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Pediatric Bone Health Update

Effective counseling for children's bone health

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ABSTRACT

Poor bone health is a significant contributing factor to the frequency and severity of many childhood injuries and fractures. Osteoporosis starts in childhood. Therefore, it is important to optimize bone health in children in order to decrease the risk of injury, improve healing, and maximize peak bone mass. To do this, pediatricians and pediatric orthopedists need to effectively counsel patients and families to give them the tools necessary to effect lasting change. Bone health is a recipe that requires ingredients including calcium, vitamin D, vitamin C, vitamin K, and physical exercise. Required amounts of each component change as children grow and are lifelong requirements. Unfortunately, at this time, there is no uniform consensus on vitamin D supplementation guidelines or optimal serum levels. Current vitamin D dosing guidelines are age-based, but vitamin D is stored in adipose tissue and higher weights/body mass index (BMI) require higher doses of vitamin D to achieve and maintain adequate serum levels. Routine monitoring of vitamin D is recommended in all patients. However, re-evaluating the dosing guidelines to base them on weight/BMI, rather than age, should be considered.

Key Concepts:

(1) Bone health needs to be prioritized from a young age because the majority of peak bone mass is attained by the end of the second decade of life.
(2) Patient counseling and patient buy-in are imperative to create lasting impact.
(3) Bone health is a recipe and the amounts of ingredients needed will vary according to growth and body size.
(4) Vitamin D dosing should take weight and body mass into consideration to achieve optimal serum levels.

Introduction

In pediatric orthopedic surgery, there is a "busy season, which, in many geographic areas occurs in the spring and summer when more children get injured, and the volume of fractures increases. It is easy to say that this happens because more children are outside playing, there is more involvement in seasonal sports, or that days are longer allowing for more outdoor playtime. All of these theories are true; however, a substantial contributing factor may be poor bone health. Bone health refers to the bone's strength and ability to resist injury. When children go through a growth spurt in adolescence, there is also a natural period of weakened bone. This phenomenon is caused by the increased cortical porosity due to increased intracortical bone turnover, creating an increased fracture risk in both males and females [1–3]. This risk is amplified in patients who are starting with poor bone health [3]. The ideal time to counsel patients and families about bone health is before the growth spurt and before an injury happens, but this conversation becomes imperative once a patient sustains a fracture or injury.

It has also been shown that the opportunity to maximize bone strength during one's lifetime is time-dependent [4,5]. The large majority of peak bone mass is obtained by the end of the second decade with women reaching peak bone mass earlier than men [3–6]. Many patients and families are unfamiliar with this concept. Unfortunately, if bone mass is not maximized by this age, it cannot be fixed later in life [4–6]. The purpose of this paper is to discuss information from the literature regarding all aspects of bone health needed to counsel patients and families to promote optimal bone health in childhood for lifelong function. Part of the review will be focused on vitamin D as related to its role in bone health.

Patient empowerment

When injured, children's bodies "want" to heal. Their bones are continuously growing and have the remarkable ability to remodel, even after significant injury [7]. Most children tend to be thought of as "healthy", but if they lack the essential components for bone health,

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they may take longer to heal after injury, heal poorly, or not heal at all. If they do heal and do not have healthy bones, they may quickly sustain subsequent injuries [8]. Consequently, it is recommended that there should be a discussion of bone health at every pediatric orthopedic office visit with every patient. Children can learn the importance of taking ownership of their own health at an early age. Education of caregivers regarding bone health does not consistently occur in the primary care setting, and orthopedists should take this opportunity to educate parents and caregivers. To be successful, the patient must be enlisted in their own care as lifestyle and diet changes are not possible without patient and parent buy-in. Strategies such as utilizing a pill box labeled by the days of the week can organize this process for parents and children and help encourage compliance. Effective and relatable strategies are needed to engage the patient. For example, their body can be compared to a house. Ask the patient: "Are you planning to move anytime soon? If not, then you need to take care of the body you live in."

AAP and bone health

Counseling patients is imperative for the pediatric orthopedist but should start with the pediatrician. The following are the 2014 American Academy of Pediatrics (AAP) guidelines for the role of the pediatrician in optimizing bone health in children and adolescents. Pediatric providers should: (1) inquire about dietary intake of calcium and vitamin D, supplements, and exercise at health maintenance visits, (2) encourage dietary intake of calcium and vitamin D, (3) encourage weight-bearing activities, (4) discourage routine screening for vitamin D deficiency in otherwise healthy patients, and (5) consider a dual-energy x-ray absorptiometry (DXA) scan in medical conditions with reduced bone mass or increased bone fragility [2].

These guidelines are insufficient to optimize pediatric bone health. Patients and families do not necessarily know which foods are good sources of calcium or vitamin D [9]. Even if they have this knowledge, they are frequently unclear on amounts present in various foods or are not familiar with the recommended daily allowance (RDA). Discussion should occur regularly at well visits and should include specific amounts.

Children of all ages are at risk for vitamin D deficiency and their needs change as they grow [10]. Up to 70% of the children in the United States are vitamin D insufficient or deficient, which is something that can be corrected and sustained in their lifetime with supplementation and monitoring of serum levels [11]. Currently, no agency recommends routine vitamin D screening. However, given the high prevalence of vitamin D deficiency, routine testing in children is something that should be considered. Children and caregivers may be more likely to take supplementation seriously if they have serum levels regularly monitored. Regular lab testing of 25(OH)D would also elucidate the need for any adjustments to ensure the levels remain within the target range. While the cost of performing a vitamin D test is low, applied up-charges can increase the expense with prices ranging from $35 to $250 depending on various factors such as specific lab used and insurance coverage [12]. The associated costs could be addressed at a government level to make vitamin D testing more affordable and accessible to patients. Government intervention has been integral in past health initiatives such as folate fortification of foods, lead poisoning prevention, and widespread COVID-19 testing and vaccination [13–15]. Adequate 25(OH)D levels are especially important goals in pediatric patients to minimize fracture severity, maximize muscle repair, strength, and stamina, and optimize bone formation [16–18]. One article reported that there is a 6x higher chance of having a severe enough fracture to require surgery if the 25(OH)D serum level is < 20 ng/mL and this was found to be 3.8x higher if the serum level was < 20 in another article [16,17]. Growing bodies need the right ingredient components and knowledge to optimize bone health and reach peak bone mass [2].

Important basic information needed to counsel patients

To be effective when counseling patients, it is important to ask questions regarding their nutritional habits and then recommend specific amounts of supplements. Patients tend to respond to specific quantifiable goals and can learn about nutrition when this conversation occurs.

Building strong bones is a "recipe" that requires several "ingredients. The main components include calcium, vitamin D, vitamin C, and vitamin K as well as physical exercise [2,19,20]. Just as in making a cake, specific amounts of ingredients are required. Too much salt can ruin the cake. Too much vitamin D can cause toxicity. However, very large amounts of vitamin D would need to be consumed to get to this point [2,10,21]. The amounts discussed in this article will not cause toxicity for healthy children and adolescents without kidney or liver problems, and these amounts are within the range quoted by the Endocrine Society [21,10,22–27].

It is also important to review if the patient is taking other prescription medications such as thiazide diuretics, or those that can negatively impact bone density including antiepileptics, glucocorticoids, antiretrovirals, and antifungals that may block the absorption of vitamin D [2,28]. The authors recognize that the need for growing bones and bodies of a healthy pediatric population is very different than that of other patient populations such as older adults or children with chronic health conditions. Bone health needs will vary significantly based on age, body size, composition, and stage of growth. Available randomized controlled trials (RCTs) focusing on the effects of vitamin D in children are limited. Therefore, findings from RCTs looking at the adult population are touched on briefly.

Focusing on a simple regimen for bone health makes it easier for children and families to implement this into their daily routines. For example, choosing round numbers for dosing (eg, choosing 1,000 rather than 1,200), can make it easier for patients to remember the dose. Fig. 1 shows an example of a bone health recipe card that can be used for discussion at every pediatric orthopedic office visit. Allowing patients and families to choose the specific brand and formulation of over-the-counter vitamins can make patient compliance more likely than if they are directed toward a specific brand or vitamin prescription. When patients can choose between formulation (ie, pills, gummies, drops) and brand, they can cater to their specific tastes and lifestyle. If a prescription is given and the child does not like it, this can be an excuse to disregard supplementation because they may not know of an acceptable alternative. Providing a "bone health" pamphlet with information that is easy to understand is also helpful.

Finally, cultivate an office culture that includes the entire office staff in the discussion surrounding bone health. This allows the conversation with the patient to flow more seamlessly between medical assistants, nurses, advanced practice clinicians, and physicians. This engages all parts of the medical team in the education and discussion regarding bone health.

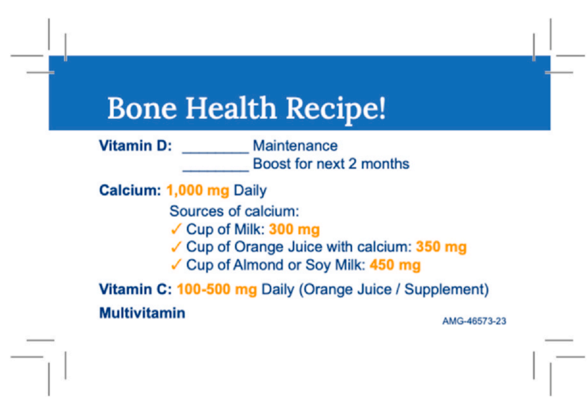

Figure 1. Example of bone health recipe card.

Table 1
Recommended Dietary Allowances (RDAs) for calcium.

Age	Calcium RDA
0-6 months	200 mg
7-12 months	260 mg
1-3 years	700 mg
4-8 years	1,000 mg
9-13 years	1,300 mg
14-18 years	1,300 mg
19-50 years	1,000 mg
51-70 years	1,000-1,200 mg
> 70+ years	1,200 mg

Bone health recipe

Calcium

The first component of the bone health recipe is calcium. It is the most abundant mineral in the body. Calcium forms the mineral composition of bones and maintains bone density, giving bones their structure and hardness [29]. RDA varies by age (Table 1) and is at minimum 1,000 mg per day by age 4 with an upper limit of 2,500 mg per day. Many children have a calciopenic diet because milk drinking is minimized or eliminated entirely at a young age, and these children do not get adequate alternative sources of calcium in their diets [29]. 1,000 mg calcium is roughly equivalent to three 8-ounce cups of milk per day. Those who are not dairy or non-dairy milk drinkers may have difficulty hitting this target and need to seek out alternative sources of calcium. Most common dietary sources of calcium and amounts are listed in Table 2. Leafy greens, beans and brocoli have calcium but it is difficult to absorb due to their oxalate content [30]. If getting adequate calcium through diet alone is not an option, many forms of supplements are available such as pills, gummies, liquids, powders, or even antacids [31].

Vitamin D

Vitamin D supplementation and serum levels

The next component of the bone health recipe is vitamin D. Vitamin D is required for calcium absorption in the intestines and for moving calcium into the bone. Without sufficient vitamin D, only 10% to 15% of calcium is absorbed from the diet [32,33]. Daily supplementation is optimal [101]. Weekly and monthly vitamin D bolus dosing are also options for administration, but there is increasing evidence that bolus dosing may be detrimental to the body’s tight hormonal control of vitamin D and may even negatively impact falls and fractures in older adults [34]. The 2 forms of vitamin D are D2 (ergocalciferol) and D3 (cholecalciferol). Vitamin D3 has a half-life of 2 to 3 weeks and reaches a steady state at 6 to 8 weeks (about 2 months). Vitamin D3 is better absorbed, lasts longer in the body than D2, and has been shown to be more effective at raising serum levels than D2 [33]. Supplementation using vitamin D3 will be used for the purpose of this review.

The active form of vitamin D in the serum is 1,25(OH)$_2$D, which is called calcitriol. This is produced by hydroxylation of D3 or cholecalciferol to 25(OH)D in the liver, which is the major circulating form of vitamin D. Hydroxylation takes place once more in the kidney to yield 1,25(OH)$_2$D. There is a small amount of calcitriol present in the serum at any time due to tight control of levels. There are nuclear vitamin D receptors for 1,25(OH)$_2$D in the intestines as well as other areas such as the pancreas, skin, brain, and activated T cells to help maintain calcium homeostasis. It is the 25(OH)D form that is measured in the serum when discussing vitamin D deficiency. Production of 25(OH)D is not tightly controlled by the body and thus reflects what is available from the diet and environment [35].

Before discussing vitamin D requirements, the current acceptable serum levels of vitamin D warrant discussion. There is controversy regarding where to set goal values for serum 25(OH)D. This is due to differing opinions of 2 different endocrine groups: the Institute of Medicine (IOM) and the Endocrine Society. The IOM set the RDA based on general population statistics as the minimal amount of vitamin D needed to have a healthy population and the Endocrine Society takes more of an individual approach to setting amounts of vitamin D needed [10,36]. The RDA for vitamin D supplementation as recommended by the IOM is assigned by age range: < 1 year (400 IU), 1 year to 70 years (600 IU), and > 70 years (800 IU); IU = International Units [36]. Conversely, the Endocrine Society provides a range for recommended daily intake to consistently maintain serum 25(OH)D levels 40 to 60 ng/mL (Table 3) [10]. The Endocrine Society's values will be used for this paper. Their values are well referenced in the literature for 25(OH)D; values < 20 ng/mL are deficient, < 30 ng/mL insufficient and levels greater than 40 ng/mL up to 100 ng/mL are acceptable [10].

Some have challenged the exact ideal serum level and aim for 50 ng/mL as the safe upper limit because studies in the adult population have shown an increased risk of kidney stones and falls at higher serum levels in certain populations [37,38]. The mechanism by which higher serum levels of vitamin D may impact fall risk has not been fully determined. However, there are limited pediatric studies in the existing literature and well-designed RCTs need to be done to better evaluate the true risk and incidence of possible side effects at higher serum 25(OH)D levels. The optimal 25(OH)D level for bone health in children and adolescents is unknown. Some of the difficulty reaching consensus on this topic is caused by the discordant information provided in vitamin D studies which may be due to factors including variable baseline 25(OH)D levels, short-term rather than long-term intervention, lack of routine serum monitoring, use of bolus rather than frequent dosing, or variable effects due to obesity or age [39].

Table 2
Food and drink sources for calcium.

Food/drink source for calcium	Amount (mg)
Low-fat vanilla yogurt—8 ounces	388
1% milk—1 cup	310
Soy milk, fortified—1 cup	299
Almond milk, unsweetened—1 cup	482
Swiss cheese—1 cup	1175
Orange juice,calcium-fortified—1 cup	349
Collard Greens, cooked—1 cup	268
Spinach, cooked—1 cup	245
Kale, cooked—1 cup	177
Broccoli, cooked—1 cup	62
Tofu, prepared with calcium sulfate—½ cup	434
Sardines, canned—3 oz	324
Salmon, canned—3 oz	181
Almonds—¼ cup	92

Table 3
Vitamin D intakes recommended by the IOM and the Endocrine Practice Guidelines Committee.

Age	IOM	Endocrine Society	
	Daily requirement	Daily requirement	Upper limit
0-6 months	400 IU (10 µg)	400-1,000 IU	2,000 IU
6-12 months	400 IU (10 µg)	400-1,000 IU	2,000 IU
1-3 y	600 IU (15 µg)	600-1,000 IU	4,000 IU
4-8 y	600 IU (15 µg)	600-1,000 IU	4,000 IU
9-13 y	600 IU (15 µg)	600-1,000 IU	4,000 IU
14-18 y	600 IU (15 µg)	600-1,000 IU	4,000 IU
19-30 y	600 IU (15 µg)	1,500-2,000 IU	10,000 IU
31-50 y	600 IU (15 µg)	1,500-2,000 IU	10,000 IU
51-70 y	600 IU (15 µg)	1,500-2,000 IU	10,000 IU
> 70 y	800 IU (15 µg)	1,500-2,000 IU	10,000 IU

IU = International Units.

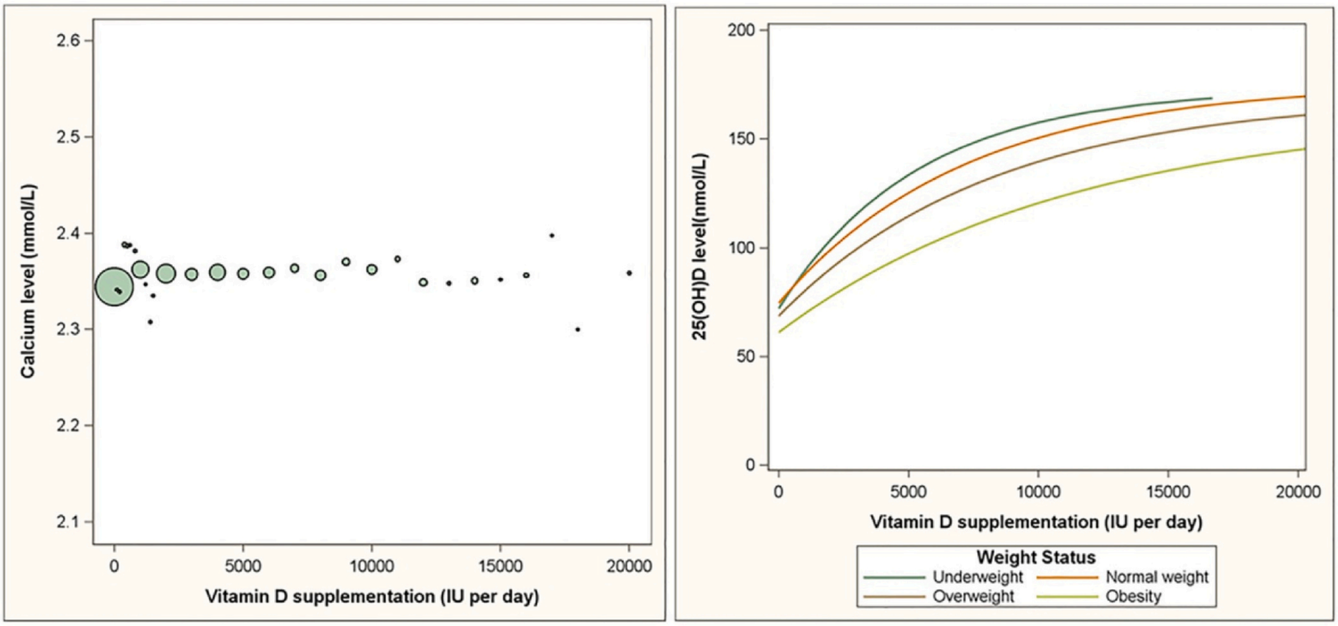

Figure 2. When discussing serum 25(OH)D levels in this paper, ng/mL is used throughout. These images use nmol/L, which is equivalent to ng/mL multiplied by 2.5. Images adapted from open access article Ekwaru et al. [41].

Toxicity

Vitamin D toxicity is uncommon and there is a large gap between acceptable vitamin D levels and levels at which clinical signs of toxicity are seen [10,40]. With a fixed vitamin D intake, (Fig. 2), serum levels of vitamin D have been shown to plateau and reach a steady state, rather than continue to rise linearly which decreases the likelihood of toxicity over time. Although there is not a clinically established upper limit for serum levels of vitamin D to avoid hypercalcemia in healthy patients, most studies have shown that 25(OH)D levels need to be > 150 ng/mL and likely even higher before there is clinical concern for hypercalcemia [10,36,41,42]. A study performed by the Mayo Clinic measured > 20,000 serum vitamin D levels in patients and only had clinical toxicity in one patient at a 25(OH)D level of 364 ng/mL [42]. Therefore, using 100 ng/mL for healthy children and adolescents as the upper limit for the acceptable range allows for a large zone of excess before there are signs of clinical toxicity [10,40]. This allows time to fine tune the amount of vitamin D ingested to safely maintain an appropriate serum level.

Although toxicity may not be seen in the zone of excess, it is important to note that some research has come out showing that higher vitamin D levels can be associated with problems in adults and has questioned the benefit of vitamin D above these levels. A large RCT performed by LeBoff et al. showed no significant reduction in fracture risk between midlife and older adults who took vitamin D without calcium compared with those who did not take any supplemental vitamin D, questioning its utility to bone health. It is also noteworthy that in this study, there were no significant differences between groups in relation to the risk of hypercalcemia or kidney stones [39]. A study in aging women (mean age 66) showed that serum levels between 32 and 38 ng/mL were associated with a significant decrease in falls, whereas serum levels exceeding 40 to 45 ng/mL were associated with a significant increase in falls [37]. Conversely, the Women's Health Initiative found that in post-menopausal women, 1 out of every 273 women taking vitamin D and calcium supplements was diagnosed with a kidney stone [43]. When considering the findings of these studies, it is necessary to consider differences in patient population (ie, children and adolescents vs older adults). The needs of their bodies will differ and recommendations for one group may not be transferrable to another.

Vitamin D intake

It is helpful to know which foods contain vitamin D (Table 4), but it is not practical for most people to take in an adequate amount of vitamin D from food alone. The most common food sources of vitamin D are shown in Table 4 [10,20]. It is estimated that 50% to 90% of vitamin D should come from production in the skin through sun exposure [44]. To get enough in this way, one must live near the equator. Living north of 37′ latitude in the Northern Hemisphere and south of 37′ latitude in the Southern Hemisphere and using protection from the sun (ie, sunscreen) makes it difficult to use the sun as the primary vitamin D source [45]. Therefore, for most of us, vitamin D needs to come from a supplement, especially for those living north or south of 37′ latitude (Fig. 3).

Table 4
Sources of vitamin D_2 and vitamin D_3.

Source	Vitamin D content
Natural sources	
Egg yolk—1 yolk	20 IU vitamin D_3 or D_2
Shiitake mushrooms, fresh—3.5 oz	100 IU vitamin D_2
Shiitake mushrooms, sun-dried—3.5 oz	1,600 IU oz vitamin D_2
Cod liver oil—1 tsp	400-1,000 IU vitamin D_3
Salmon, fresh wild caught—3.5 oz	600-1,000 IU vitamin D_3
Salmon, fresh farmed—3.5 oz	100-250 IU vitamin D_3, vitamin D_2
Salmon, canned—3.5 oz	300-600 IU vitamin D_3
Sardines, canned—3.5 oz	300 IU vitamin D_3
Mackerel, canned—3.5 oz	250 IU oz vitamin D_3
Tuna, canned—3.5 oz	236 IU oz vitamin D_3
Fortified foods	
Fortified milk—8 oz	100 IU vitamin D_3
Fortified orange juice—8 oz	100 IU vitamin D_3
Infant formulas—8 oz	100 IU vitamin D_3
Fortified yogurts—8 oz	100 IU vitamin D_3
Fortified butter—3.5 oz	56 IU vitamin D_3
Fortified breakfast cereals—1 serving	100 IU vitamin D_3

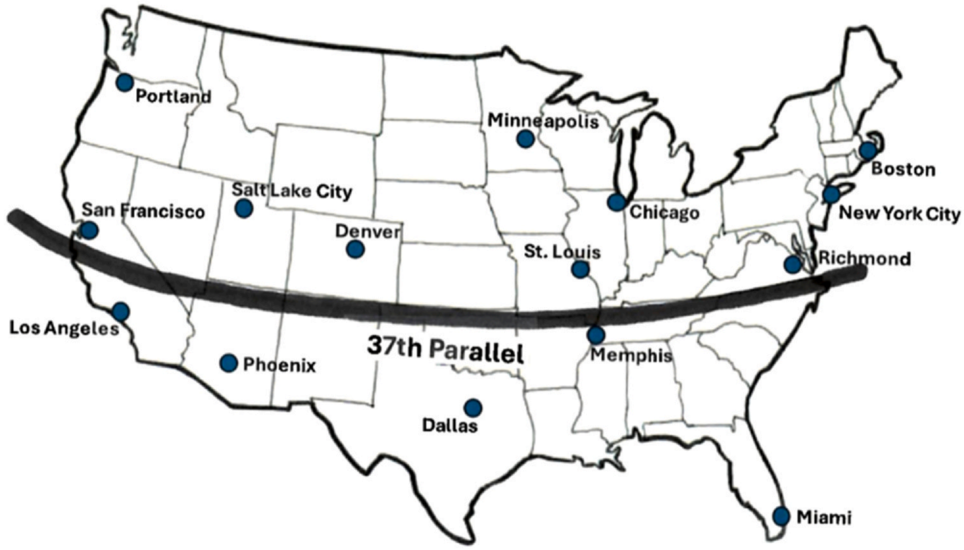

Figure 3. 37th-degree latitude division in the United States. Image created by C. Spingarn.

Recommendation for vitamin D supplementation in infants and breast-feeding women

It is well established that human milk generally does not contain enough vitamin D to support exclusively breast-fed infants, and it is necessary that infants receive adequate vitamin D in order to prevent rickets. The AAP recommends that every nursing infant receive 400 IU of supplemental vitamin D daily. [46] This recommendation is inconsistently followed, which is highlighted by a study conducted by Hollis et al. in which only 12% of study infants were receiving vitamin D supplementation at baseline. This study also confirmed that the IOM recommendation of vitamin D supplementation for the lactating mother, 400 IU daily, is too low, and maternal daily supplementation of 6400 IU per day is both safe for the mother and results in adequate vitamin D expressed in the breastmilk, providing an alternative to direct infant supplementation [47]. It is important to note, however, that in the absence of routine serum vitamin D monitoring for breastfeeding mothers and infants, 6400 IU vitamin D per day may not be sufficient for everyone and factors such as body size and individual absorption may affect vitamin D requirements.

Vitamin D3 supplementation by weight

The dosing recommendations from both the IOM and Endocrine Society do not account for weight/BMI [10,41]. Vitamin D is a fat-soluble vitamin distributed in the body in adipose tissue before circulating in the blood. This means that heavier patients need higher doses of vitamin D to reach and maintain adequate serum levels [41,48–50]. Absorption of vitamin D can vary from patient to patient and in an obese patient, maintenance demand for vitamin D may decrease after adipose tissue is loaded with vitamin D, supporting the need for routine monitoring. Consideration of the fat-soluble properties of vitamin D aligns with the Endocrine Society's guideline of a range for daily requirements and a more reasonable upper limit (UL) compared to the Institute of Medicine recommendations. Even though these values are a wide range, they are not specifically assigned by weight/BMI and may still be too low for higher weights [10,41]. The physiology of obesity also affects bone metabolism, which negatively impacts the growing skeleton and has other negative effects in pediatric orthopedic conditions [51]. For more information see Kreutzer et al.'s article included in this bone health segment.

The current RDAs for vitamin D (Table 3) are too low for many people to obtain and maintain adequate serum levels. Many studies have shown that taking higher daily amounts of vitamin D is safe [10,36,40–42,48–50]. A study performed in Finland showed that infants who received at least 2000 IU/day of vitamin D during the first year of life reduced their risk of developing type 1 diabetes in the following 3 decades by 88% [24]. There were no reports of toxicity. A study performed in Japan with children between 6 and 15 years old who received 1200 IU/day vitamin D from December through March reduced their risk of influenza A by 42% and reduced the viral load for those who did get sick without any reports of toxicity [23]. Preteen and teen girls who received 2,000 IU/day vitamin D showed improvement in muscle mass with no toxicity. Vitamin D supplementation of 2,000 IU/day was shown to improve trabecular bone mineral density and muscle power in pediatric patients with Irritable Bowel Disease [52]. An additional study showed that children receiving 2,000 IU/day vitamin D compared with 400 IU/day vitamin D for 16 weeks had significantly lower arterial wall stiffness with no toxicity [25]. In Turkish children 12 to 17 years old, 2,000 IU/d vitamin D was needed to maintain serum levels above 30 ng/mL [53]. A 6-year study looking at adults aged 18 to 84 who received 3,000 IU/d vitamin D had no change in serum calcium levels and no increased risk of kidney stones from hypercalcemia [54]. Another study showed that healthy adults who received 10,000 IU/d vitamin D had no hypercalcemia or urinary calcium excretion [55].

Ekwaru et al. published the first body weight characterization of the dose-response relationship between vitamin D supplementation and serum vitamin D levels (Fig. 2). This study confirms the need for higher doses of vitamin D in overweight and obese patients, with overweight individuals requiring 1.47 times and obese individuals requiring 2.6 times the dose of normal weight individuals to achieve the same serum vitamin D levels. Average serum 25(OH)D levels of 40 ng/mL are estimated to require daily supplementation with 2,080 IU, 3,065 IU and 5,473 IU vitamin D for normal weight, overweight, and obese individuals, respectively [41].

Dosing by age has been researched and established by the Endocrine Society using studies mentioned above and others [10]. Studies using weight-based dosing with vitamin D monitoring at regular intervals are lacking in the current literature. Weight-based dosing is the usual and customary way to determine medication dosages in children. Given the fat-soluble properties of vitamin D and the need for higher doses at heavier weights, vitamin D should be administered in the same way using all the information provided above.

Table 5 shows suggested vitamin D doses based on weight range. These values are a place to empirically start supplementing children, adolescents, and young adults seen in pediatric practice. These dosing ranges work well in a clinical setting and adhere to the ranges and

Table 5
Suggested dosing regimen for daily vitamin D3 supplementation.

Weight range	Vitamin D_3 supplementation/day
0-89 lbs	1,000 IU
90-149 lbs	2,000 IU
150-199 lbs	5,000 IU
200+ lbs	Start at 5,000 IU; may need up to 10,000 IU*
	**UL as reported by the Endocrine Society*

upper limits of dosing described by the Endocrine Society [10]. They are individualized and are specific to the weight of the patient. As mentioned above, there are studies showing possible adverse effects of higher serum vitamin D levels in older adults. As such, this recommendation is only meant to apply to the healthy pediatric population. Serum 25(OH)D levels should be obtained after 2 to 3 months of following the regimen when values reach a steady state [41,56]. Patients may need more or less supplementation at that time depending on their serum levels. Some patients may choose a holiday from supplementing vitamin D in the summer due to the belief that they will get too much while in the sun. However, vitamin D can be dosed consistently all year. The sun will not push patients to toxicity due to the body's tight control of the conversion of vitamin D to its inactive metabolites [40,57].

Long-term supplementation studies in children and obese adults are lacking [10]. Studies are needed to validate this regimen in healthy children and adolescents and determine if weight-based dosing can better address the high rates of vitamin D deficiency and keep serum levels of 25(OH)D consistently in an acceptable range. Studies should include close monitoring for signs of toxicity and ultimately aim to determine if there is a sweet spot for vitamin D as it relates to bone health. In the meantime, this counseling review proposes a reasonable empiric dosing regimen (Table 5) that can be used to treat patients and can be validated by vitamin D serum monitoring.

Vitamin C

Vitamin C, a water-soluble vitamin, is another essential ingredient for healthy bones. It is a key factor for cross-linking collagen, is involved in the production of collagen in the bone matrix, and has an anabolic effect on bone where it is involved in the formation of osteoblasts and osteoclasts [20,58–61]. Studies have shown that increased levels of vitamin C are associated with greater bone mineral density [58]. It is known that vitamin C is advantageous to bone health and healing, however, there is no consensus or recommended dose of vitamin C to support bone health [59]. A large 17-year follow-up study by Sahni et al. showed a significant protective effect of vitamin C with fracture rate in the elderly population [61]. Studies researching the specific dosage of vitamin C needed for bone health are confounded by levels of vitamin C already found in the diet [60]. Given its benefits to bone health, low cost, easy accessibility, and favorable safety profile, vitamin C supplementation or dietary modifications should be recommended [58,59]. Empiric values chosen for supplementation take into consideration the RDA upper limits for daily intake of vitamin C as seen in Table 6 from the National Institute of Health. It is reasonable to recommend that patients take between 100 and 500 mg vitamin C daily as part of the bone health regimen.

Vitamin K

Vitamin K rounds out the supplement portion of the bone health regimen. Vitamin K helps with the regulation of proteins for osteoclastic and osteoblastic activities. It is involved with the production of proteins in the bone including osteocalcin, which is needed to prevent weakening of the bone [3,62]. Without vitamin K, the body can't effectively resorb old bone causing decreased bone turnover, brittle bones, and potential for increased fracture risk at low levels [20,62]. Vitamin K also helps promote calcium accumulation in the bone [62]. It is reasonable to obtain vitamin K in appropriate amounts from the diet with foods such as leafy green vegetables and soy. If these are included in the diet, then most people are able to maintain adequate levels [20]. As an alternative, it is also a component in many multivitamins.

Table 6
Recommended daily allowance (RDA) of vitamin C (ascorbic acid).

Age	Vitamin C RDA (mg) Male	Female	Upper limit (mg)
0-6 months	40	40	N/A
7-12 months	50	50	N/A
1-3 years	15	15	400
4-8 years	25	25	650
9-13 years	45	45	1,200
14-18 years	75	65	1,800
19+ years	90	75	2,000

Physical exercise

A final necessary component for bone health is physical exercise. Numerous studies have shown that putting stress on bone through weight-bearing exercises can prevent bone loss and even build bone [2,3]. Bone remodels according to stress and activity. It takes 3 to 6 weeks for bones to remodel stronger in response to activity [63,64]. Patients are counseled to stay active. Just 3 days of bed rest causes muscle loss and with continued bed rest, there is associated loss of bone [65]. Weight-bearing and resistance training activities such as walking, running, jumping, and weightlifting are best [66,67]. This added stress stimulates the bone to become stronger and denser [2,3]. Weekend-only activity with rapid acceleration of activity over a short period should be avoided. Overdoing it, especially in someone who does not have great bone health, leads to more frequent injuries and fractures [68].

Why is so much emphasis placed on vitamin D?

Vitamin D is important for many reasons beyond bone health. Emphasis on its importance in relation to bone, brain, and the immune system is paramount for patient counseling. Many tissues and cells in the body have a vitamin D receptor and it has been shown that $1,25(OH)_2D$ can play a role in the expression of a large part of the human genome [69,70]. Additionally, there appears to be a dose-dependent effect with a greater influence on gene expression with higher doses of vitamin D with pronounced expression of over 1,200 genes [70]. Many studies have shown a link between vitamin D levels and various allergy and autoimmune conditions, acute illness, cancers, cardiovascular disease, and neurologic conditions [40,70,71]. Controversy and mixed results can be found in all areas of vitamin D research, but ongoing research is giving a better picture of the full impact of vitamin D. For more detailed information of possible extraskeletal effects of vitamin D and ongoing research in these fields, see Appendix 1.

Summary

More emphasis needs to be placed on the discussion of bone health between clinicians and patients. This is especially important in pediatrics because it is the time of highest impact. During childhood, the bones are growing and kids are gearing up to reach their peak bone mass that will provide the foundation for the rest of their lives. Peak bone mass should be optimized to set children up to lead a life with as much protection from injury as possible. The conversation needs to start with the pediatrician and needs to happen at every office visit for the pediatric orthopedist. Both the pediatricians and the orthopedists need the appropriate tools to make these conversations effective and create lasting changes from a young age.

To get here, multiple steps need to be taken. The AAP recommendations on optimizing bone health in children and adolescents should be updated. Conversations need to include individualized recommendations and amounts for calcium and vitamin D supplementation. The pediatric provider needs to have more concrete guidelines. Providers can be frustrated by the inability to adequately raise a patient's vitamin D levels by following the guidelines put forth by the IOM. There are gaps in the literature looking at optimizing the intake of various supplements in relation to bone health. Studies need to be conducted to give clinicians accurate and concrete guidelines to help patients meet their daily requirements. For example, studies to validate dosing vitamin D supplementation by weight rather than age to maintain adequate serum vitamin D levels are needed. This is especially important since pediatric obesity is on the rise and significant variation of body mass index within age groups needs to be accounted for in the pediatric population. It is not effective to treat an 8-year-old that weighs 60 lbs the same as an 8-year-old that weighs 160 lbs. Vitamin D testing should be performed routinely on children because their height, weight, and diet are all in a state of constant flux. Many patients are not identified as at risk because they are "healthy children. Currently, the general population is at risk for deficiency and should be treated as such. Osteoporosis starts in childhood when children do not reach their peak bone mass [3,6]. Although recommending routine testing is not a common stance, this tactic is one that would have a high impact on children's health and avert many potential future health care problems.

Author contributions

Barbara Minkowitz: Conceptualization, Writing – original draft, Writing – review & editing. **Colleen M Spingarn:** Conceptualization, Writing – original draft, Writing – review & editing.

Declarations of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix 1

Allergy and autoimmune diseases

Vitamin D appears to be an essential component of immune system health and integrity [70,71]. Studies show that $1,25(OH)_2D_3$ plays a role in both active and passive immunity. There is a vitamin D receptor (VDR) present on activated T cells, and animal studies have shown that $1,25(OH)_2D_3$ can protect against a number of autoimmune diseases by shifting proinflammatory immune responses to anti-inflammatory immune responses [35,72]. Atopic dermatitis has been associated with vitamin D deficiency [73,74]. Studies looking at relative risk reduction of vitamin D in relation to atopic dermatitis and asthma are mixed, but the association of low vitamin D levels and atopic dermatitis suggest that vitamin D may be helpful as an adjuvant therapy [74]. Additionally, vitamin D may decrease the severity and duration of asthma and allergy symptoms [75]. It is hypothesized that low levels of vitamin D play a role in the development of childhood food allergies, asthma, and fetal lung development [76]. Studies are needed to better quantify these relationships and consider whether higher doses of vitamin D during pregnancy and early childhood can be an adjunctive therapy or preventative treatment [75]. Study data are currently not strong enough to recommend vitamin D supplementation for prevention of these conditions [77,78]. However, animal studies have shown that vitamin D has an impact on early lung development, and it is possible that elevated vitamin D levels in pregnancy may positively impact certain allergic phenotypes [78].

There has been research into Multiple Sclerosis (MS) and its relationship to vitamin D. Low vitamin D is a risk factor for expressing the genes causing MS and relapses [79,80]. It appears to be involved in its immunomodulation within the central nervous system [79]. Seasonal changes in vitamin D concentrations are associated with relapse rate [81]. Multiple statistical models have shown a favorable vitamin D relationship and reduction in MS relapse rate by 50% to 70% [79]. There is a Mendelian randomization study that shows causal relationship between genetically increased serum vitamin D and reduced MS in the European population [82].

Type 1 diabetes mellitus (DM) is another autoimmune disease that appears to have ties to vitamin D [83]. In people with the DM type 1 gene, early supplementation appears to decrease gene expression [84]. This is seen as a correlation with vitamin D supplementation in infancy and reduced risk of DM1 [24].

In people with DM type 2, vitamin D is necessary for insulin release in response to glucose. It acts through vitamin D receptors on the pancreas and has a nongenomic effect on levels of calcium that would reduce insulin secretion [83]. In another study, there was a decreased risk for diabetes by administration of vitamin D in prediabetics [85]. This research is ongoing and adequately powered RCTs are needed to demonstrate the suggested benefit of vitamin D for both Type I and Type II diabetes as well as other autoimmune diseases.

Acute illnesses

Vitamin D was found to prevent and improve symptoms of flu in infants < 1 year of age given 1,000 IU/d vitamin D. There was a shorter duration of fever, cough, wheezing and a lower viral load [86]. A review of 25 randomized controlled trials revealed that there is a reduced risk of upper respiratory infection with vitamin D supplementation [87]. Additionally, vitamin D deficiency was reported to be a possible risk factor for more severe COVID-19. Studies have shown improved outcomes after vitamin D supplementation and increased severity and mortality in hospitalized patients with low vitamin D levels [88]. While these associations are promising, further studies are needed to support the relationship between vitamin D and host resistance to infection.

Cancers

There is interest surrounding the anticancer properties or vitamin D and its potential ability to impact the development and progression of cancer [35,89]. Numerous studies have shown that 1,25(OH)2D3 can slow down cancer cell growth, inducing cell death, and even alter the invasiveness of cancer cells [35]. Proposed mechanisms for risk reduction include reduction in inflammation, and effect on cellular differentiation, progression and apoptosis [90,91].

A recent meta-analysis looking at the impact of vitamin D3 supplementation on cancer mortality found a nonsignificant risk reduction of 6% for those taking vitamin D supplementation compared to placebo and a significant subgroup analysis of 12% risk reduction for those taking daily supplementation compared to bolus dosing of vitamin D [92]. A risk reduction for colorectal cancer and breast cancer has been previously reported in the literature [93–95]. A recent literature review challenged the significance of this relationship but did find that supplementation may be associated with improved outcomes for those with breast or colorectal cancer [96]. An additional 2023 review supports a possible association between vitamin D supplementation and improved clinical outcomes as well as a link between low vitamin D levels and increased risk for cancer [97]. The interplay of variables contributing to cancer risk, progression, and clinical outcomes is incredibly complex, and while these relationships are promising, significant research is needed before any definitive benefit is established.

Cardiovascular disease

Vitamin D receptors have been reported in myocardium [98]. Epidemiologic and observational studies have shown a significant association between low vitamin D levels and cardiovascular risk factors, severity of cardiovascular events and predisposition to increased morbidity and mortality [35,98,99]. Low vitamin D levels may be an independent risk factor for acute myocardial infarction and worse associated outcomes [98]. Studies have also shown a positive association between low vitamin D levels and hypertension [100,101]. Animal studies have confirmed a protective role of vitamin D through mechanisms such as decreased arterial wall stiffness and improved systolic and diastolic function [35]. However, there is not currently enough evidence to support vitamin D supplementation for cardiovascular risk reduction at the population level [35,98,99].

Nervous system and mental health

The involvement of vitamin D and its impact on the central nervous system is controversial. Vitamin D may be important for brain development and may have effects on cellular proliferation and differentiation, impacting neurophysiology and neuroprotection. Part of its suggested mechanism involves neurotransmission, synaptic plasticity, and synthesis of neurotransmitters and neurotrophins [102,103]. There is research being conducted looking at the association between vitamin D and its effects on mental health, autism, dementia, and schizophrenia [102–104]. It has been suggested that low vitamin D is associated with depressed mood [105]. In early childhood, supplementation with 1200 IU/d vs 400 IU vitamin D supplementation was associated with fewer cases of depressed mood, anxiety, and withdrawn behavior [106]. A study in veterans who are 1.5x more likely to die by suicide suggests a link between vitamin D deficiency and depression or other forms of mental illness. Taking vitamin D lowered the rates of attempted suicide and intentional self-harm. Self-harm was found in 0.36% of the untreated group and 0.2% in those given vitamin D [107]. Some feel low vitamin D may precipitate mental health disorders and higher doses of vitamin D may be protective [108]. This research is ongoing; it has not been determined if there is a specific serum level of vitamin D needed for mental health and neurologic benefit.

There is substantial research and interest in the extraskeletal effects of vitamin D, but with most body systems and reported associations of the effects of vitamin D, the number of contributing factors is extremely complex and very patient dependent. Therefore, it is difficult to parse out how much is truly attributable to vitamin D. Further studies are needed to understand vitamin D's extraskeletal interactions.

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