are limited but include cod liver oil, fatty fish (eg, salmon, sardines, tuna), and fortified foods. Farm-raised salmon has lower concentrations of vitamin D than does fresh, wild-caught salmon.<sup>31</sup> Human milk does not provide adequate amounts of vitamin D (approximately

20 IU/L). In the United States and Canada, all infant formula is fortified with vitamin D. Cow milk, infant formula, and fortified fruit juices each contain approximately 100 IU of vitamin D per 8 oz (Table 4).

## Recommended Daily Intake and Vitamin D Supplementation

Adequate vitamin D intake for infants younger than 1 year is 400 IU/d. The RDA is 600 IU for children 1 year and older. Because human milk contains inadequate amounts of vitamin D (unless the lactating mother is taking supplements of approximately 6000 IU/d), breastfed and partially breastfed infants should be supplemented with 400 IU of vitamin D per day beginning in the first few days of life and continued until the infant has been weaned and is drinking at least 1 L/d of vitamin D–fortified infant formula or cow milk. Daily supplementation of breastfed infants with 400 IU of vitamin D during the first months of life increases 25-OH-D amounts to normal concentrations.<sup>46,47</sup> Although the RDA

for children older than 1 year and for adolescents is 600 IU, children who are obese and children on anticonvulsant, glucocorticoid, antifungal, and anti-retroviral medications may require 2 to 4 times the recommended dose of vitamin D to achieve serum 25-OH-D values the same as children without these conditions; at this time, however, definitive recommendations for these children remain unavailable.

Although approximately 98% of cow milk in the United States is fortified with vitamin D, some yogurts, cheeses, juices, and breakfast cereals are also fortified with similar amounts of vitamin D (Table 4) and can generally be recommended in preference to nonfortified foods. For those who are unable to achieve adequate amounts of vitamin D in their diet or who have vitamin D deficiency, vitamin D supplements are available in 2 forms: vitamin D<sub>2</sub> (ergocalciferol), derived from plants, and vitamin D<sub>3</sub> (cholecalciferol), synthesized by mammals. Drisdol (Sanofi-Aventis US,

**TABLE 4** Sources of Vitamin D

Food	Serving Size	Vitamin D Content <sup>a</sup> (IU)
Natural sources		
Salmon		
Fresh wild	3.5 oz	600–1000
Fresh farmed	3.5 oz	100–250
Sardines, canned	3.5 oz	300
Mackerel, canned	3.5 oz	250
Tuna, canned	3.5 oz	236
Shitake mushroom		
Fresh	3.5 oz	100
Canned	3.5 oz	1600
Egg, hard-boiled	3.5 oz	20
Vitamin D–fortified foods		
Infant formula	1 cup (8 oz)	100
Milk	1 cup (8 oz)	100
Orange juice <sup>b</sup>	1 cup (8 oz)	100
Yogurts <sup>b</sup>	1 cup (8 oz)	100
Cheeses <sup>b</sup>	3 oz	100
Breakfast cereals <sup>b</sup>	1 serving	40–100
Pharmaceutical sources in the United States		
Vitamin D <sub>2</sub> (ergocalciferol)	1 capsule	50 000
Drisdol (vitamin D <sub>2</sub> ) liquid	1 cc	8000
Supplemental sources		
Multivitamin		400, 500, 1000
Vitamin D <sub>3</sub>		400, 800, 1000, 2000, 5000, 10 000, 50 000

<sup>a</sup> The activity of 40 IU of vitamin D is equivalent to 1 µg.

<sup>b</sup> Not all brands of orange juice, yogurt, and cheese are fortified with vitamin D.

Bridgewater, NJ) is a vitamin D<sub>2</sub> preparation that contains 8000 IU/mL, and most multivitamins contain 400 IU per tablet. Some calcium preparations also contain vitamin D. In adolescent girls, supplementation of 200 to 400 IU of vitamin D<sub>3</sub> was effective in increasing BMD in a dose-response manner.<sup>48</sup> The daily upper limits are as follows: infants up to 6 months of age: 1000 IU; infants 6 to 12 months of age: 1500 IU; children 1 through 3 years of age: 2500 IU; children 4 through 8 years of age: 3000 IU; and children and adolescents 9 through 18 years of age: 4000 IU (Table 2).

### Assessment of Vitamin D Status

Measurement of serum 25-OH-D concentration reflects both endogenous synthesis and dietary intake of vitamin D and is the optimal method of assessment of vitamin D status.<sup>45</sup> The 2011 RDAs were selected to ensure that nearly all those who receive the RDA will have a serum 25-OH-D concentration greater than 20 ng/mL. This value was derived on the basis of an assumption of minimal exposure to sunlight and minimal solar vitamin D conversion. The 25-OH-D concentration of 20 ng/mL was also set as a target by the Pediatric Endocrine Society and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition.<sup>44,49</sup> In contrast, the Endocrine Society has defined vitamin D deficiency as a 25-OH-D concentration <20 ng/mL (50 nmol/L) and insufficiency as a 25-OH-D concentration between 21 and 29 ng/mL (52.3–72.5 nmol/L).<sup>45</sup> Controversy remains as to whether there are specific health benefits to a higher target, such as 30 ng/mL or higher, for healthy children. In a population of healthy white Danish and Finnish girls, a daily intake of approximately 750 IU of vitamin D was necessary to enable 97.5% of the subjects to achieve a 25-OH-D concentration above 20 ng/mL, in support of the IOM recommendations.<sup>50</sup>

### Screening for Vitamin D Deficiency

Evidence is insufficient to recommend universal screening for vitamin D deficiency. The Endocrine Society recommends that “at-risk individuals” should be screened; these include children with obesity, black and Hispanic children, children with malabsorption syndromes, and children on glucocorticoid, anticonvulsant, antifungal, and antiretroviral medications.<sup>45</sup> There is concern, however, with these recommendations, because they would involve screening, treating, and retesting large numbers of children without good evidence of the cost–benefit in reducing fracture risk (as opposed to improving serum 25-OH-D concentrations) in a healthy population.<sup>51</sup> For example, black youth have lower 25-OH-D concentrations than do white youth, but black subjects also have higher bone mass and reduced fracture risk. The IOM and existing AAP reports do not make recommendations specific to screening. In the absence of evidence supporting the role of screening healthy individuals at risk for vitamin D deficiency in reducing fracture risk and the potential costs involved, the present AAP report advises screening for vitamin D deficiency only in children and adolescents with conditions associated with reduced bone mass and/or recurrent low-impact fractures. More evidence is needed before recommendations can be made regarding screening of healthy black and Hispanic children or children with obesity. The recommended screening is measuring serum 25-OH-D concentration, and it is important to be sure this test is chosen instead of measurement of the 1,25-OH<sub>2</sub>-D concentration, which has little, if any, predictive value related to bone health.

### Treatment of Vitamin D Deficiency

Both vitamin D<sub>2</sub> and vitamin D<sub>3</sub> increase serum 25-OH-D concentrations. In adults, some<sup>52,53</sup> but not all<sup>54</sup> studies

have suggested that vitamin D<sub>3</sub> is more effective in increasing serum 25-OH-D concentrations than is vitamin D<sub>2</sub>. In infants and toddlers, 2000 IU of vitamin D<sub>2</sub> daily, 2000 IU of vitamin D<sub>3</sub> daily, and 50 000 IU of vitamin D<sub>2</sub> weekly were equivalent in increasing serum 25-OH-D concentrations.<sup>55</sup> Infants and toddlers with vitamin D deficiency can be given 50 000 IU of vitamin D<sub>2</sub> or vitamin D<sub>3</sub> weekly for 6 weeks or 2000 IU of vitamin D<sub>2</sub> or vitamin D<sub>3</sub> daily for 6 weeks, followed by a maintenance dose of 400 to 1000 IU/d. Children and adolescents can be treated with vitamin D<sub>2</sub> or vitamin D<sub>3</sub> (50 000 IU, 1 capsule weekly) for 6 to 8 weeks or 2000 IU of vitamin D<sub>2</sub> or vitamin D<sub>3</sub> daily for 6 to 8 weeks to achieve a serum 25-OH-D concentration greater than 20 ng/mL, followed by a maintenance dose of 600 to 1000 IU/d (Table 5).<sup>18,45</sup> After completion of treatment, repeat serum 25-OH-D concentrations should be obtained. It is not unusual for a second course of treatment to be necessary to achieve adequate concentrations of serum 25-OH-D. There is no strong evidence about whether to treat healthy children who have serum 25-OH-D concentrations between 21 and 29 ng/mL.

### SODA CONSUMPTION, PROTEIN, AND OTHER MINERALS

In 2010, 24.3% of US high school students drank at least 1 serving of soda daily.<sup>56</sup> A recent meta-analysis of 88 studies reported that soda consumption is associated with lower intake of milk and calcium, and larger effect sizes were found with longitudinal and experimental studies compared with cross-sectional studies. The replacement of milk in the diet by soda can prevent adolescents from achieving adequate calcium and vitamin D intake, and because soda consumption has no health benefit, it should be avoided.<sup>57</sup>

Diets low in protein or high in sodium will predispose subjects to reduced

calcium retention.<sup>58,59</sup> Sodium and calcium share the same transport system in the proximal tubule, and a high-sodium diet promotes increased urinary calcium excretion and should be avoided.

## EXERCISE AND LIFESTYLE

Mechanical forces applied to the skeleton (mechanical loading) increase bone formation, and weight-bearing exercise improves bone mineral accrual in children and adolescents.<sup>60</sup> In healthy children, an exercise program incorporating high-impact, low-frequency exercises such as jumping, skipping, and hopping for 10 minutes 3 times a week increased BMD of the femoral neck in the intervention group compared with control subjects.<sup>61–63</sup> The greatest effect was observed in children in early puberty. A population-based prospective controlled trial in Sweden demonstrated that a school-based, moderately active, 4-year exercise program increased bone mass and size in children aged 7 through 9 years without increasing fracture risk.<sup>64</sup> Adolescent female athletes have higher BMD than nonathletes, provided they are menstruating regularly. When female athletes become amenorrheic, the protective effect of exercise on BMD is lost.<sup>65</sup> Children who are immobilized have rapid declines in bone mass.

Increases in BMD are site specific, depending on the loading patterns of the specific sport. For example, BMD is greater in gymnasts at the hip and spine, in runners at the femoral neck, and in rowers at the lumbar spine; tennis players have higher radial BMD in the

dominant arm than in the nondominant arm. High-impact sports (eg, gymnastics, volleyball, karate) or odd-impact sports (eg, soccer, basketball, racquet sports) are associated with higher BMD and enhanced bone geometry.<sup>66</sup>

For most children and adolescents, walking, jogging, jumping, and dancing activities are better for bone health than are swimming or bicycle riding. Excessive high-impact exercise can, however, increase fracture risk. A prospective longitudinal study of 6831 high school girls found that those who participated in more than 8 hours per week of running, basketball, cheerleading, or gymnastics were twice as likely to sustain a fracture compared with less active girls. The authors suggested that girls who participate in these sports should also include cross-training in lower impact activities.<sup>67</sup>

Lifestyle choices may also confer additional risk for BMD deficits. In adults, smoking, caffeine, and alcohol intake are all associated with reduced BMD,<sup>68–70</sup> and these behaviors should be avoided in children and adolescents.

## BODY WEIGHT

Body weight and composition are important modifiable determinants of bone mass. Mechanical loading during weight-bearing activities stimulates bone formation, and multiple studies in healthy adolescents<sup>8,71–73</sup> and in those with anorexia nervosa<sup>74–77</sup> have demonstrated that BMD is directly correlated with BMI. Lean body mass is most strongly associated with BMD,<sup>78</sup> but increased adiposity can also be associated with

increased fracture risk.<sup>79</sup> Maintenance of a healthy body weight during childhood and adolescence is therefore recommended to optimize bone health.

## HORMONAL STATUS

Several hormones affect bone mass. Estrogen plays an important part in maintaining BMD in women, and estrogen deficiency is associated with increased bone resorption and increased fracture risk. Testosterone, growth hormone, and IGF-1 all promote bone formation, whereas glucocorticoid excess both increases bone resorption and impairs bone formation.

## SECONDARY PREVENTION: ASSESSMENT OF POPULATIONS AT RISK FOR INCREASED BONE FRAGILITY

### Conditions Associated With Reduced Bone Mass in Children and Adolescents

Conditions associated with reduced bone mass and increased fracture risk in children and adolescents are listed in Table 6. Osteogenesis imperfecta, idiopathic juvenile osteoporosis, and Turner syndrome are rare conditions with increased bone fragility, best managed by pediatric endocrinologists, geneticists, and specialists in pediatric bone health. Children with chronic illnesses are, however, frequently managed by general pediatricians. Cystic fibrosis, systemic lupus erythematosus, juvenile idiopathic arthritis, inflammatory bowel disease, celiac disease, chronic renal failure, childhood cancers, and cerebral palsy

**TABLE 5** Treatment of Vitamin D Deficiency

Age	Preparation and Dose <sup>a</sup>	
Infants, 0–12 mo	Vitamin D <sub>2</sub> or D <sub>3</sub> 50 000 IU weekly for 6 wk Followed by a maintenance dose of 400–1000 IU daily	or Vitamin D <sub>2</sub> or D <sub>3</sub> 2000 IU daily for 6 wk
Children and adolescents, 1–18 y	Vitamin D <sub>2</sub> or D <sub>3</sub> 50 000 IU weekly for 6–8 wk Followed by a maintenance dose of 600–1000 IU daily	or Vitamin D <sub>2</sub> or D <sub>3</sub> 2000 IU daily for 6–8 wk

Vitamin D<sub>2</sub>, ergocalciferol; vitamin D<sub>3</sub>, cholecalciferol.

<sup>a</sup> Vitamin D<sub>3</sub> may be more potent than vitamin D<sub>2</sub>.

can all be associated with reduced bone mass.<sup>78,80–84</sup> Risk factors include malnutrition, increased metabolic requirements, intestinal malabsorption, low body weight, chronic inflammation with increased cytokine production, hypogonadism, immobilization, and the effects of prolonged glucocorticoid therapy. Children with cerebral palsy are at particular risk. One study found that 77% of children with cerebral palsy had a femoral neck BMD z score less than –2.0, and 26% of children older than 10 years had sustained a fracture.<sup>84</sup>

Eating disorders are prevalent in adolescents.<sup>85</sup> Anorexia nervosa is associated with reduced BMD and increased fracture risk,<sup>74–76,86–89</sup> and the reduction in bone mass occurs after a relatively short duration of illness.<sup>74,90</sup> Etiologic

factors include poor nutrition, low body weight, estrogen deficiency, and hypercortisolism. The degree of reduction of BMD is directly related to the degree of malnutrition, and in girls, is related to the duration of amenorrhea. Low BMD is also found in boys with anorexia nervosa and is associated with low testosterone concentrations.<sup>91</sup> Patients with partial eating disorders or those with bulimia nervosa may also have reduced bone mass, especially if they are or have been of low weight.<sup>89,92,93</sup> The “female athlete triad” refers to 3 interrelated conditions seen in female athletes: low energy availability, menstrual dysfunction, and reduced BMD.<sup>94</sup> Low energy availability refers to inadequate energy intake for the level of physical activity. The energy deficit may be unintentional secondary to a lack of knowledge regarding the increased energy requirements of athletes or it may be intentional and associated with an underlying eating disorder. There is suppression of the hypothalamic-pituitary-ovarian axis, resulting in amenorrhea, a low estrogen state, reduced bone mass, and increased fracture risk.

Endocrine conditions associated with glucocorticoid or PTH excess, hypogonadism, hyperthyroidism, or deficiency of growth hormone or IGF-1 are all associated with low bone mass (Table 6). Certain medications, including anticonvulsants and chemotherapeutic agents, prolonged use of proton pump inhibitors, and selective serotonin reuptake inhibitors, can also have a negative effect on bone mass. Depot medroxyprogesterone acetate (DMPA) is a very effective long-acting contraceptive that has been credited, to some degree, for the reduction in adolescent pregnancy rates in the United States over the past decade. Prolonged use of DMPA in adolescent girls is associated with hypothalamic suppression and reduced bone mass, however.<sup>95</sup> In 2004, the US Food and

Drug Administration issued a black box warning to inform practitioners about the negative effects of DMPA on bone mass. Discontinuation of DMPA is associated with rapid improvements in bone mass, although it is not known how much of potential maximum peak bone mass is recovered.<sup>96</sup> For most adolescents, the risk of fracture while taking DMPA is low, and the benefit of taking the medication outweighs the risks. The Society for Adolescent Health and Medicine recommends continuing to prescribe DMPA to adolescent girls needing contraception but recommends explanation of the risks and benefits.<sup>97</sup> The American College of Obstetrics and Gynecology further states that concerns about the effect of DMPA on BMD should neither prevent practitioners from prescribing it nor limit its use to 2 consecutive years.<sup>98</sup> In adolescent girls, low-dose oral contraceptives containing less than 30 µg of ethinyl estradiol may interfere with peak bone mass acquisition compared with oral contraceptives containing ≥30 µg of ethinyl estradiol.<sup>99,100</sup> Despite a possible reduction in BMD in oral contraceptive users, a recent Cochrane review of observational studies found no association between oral contraceptive use and increased fracture risk.<sup>101</sup>

### Assessment of Bone Health

The ideal method of assessment of clinically relevant bone health is determination of fracture risk on the basis of longitudinal data. However, there is a paucity of longitudinal studies examining factors affecting bone health in children on the basis of incidence of fractures. Fracture risk depends not only on skeletal fragility but also on age, body weight, history of fractures, and the force of an injury. Skeletal fragility, in turn, is dependent on a number of factors in addition to bone mass, including bone size, geometry, microarchitecture, and bending strength. For example, bending strength depends on the radius of a bone,

**TABLE 6** Conditions Associated With Reduced Bone Mass in Children and Adolescents

Genetic conditions
Osteogenesis imperfecta
Idiopathic juvenile osteoporosis
Turner syndrome
Chronic illness
Cystic fibrosis
Connective tissue disorders (lupus, juvenile idiopathic arthritis, juvenile dermatomyositis)
Inflammatory bowel disease, celiac disease
Chronic renal failure
Childhood cancer
Cerebral palsy
Chronic immobilization
Eating disorders, including anorexia nervosa, bulimia nervosa, eating disorders not otherwise specified, and the female athlete triad
Endocrine conditions
Cushing syndrome
Hypogonadism
Hyperthyroidism
Hyperparathyroidism
Growth hormone deficiency
Diabetes mellitus
Medications
Glucocorticoids
Anticonvulsants
Chemotherapy
Leuprolide acetate
Proton pump inhibitors
Selective serotonin reuptake inhibitors
DMPA



and a large bone will be more resistant to fracture than a smaller bone, even when both bones have the same BMC or BMD. Bone mass, which accounts for approximately 70% of bone strength, can be used as a surrogate measure of bone health, recognizing that a low bone mass in children does not necessarily translate to increased fracture risk.

Dual-energy x-ray absorptiometry (DXA) is the preferred method of assessment of bone mass because of its availability, speed, precision, and low dose of radiation (5–6 mSv for the lumbar spine, hip, and whole body, which is less than the radiation exposure of a transcontinental flight and one-tenth that of a standard chest radiograph).<sup>102</sup> DXA measures BMC and calculates areal BMD by dividing BMC by the area of the region scanned. DXA machines are widely available, and robust pediatric reference databases for children older than 5 years are included with the software of the major DXA manufacturers.<sup>103–106</sup> In pediatric patients, the preferred sites of measurement are the lumbar spine and whole body.<sup>107</sup> In children, the hip is less reliable because of variability in positioning and difficulties identifying bony landmarks. Scanning time of the hip or spine is less than 1 minute; for the whole body, it is approximately 5 minutes. In adults, each SD reduction in BMD below the young adult mean doubles the fracture risk. Osteoporosis is operationally defined as a BMD 2.5 or more SDs below the young adult mean (a T score less than  $-2.5$ ), and osteopenia is defined as a BMD  $\geq 1$  SD below the young adult mean (a T score of less than  $-1.0$ ). However, caution should be used in interpreting DXA results in children. First, because children have not yet achieved peak bone mass, z scores (the number of SDs below the age-matched mean) should be used instead of T scores. Second, DXA measures 2-dimensional areal BMD (expressed as grams per square centimeter), as

opposed to 3-dimensional volumetric BMD (expressed in grams per cubic centimeter), and areal BMD underestimates true volumetric BMD in subjects with smaller bones. Third, many children with chronic illness have growth retardation and delayed puberty. Therefore, a correction should be made for height or height age, and a number of mathematical corrections have been proposed.<sup>108–110</sup>

The International Society for Clinical Densitometry recommends that the term “osteopenia” no longer be used in pediatric DXA reports and that the diagnosis of osteoporosis not be made on the basis of DXA results alone.<sup>107</sup> In the pediatric age group, the diagnosis of osteoporosis requires both a low BMD or BMC (defined as a z score less than  $-2$ ) and a clinically significant fracture (defined as a long-bone fracture of the lower extremity, a vertebral compression fracture, or 2 or more long-bone fractures of the upper extremity).<sup>107,111</sup> Longitudinal studies in children and adolescents have demonstrated a high degree of tracking over a period of 3 years.<sup>112</sup> In other words, children with low bone density continue to have low bone density over time. In contrast to adults, in pediatrics, there is no specific BMD z score below which fractures are more likely to occur, but there is a growing body of literature demonstrating an association between low bone mass measured by using DXA and fracture risk in children.<sup>113–115</sup>

Limited evidence is available to guide pediatricians regarding when to order a DXA. In general, a DXA should be performed to identify children and adolescents at risk for skeletal fragility fractures and to guide treatment decisions. The AAP’s “Clinical Report—Bone Densitometry in Children and Adolescents” recommends ordering a DXA for children and adolescents with clinically significant fractures (defined earlier) sustained after minimal trauma

(defined as falling from standing height or less) and in those with medical conditions associated with increased fracture risk.<sup>116</sup> Evidence is insufficient to support obtaining a DXA in children and adolescents taking medications that can adversely affect bone or in healthy children with recurrent traumatic fractures of the fingers or toes. DXA scans are usually repeated after 1 year and should not be repeated at an interval of less than 6 months.

Quantitative computed tomography measures true volumetric BMD, but the radiation exposure dose is high (30–7000 mSv). Newer modalities, such as peripheral quantitative computed tomography, can measure volumetric BMD of the appendicular skeleton with much lower radiation doses but are not widely available for clinical use. Quantitative ultrasonography is a noninvasive method of assessing bone health by measuring speed of an ultrasound wave as it is propagated along the surface of bone. This method is difficult to interpret because of a lack of pediatric reference data, however, and poor precision in the pediatric population.

### **TERTIARY PREVENTION: SPECIFIC TREATMENTS TO INCREASE BONE MASS IN POPULATIONS AT INCREASED RISK OF FRACTURE**

In most chronic diseases associated with low BMD, treatment of the underlying condition helps improve bone mass, and specific interventions will depend on the underlying condition.

#### **Calcium Supplementation**

Depending on the medical condition, for those children and adolescents who are unable to consume enough calcium from dietary sources, including fortified foods, calcium supplementation can be prescribed. The most common forms of supplemental calcium are calcium carbonate (40% elemental calcium) and calcium citrate (21% elemental calcium).

Calcium carbonate should be taken with meals to promote absorption, but calcium citrate does not require gastric acid for absorption and can be taken on an empty stomach.<sup>117</sup> Calcium supplements are available in liquid, tablet, and chewable preparations.

### Treatment of Vitamin D Deficiency

Screening for vitamin D deficiency by obtaining a serum 25-OH-D concentration is recommended in patients at increased risk of bone fragility and in those with recurrent low-impact fractures. Although a serum 25-OH-D concentration of 20 ng/mL is considered normal for healthy children and adolescents, some experts aim for achievement of a serum 25-OH-D concentration above 30 ng/mL in populations at increased risk of fracture, given the potential benefits and unlikely risk of toxicity of doses required to achieve this concentration (the upper limit for a child older than 9 years is 4000 IU/d).<sup>118</sup> Pediatric treatment regimens for vitamin D deficiency are outlined in Table 5.

### Bisphosphonates

Bisphosphonates inhibit osteoclast-mediated bone resorption and have been used to increase BMD and reduce fracture risk in children with osteogenesis imperfecta,<sup>119–121</sup> cerebral palsy,<sup>122</sup> and connective tissue disorders<sup>123,124</sup> and children treated with corticosteroids.<sup>123,125–127</sup> Pilot studies have also been conducted in adolescents with anorexia nervosa.<sup>128</sup> In osteogenesis imperfecta, an open-label study examining the use of cyclic administration of intravenous pamidronate reported reduced pain and fractures associated with dramatic increases in BMD.<sup>119</sup> A recent multicenter, randomized controlled trial found increases in lumbar spine BMD (51% vs 12% in control subjects) with oral alendronate but no significant change in fracture incidence.<sup>121</sup> Use of bisphosphonates in children remains controversial because

of the potential adverse effects of these agents and their long half-lives. Bisphosphonates are incorporated into bone and may be slowly released from the bone even after the medication has been discontinued. Because of the paucity of studies on efficacy and long-term safety, at this time these agents should not be used to treat asymptomatic reduction in bone mass in children, and their use should be restricted to osteogenesis imperfecta and other select conditions with recurrent fractures, severe pain, or vertebral collapse.<sup>129,130</sup>

### Oral Contraceptives

Adolescent girls with anorexia nervosa or the female athlete triad are frequently prescribed oral contraceptives to improve bone mass, even with no evidence of their efficacy.<sup>131</sup> Prospective cohort studies and randomized controlled trials have both shown that oral contraceptives do not increase bone mass in subjects with anorexia nervosa or in female athletes.<sup>75,132–135</sup> Because of this lack of demonstrated efficacy, their use is not recommended to increase bone mass. In girls with anorexia nervosa, oral contraceptives will induce monthly menstruation, which may be incorrectly interpreted as an indication of adequate weight restoration.

## THE ROLE OF THE PEDIATRICIAN

1. Ask about dairy intake, nondairy sources of calcium and vitamin D, use of calcium and/or vitamin D supplements, soda consumption, and type and amount of exercise at health maintenance visits. Suggested ages to ask these questions are 3 years, 9 years, and during the annual adolescent health maintenance visits.
2. Encourage increased dietary intake of calcium- and vitamin D-containing foods and beverages. Dairy products constitute the major source of dietary calcium, but calcium-fortified

drinks and cereals are available. Low-fat dairy products, including nonfat milk and low-fat yogurts, are good sources of calcium. Children 4 through 8 years of age require 2 to 3 servings of dairy products or equivalent per day. Adolescents require 4 servings per day (Table 3). Suggested targeted questions include: “What kind of milk or dairy products do you consume?” “How many servings do you consume a day?” (One serving is an 8-oz glass of milk, an 8-oz yogurt, or 1.5 oz of natural cheese.) “In addition to dairy, what calcium-fortified foods do you buy or have you thought about buying?” Current data do not support routine calcium supplementation for healthy children and adolescents. The RDA of vitamin D for children 1 year and older is 600 IU. Children who are obese and children on anticonvulsant, glucocorticoid, antifungal, or retroviral medications may require higher doses, but specific end points and targets remain poorly defined.

3. Encourage weight-bearing activities. Walking, jumping, skipping, running, and dancing activities are preferable to swimming or cycling to optimize bone health.
4. Routine screening of healthy children and adolescents for vitamin D deficiency is not recommended. Those with conditions associated with reduced bone mass (Table 6) or recurrent low-impact fractures should have a serum 25-OH-D concentration measured. Those who have vitamin D deficiency should be treated and have 25-OH-D concentrations measured after completion of treatment.
5. Consider a DXA in medical conditions associated with reduced bone mass and increased bone fragility and in children and adolescents with clinically significant fractures sustained after minimal trauma. In

children, z scores should be used instead of T scores. In those with growth or maturational delay, corrections should be made for height or height age.

6. In adolescent female subjects, discourage preoccupation with extreme thinness. A DXA should be considered in an adolescent athlete who has been amenorrheic for more than 6 months. Athletes, parents, and coaches should be educated about the female athlete triad. There is no evidence to support prescribing oral contraceptives to increase bone mass in those with anorexia nervosa or the female athlete triad.
7. Until more studies demonstrating safety and efficacy in other popula-

tions have been conducted, use of bisphosphonates in children and adolescents should be restricted to osteogenesis imperfecta and conditions associated with recurrent fractures, severe pain, or vertebral collapse.

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