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Underweight, Overweight, and Pediatric Bone Fragility: Impact and Management

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Abstract

Skeletal health is modulated by a variety of factors, including genetic makeup, hormonal axes, and environment. Across all ages, extremes of body weight may exert a deleterious effect on bone accretion and increase fracture risk. The incidence of both anorexia nervosa and obesity, each involving extreme alterations in body composition, is rising among youth, and secondary osteoporosis is increasingly being diagnosed among affected children and adolescents. Compared with the elderly, the definition of osteoporosis that stems from any underlying condition differs for the pediatric population and special precautions are required with regard to treatment of young patients. Early recognition and management of both underweight and overweight youth and the accompanying consequences on bone and mineral metabolism are essential for preservation of skeletal health, although prevention of bone loss and optimization of bone mineral accrual remain the most important protective measures.

Keywords

Osteoporosis; Pediatric; Anorexia nervosa; Overweight; Obese; Bonemineral density; Fracture; Weight loss; Weight gain; Exercise; Calcium; Vitamin D; Bisphosphonate

Introduction

The pathophysiology of bone disease across all ages is influenced by genetic, environmental, and hormonal factors [1]. Body composition, especially in individuals at extremes of the weight spectrum, exerts a significant effect on bone accrual, geometry, and subsequent fracture risk. Anorexia nervosa, the most extreme example of malnutrition, has a lifetime prevalence of 0.3 % in 13- to 18-year-old adolescents among both sexes [2], and the

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Compliance with Ethics Guidelines

Conflict of Interest S. R. Bialo and C. M. Gordon declare that they have no conflicts of interest.

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incidence is increasing in this age group [3]. The disease is associated with low bone mineral density (BMD) and bone mineral content (BMC) in both adolescent boys and girls [4–6], thus predisposing them to significant skeletal morbidity [7]. At the opposite end of the spectrum, the incidence of overweight and obesity is also increasing at alarming rates. The World Health Organization (WHO) reports a near doubling of worldwide obesity since 1980 [8]. Between 2011 and 2012 in the United States, 16.9 % of 2- to 19-year-olds were noted to be obese [9]. Obesity was once thought to be protective in the development of osteoporosis in adults [10], but this assumption has not proven to be true either in adults or the pediatric population. Obese individuals of all ages are more likely to be deficient in micronutrients such as vitamin D [11•], and obese children have a higher fracture incidence than their healthy weight counterparts [12]. Given that the vast majority of peak bone mass is achieved during puberty [13], prevention and optimal management of bone disease among underweight and overweight youth is imperative for healthy long-term outcomes.

Diagnosis of Pediatric Osteoporosis

There is no WHO definition for osteoporosis for children or adolescents. Among the pediatric population, use of Z-scores is recommended over T-scores as the former employ age and sex-specific BMC/BMD distributions [1, 14]. Furthermore, the diagnosis of osteoporosis in children and adolescents cannot be made based on a BMD Z-score alone, as the clinical relevance of an uncomplicated low bone density in the pediatric population and its long-term consequences have yet to be fully elucidated. The definition of osteoporosis among youth was recently revised at the 2013 International Society for Clinical Densitometry (ISCD) Pediatric Position Development Conference, and is indicated by the presence of a BMD Z-score -2.0 , as well as a clinically significant fracture history (Table 1) [15•]. Of note, a low-trauma vertebral compression fracture may now be used as a sole criterion in reaching a diagnosis of osteoporosis, independent of BMD Z-score. The interpretation of densitometric data in children is complicated by continuously changing values with age and the effect of variables such as ethnicity, gender, pubertal staging, skeletal maturation, and body composition. The adjustments that yield the most accurate BMD Z-score in the face of variable bone size is an area of fervent research, but height corrections appear to be particularly informative [16].

There are a number of methods available for the measurement of BMD [1]. The most widely used tool is dual-energy x-ray absorptiometry (DXA), which provides a measure of areal bone density (BMC/projected area; g/cm^2). DXA studies are easily accessible, inexpensive, fast, involve low doses of radiation, and have good reproducibility. However, because DXA does not measure volumetric density, the measurements underestimate the true density value for smaller bones and overestimate that of larger bones. DXA can thus be problematic in young patients with constantly changing bone dimensions. Use of calculations that estimate volumetric bone density, such as bone mineral apparent density (BMAD, g/cm^3), can be helpful as they help to explain the extent to which an areal bone density measure may be confounded due to bone size [17]. In children with short stature or growth delay, spine and total body less head (TBLH) BMC and areal BMD results should be adjusted. The ISCD recommends that TBLH be adjusted using the height Z-score and that of the spine using either the height Z-score or BMAD [14]. Peripheral quantitative computerized tomography

(pQCT) is a tool that produces three-dimensional images of peripheral bones and their adjacent muscle mass. Unlike DXA, it distinguishes cortical from trabecular bone and allows for the assessment of bone geometry. However, pQCT is more costly and fewer normative data are available. Therefore, pQCT is not used as widely as DXA, especially for clinical purposes. In the pediatric population, pQCT is generally limited to investigational use. Bone mineral status during childhood tracks through young adulthood [18•], thus, supporting the use of DXA for early identification of children at risk for osteoporosis later in life. However, there is evidence that DXA precision declines with increasing BMI [19] and that pQCT may be a better tool for obese patients as it is less susceptible to artifacts arising from excess soft tissue and changing body composition [20].

Impact of Body Composition on the Skeleton

Weight changes are associated with alterations in several hormonal axes that, in turn, affect bone. Individuals with anorexia nervosa (AN) have reduced caloric intake accompanied by low serum insulin-like growth factor I (IGF-I) levels and growth hormone resistance, decreased fat mass with low leptin levels, impaired thyroid function, hypogonadotropic hypogonadism with low serum sex steroid and adrenal androgen levels, and high circulating cortisol [21, 22]. The positive relationship between body mass and bone density is not present in AN [23], suggesting that these hormonal abnormalities, alongside other factors, impact bone accrual in both sexes with this disease.

Adolescent girls with AN have reduced areal BMD [24], suppression of bone formation and resorption markers [25], and reduced bone accrual as measured by lumbar spine BMD [6]. One study found that BMD is reduced by 1.0 SD in at least one skeletal site in 92 % and by at least 2.5 SD in 38 % of adult women with anorexia nervosa (AN) [26]. Decreased indices of both whole and relative bone strength have been demonstrated in adolescent girls with AN compared with healthy control subjects [27]. Adolescent girls with AN who have undergone high-resolution pQCT assessments show impaired cortical and trabecular microarchitecture and reduced bone strength at the distal radius [28]. Adolescent boys with AN also have lower BMD at multiple sites, a reduced bone turnover rate, and impaired hip structure and strength compared with healthy controls [4, 5]. These changes predispose youth with AN to an increased risk of fracture and related morbidity.

Obesity is associated with increased fat mass and elevated concentrations of leptin, IGF-I, insulin, and estrogen [21]. In affected children and adolescents, hyperinsulinemia may be secondary to insulin resistance and increased estrogen concentrations can be seen due to aromatization of androgens within adipose tissue. These changes accelerate pubertal development and bone maturation in both sexes. A high body mass also increases mechanical loading on weight-bearing bones, resulting in increased BMD in obese children compared with their healthy weight counterparts [29], although hip structural analysis in overweight children has shown that bone strength adapts primarily to muscle forces independent of fat load [30]. Obese male adolescents have been shown to have greater cortical area and periosteal and endosteal circumference dimensions at the radius and tibia on pQCT compared with healthy age-matched controls, which is attributed to larger muscle area [31]. The definitive effect of pediatric obesity on bone mass, however, remains

controversial. There is evidence that obese children have significantly greater vertebral density, whole-body bone area and BMC for age and for height [29], while other studies describe lower bone mass and bone area in obese children compared with healthy weight controls [32] and that BMC decreases with increasing fat mass [33]. Further investigation is needed to clarify the direct effect of increased fat mass in the pediatric population on immediate and future bone health.

The bone marrow cavity contains significant fat tissue, which may modulate bone remodeling, although the metabolic function of marrow fat remains under active investigation [34]. Mesenchymal stem cells within bone marrow differentiate to become either adipocytes or osteoblasts. The adipocytes formed secrete cytokines and adipokines that may either stimulate or inhibit adjacent osteoblasts. The relationship of marrow adipose tissue to fat depots in other parts of the body is complex and may play a distinct role in metabolic homeostasis, hematopoiesis, and osteogenesis [35]. Fully differentiated bone cells secrete factors that influence insulin sensitivity, and fat cells synthesize cytokines that regulate osteoblast differentiation; thus, the two pathways are closely interrelated. States of malnutrition, such as restrictive eating disorders, have been shown to increase marrow adiposity accompanying concurrent losses of subcutaneous adipose tissue, and there is an inverse association between marrow fat and areal BMD measures in adults with AN [36, 37]. In adolescents and young women, increased marrow fat has been documented to be present in the peripheral skeleton [38] as well as lumbar spine [37]. The emerging importance of bone-fat interactions suggests that novel molecules could emerge as targets to enhance bone formation and possibly prevent bone loss and fractures [35].

Over-nutrition, on the other hand, does not appear to contribute to the development of marrow adiposity [36]. In healthy adolescents and young adults, significant marrow adiposity has been identified in the appendicular skeleton without relation to the subcutaneous or visceral fat depots [39], which may be explained by the infiltration of marrow adipocytes during the time of peak bone acquisition. The role of visceral and intramuscular fat has also been a topic of investigation. Gilsanz et al. obtained QCT measures of femur cortical area and body composition in 100 healthy adolescents and young women, ages 15–25 years, and reported that thigh muscle area and subcutaneous fat were significantly, positively, and independently associated with cortical dimensions, while there was a negative association between visceral subcutaneous fat and cortical bone. Interestingly, visceral and subcutaneous fat had opposite effects on the peripheral skeleton, with subcutaneous fat being beneficial to bone structure and strength, whereas visceral fat representing a pathogenic depot [40]. Further investigation is needed to define the relationship between bone marrow composition, visceral, intramuscular, and subcutaneous adiposity and their subsequent effects on bone accrual and strength.

Fracture Prevalence and Risk in Underweight and Overweight Children

Up to half of otherwise healthy children experience at least one fracture before adulthood [41]. Goulding et al. carried out important DXA studies of bone density and body composition in both girls and boys, associating lower areal BMD with increased risk of distal forearm fracture [42]. A systematic review and meta-analysis of the association

between bone density and fractures in otherwise healthy children also suggests that low bone mass may contribute to fracture risk in childhood [43]. An 8-year, prospective study revealed that a single, prepubertal DXA measure of BMD can predict fracture risk in boys and girls during puberty [44], although only healthy cohorts were examined.

Adolescents with malnutrition and AN are at high risk for insufficient bone accrual. In adolescent girls with AN, fracture prevalence remains higher than in healthy weight controls even without significant reductions of whole body areal BMD [7]. In one cross-sectional study of women with AN, 30 % suffered fractures and 36 % had histories of multiple fractures over their lifetime. Of those reporting fractures, 42 % were sustained in the absence of trauma or were fractures resulting from minor injuries that would not be expected to result in fracture in otherwise healthy individuals [45]. Young women with AN have a cumulative incidence of fracture as high as 57 %, with fracture incidence peaking after the diagnosis of an eating disorder [46]. The distal upper extremity is the most common site for fracture, although up to 9 % of reported stress fractures were vertebral [46].

Overweight children have greater bone strength as measured by bone strength index on pQCT than healthy weight counterparts, but this increased strength remains disproportionate to their overall body mass and may contribute to an increased risk of fracture [47]. This fracture risk increases uniformly with increasing weight [12] and is likely influenced by multiple factors. Compared with nonobese cohorts, obese children and adolescents report poorer mobility and balance [48]. Also, obese children generate significantly greater force while falling on outstretched limbs and are at greater risk for fractures from low-fall heights and softer-impact surfaces [49]. Obese and overweight children with low to moderate-energy fractures do not heal more slowly than children of a normal weight [50], but obese children with traumatic long-bone fractures sustain more severe injuries, thus, predisposing them to greater inpatient morbidity and mortality than healthy-weight counterparts [51]. The effect of obesity on life-long fracture risk is not yet known.

Management

Body Weight Optimization

As with any process that negatively affects health, the best strategy is prevention. For those who are already affected, treatment of the underlying issue is the most prudent approach. Underweight and overweight individuals may both suffer adverse skeletal consequences. Therefore, the logical first step in management is to work toward achieving a healthy weight.

The cornerstone of treatment for patients with AN is weight restoration, and early action is indicated in order to prevent bone disease. Data on the direct effect of weight gain on bone mass, however, are conflicting (Table 2). In an early study, all recovered women with AN who maintained normal weight at 3.6 years of follow-up were found to maintain nonosteoporotic T-scores at the lumbar spine compared with women with ongoing AN who demonstrated worsening osteoporotic T-scores at the lumbar spine [52]. A later study examined DXA measures in patients 8 years after the diagnosis of adolescent-onset AN; those who successfully recovered had significantly higher BMD at both the spine and the hip compared with patients with a persistently low BMI [53]. This finding is incongruent with

an earlier study of women with adolescent-onset AN showing that subsequent weight restoration did not allow for normalization of total body BMD compared with women with ongoing AN [54]. A recent prospective study of 79 adolescents with AN demonstrated no improvement in lumbar BMD nor BMD Z-score one year after a sustained, statistically significant increase in BMI [55].

Recovery from AN is difficult to achieve and sustained success is low. In a 6-year follow-up of patients with AN undergoing cognitive behavioral therapy, 48 % still met both DSM-IV and DSM-V diagnostic criteria for AN [56]. Likewise, successful weight loss in the management of overweight and obesity is difficult to attain. Decreased caloric intake, increased exercise, behavior modification, and medication do not frequently result in significant long-term improvement [57, 58].

Obese male adolescents who have achieved one year of successful weight loss through lifestyle modification demonstrate increased whole body and lumbar spine BMC, but lower limb and upper limb BMC decreases relative to height. Overall, however, their BMC measurements remained above average compared with nonobese counterparts [59]. With the obesity incidence rising among adolescents, obese youth are increasingly electing to undergo bariatric surgery. These procedures successfully result in rapid weight loss, but not without skeletal effect. Within the first 9 months after Roux-en-Y gastric bypass, adult patients had significant decreases in BMD and BMC at the total hip, trochanter, and total body compared with baseline [60]. Adolescents who undergo gastric bypass surgery have been found to maintain normal whole-body BMD Z-scores two years after the surgery, but whole-body BMC decreases significantly, which is likely a consequence of the high BMC and BMD before surgery in this extremely obese population [61]. Despite the observed bone loss, there are no conclusive data to support increased incidence of osteoporosis or increased fracture risk in postbariatric patients [62, 63]. The type of intervention may also be predictive, with malabsorptive procedures such as biliopancreatic diversion and Roux-en-Y causing a greater decline in femoral neck and lumbar spine areal BMD measures than predominantly restrictive procedures such as vertical banded gastroplasty, sleeve gastrectomy, and adjustable gastric banding [62].

Calcium and Vitamin D

Historically, the mainstay of prevention and treatment of osteoporosis is calcium and vitamin D supplementation [64]. Vitamin D is essential for efficient calcium absorption that contributes to bone mineralization, and is dependent on adequate calcium provision through the diet or from supplementation. The skeleton appears to be most receptive to calcium and vitamin D supplementation during the late prepubertal period [65], although data on the sustained effect of calcium and vitamin D supplementation on BMD are conflicting. In adolescent girls with AN, calcium intake and vitamin D levels did not correlate with lumbar BMD nor markers of bone turnover [6]. Surprisingly, one study showed the prevalence of vitamin D deficiency among adolescent girls with anorexia nervosa to be only 2 % compared with 24 % in healthy controls [66]. This finding is attributed to exceptional compliance with vitamins and supplements, which girls with AN likely perceive to be an adequate noncaloric nutritional substitute. Despite their severe malnutrition, patients with

AN have a similar bioavailability of oral ergocalciferol as healthy-weighted controls [67•]. Given that AN confers a low percentage body fat and that vitamin D is a fat-soluble vitamin, the low prevalence of vitamin D deficiency may be attributable to a higher concentration of circulating 25OHD.

This theory may also apply inversely to obese children. The prevalence of vitamin D deficiency is 29 % in overweight children and 34 % in obese children, and it increases linearly with increasing BMI [11•]. This can be explained by excess adipose tissue sequestering fat-soluble vitamin D and resulting in lower circulating concentrations. Obese children are also more likely to have less nutrition-dense diets, and sedentary lifestyle also limits sun exposure and may decrease peripheral conversion of vitamin D [68]. Compared with healthy weight children, normalizing deficient vitamin D levels in overweight and obese children can be challenging, as they often require two to three times higher doses; at least 6,000–10,000 IU per day followed by maintenance therapy of at least 3,000–6,000 IU per day [69].

Despite the controversial association between these micronutrients and bone outcomes, preventing vitamin D deficiency and optimizing 25OHD concentrations, and ensuring adequate dietary calcium intake remains the standard of care for bone health maintenance in both underweight and overweight youth.

Physical Activity

It is well known that skeletal strength and development is largely influenced by mechanical loading activity on bone. Children and adolescents who engage in physical activity have an increased adjusted BMC at the total hip and femoral neck [70], and adolescents who regularly exercise have increased size and density of the cortical bone of the tibia, as well as increased density of the trabecular bone of the tibia [71]. Compared with children engaged in physical education only 60 minutes per week, prepubertal boys and girls with daily, 40-minute school-based physical education have higher annual accrual of spine BMD without affecting vertebral and nonvertebral fracture risk [72]. In both sexes, physical activity during childhood also exerts a strong linear association with cortical bone size in adulthood [73–75].

While mechanical loading activities offer substantial benefits to bone and overall health, extreme exercise can mitigate those effects. Stress fractures result when bone remodeling cannot keep up with repetitive loading, such as in long-distance running. When excessive exercise is paired with inadequate caloric intake, gonadal dysfunction can ensue in males and hypothalamic amenorrhea in females. The ‘female athlete triad’ is a term that describes the spectrum of dysfunction related to energy availability, menstrual function and impaired BMD that places adolescents and young adults at increased risk of suboptimal peak bone mass with lasting impact on their bone health through adulthood [76].

It has been shown that women with AN who engage in moderate bone loading exercise have lower lumbar spine and total body BMD compared with nonexercising controls [77]. Interestingly, recovered AN patients with high bone loading exercise regimens have higher

BMD at the femoral neck and whole body than controls. These contrasting results further highlight the danger malnutrition imposes on skeletal health.

In contrast, overweight youth tend to be more inactive than their healthy-weight counterparts [78], and BMI increases linearly with increasing sedentary time [79]. Not only are inactive children not attaining the skeletal benefits of mechanical loading, it is now known that increased sedentary time alone is related to decreases in whole-body BMD, as well as lumbar spine and femoral neck BMD and BMC [80]. Obese children can capitalize on the bone and weight-related advantages of exercise, although precautions must be taken given their increased risk of fractures related to poor balance and forceful falls.

A less intensive form of physical activity that offers skeletal benefits may be a safer option for youth with severe malnutrition and promote adherence in otherwise inactive, obese children. One such example is low-magnitude, high-frequency whole body vibration (WBV) platforms for treatment of diminished bone density. WBV is still investigational although preliminary bone-related results in some patient populations are encouraging. Girls with adolescent idiopathic scoliosis and documented low bone mass who stood on the vibrating platform for 20 minutes per day, 5 days per week for 1 year showed significant increases in femoral neck areal BMD and lumbar spine BMC compared with controls [81]. The effect of WBV in malnourished and overweight populations remain to be investigated.

It is noteworthy that some studies suggest that physical activity results in a beneficial effect on BMD only when calcium intake is over 1,000 mg per day, indicating a synergistic relationship between exercise and nutrition [82, 83]. Thus, in conjunction with other measures and with special precaution in cases of extreme malnutrition, weight-bearing activity can augment treatment and prevention of osteoporosis in under- and overweight youth. A fracture risk assessment should take place on an individual basis and factor in previous injuries, calcium and vitamin D status, and other evidence of skeletal fragility. Referral to a physical therapist can facilitate an appropriate activity plan for pediatric patients with bone fragility and result in effective strengthening of the muscle-bone unit.

Pharmacologic Agents

When patients fail to adequately respond to general measures in treatment of osteoporotic fractures, pharmacologic agents may be indicated. Treatment of bone loss targets either inhibition of further bone loss or stimulation of bone formation. However, caution should be exercised when considering these agents in a growing child or adolescent as both their efficacy and associated risks may differ than in an adult.

Teriparatide [hPTH(1–34)] is a potent anabolic agent that has been shown to substantially increase spine BMD after six months of therapy in women with AN [84]. Animal studies of teriparatide resulted in dose-dependent skeletal neoplasms [85], although post-marketing safety studies have yet to show an association between osteosarcoma and teriparatide use in adults [86]. Nevertheless, teriparatide use in the pediatric population is cautioned against with a black box warning and has not been widely studied for indications other than hypoparathyroidism [87].

Bisphosphonates are synthetic analogs of pyrophosphate that exert an antiresorptive effect. Use of intravenous pamidronate therapy has proven effective in decreasing bone resorption and improving low BMD, fracture risk and bone pain in children with a variety of diseases that affect bone health including osteogenesis imperfecta, acute lymphoblastic leukemia, and non-Hodgkin lymphoma [88, 89]. Cycled IV bisphosphonates have been more widely studied than oral preparations, with the balance of evidence to date suggesting that the IV forms confer the most skeletal benefit in the pediatric population [90, 91]. However, further data are needed from ongoing clinical trials in specific patient groups to strengthen recommendations for children.

The study of both oral and IV bisphosphonate use in underweight and overweight children with osteoporosis is limited. At this time, the use of bisphosphonate therapy is not indicated in overweight or underweight children with low bone mineral density without osteoporotic fractures. A small study of ten adult women with AN who received oral risedronate for 9 months showed a significant increase in spine BMD without adverse effect [92]. Soon after, however, a randomized, double-blind, placebo-controlled study of alendronate use in 32 adolescents with AN showed no significant difference in lumbar spine and femoral neck BMD or markers of bone resorption or formation after one year of therapy [93]. The effect of bisphosphonate use in overweight, osteoporotic children or adults has not yet been investigated.

Without significant benefit, the potential adverse effects of bisphosphonates become a greater concern although, overall, bisphosphonate agents have been well-tolerated in the pediatric population [94]. Immediate reactions include nausea, fever, diarrhea, and muscular or bone pain that begins within hours or days of the therapy's initiation, but subside quickly and rarely recur. More severe effects include thrombocytopenia, uveitis, mucosal ulcerations, and avascular skeletal necrosis and have not been reported in children [94]. One case-control study demonstrated a significant association between obesity and risk of osteonecrosis of the jaw in adult cancer patients treated with zoledronate [95], but the pathophysiology is unclear and osteonecrosis related to bisphosphonate therapy has not been reported in pediatric patients, including obese, underweight nor healthy youth.

Adverse effects of bisphosphonate therapy have not been reported in children treated at published doses and intervals, but the literature contains only sparse data from controlled, long-term intervention trials. More data are necessary concerning the safety and efficacy of bisphosphonate therapy in children and adolescents.

Hormonal Replacement

Due to the high-normal circulating levels of estrogen and IGF-I in children with excessive adipose tissue, hormonal supplementation is not a treatment option for bone disease in overweight youth. On the contrary, physiologic replacement of low hormone levels secondary to malnutrition has been widely studied.

Administration of oral contraceptive pills containing estrogen and progestin does not improve lumbar spine or femoral neck BMD [96–98], but physiologic transdermal estradiol replacement in young adolescent girls with AN has been shown to increase spine and hip

BMD [99••]. Nevertheless, post-treatment BMD remained lower than in normal-weight controls. Oral DHEA has a similar effect on hip and lumbar spine BMD as a combined oral contraceptive pill after controlling for weight [22]. However, when DHEA is given in conjunction with a combined oral contraceptive pill, bone loss appears to be prevented [100] and femoral neck cross-sectional geometry increased in adolescents with AN compared with placebo [101••]. When a 9-day course of injected recombinant human insulin-like growth factor I (rhIGF-I) was administered to adolescents with AN, they exhibited high normal levels of IGF-I, as well as an increase in markers of bone formation, without an increase in markers of bone resorption [102]. A follow-up study examining a 3-month course of rhIGF-I in women with AN demonstrated no difference in IGF-I levels or markers of bone formation, and resulted in a significant decrease in fat mass in the AN group compared with placebo [103]. Overall, hormonal replacement for adolescents with AN has only a weakly positive skeletal benefit, with estrogen mono-therapy not resulting in significant skeletal gains despite the misconception that it is the standard of care. More advantageous long-term outcomes will need to be described before hormone replacement therapy is commonly prescribed in the pediatric population.

Conclusions

As the incidence of underweight and overweight in the pediatric population grows, that of pediatric osteoporosis will likely increase significantly. Children at both ends of the weight spectrum may have compromised bone strength development during their most vital period of bone accrual. Early nutritional intervention for optimal weight management, consistent monitoring of bone health, and conservative treatment with pharmacologic options presently available are important to circumvent future impaired bone strength. More rigorous, multi-center research, including intervention and prevention trials with long-term follow-up, are needed to determine the most effective means of bone loss prevention and catch-up bone accrual.

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Table 1

Definition of osteoporosis in children and adolescents [15••]

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<ul style="list-style-type: none">•••••	The diagnosis of osteoporosis in children and adolescents should NOT be made on the basis of densitometric criteria alone.
	In the absence of vertebral compression (crush) fractures, the diagnosis of osteoporosis is indicated by the presence of both a clinically significant fracture history and BMD Z-score of -2.0 .
	A clinically significant fracture history is one or more of the following: (1) two or more long bone fractures by age 10 years; (2) three or more long bone fractures at any age up to age 19 years.
	A BMC/BMD Z-score >-2.0 does not preclude the possibility of skeletal fragility and increased fracture risk.
	The finding of one or more vertebral compression (crush) fractures is indicative of osteoporosis, in the absence of local disease or high energy trauma.
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Table 2

Effect of weight optimization on bone mineral density measures

Weight recovery in anorexia nervosa				
Follow-up	Age at onset of AN	Bone mineral density outcomes	Mean BMD and SD	Ref.
1 y	16.0±3.1 y	No significant changes at the lumbar spine compared with baseline measurements	Not available	[55]
3.6 y	17.8±3.7 y	Significant increase at lumbar spine ($P<0.01$) compared with former AN patients with persistently low BMI	Lumbar spine T-score: 1.14±0.13 vs 0.93±0.13	[52]
4 y	16 y	15.8 y after onset of AN, 8 of 11 women still met criteria for low BMD despite recovery	Total body T-score: -1.3 at baseline -1.01 at follow-up Lumbar spine T-score: -0.94 at baseline -0.62 at follow-up Hip T-score: -1.38 at baseline -1.32 at follow-up	[54]
8 y	15.0±1.9 y	Significant increase at hip ($P<0.001$) and spine ($P<0.01$) compared with former AN patients with persistently low BMI	Hip Z-score: -0.02±1.11 vs -0.97±0.91 Spine Z-score: -0.62±1.31 vs -1.41±1.10	[53]
Weight loss in obesity				
Follow-up	Age at weight loss	Bone mineral density outcomes	BMD changes	Ref.
12 mo	14.5±1.1 y	Whole body BMD did not change significantly from baseline in children who underwent an intensive weight loss trial	Whole body BMC: 1.08±0.67 at baseline 1.06±0.67 at follow-up	[59]
9 mo	51±8 y	Compared with baseline, adults who underwent bariatric surgery had significant decreases in their lumbar spine, femoral neck, total hip, trochanter, and total body BMD	Lumbar spine: -3.3 %±2.6 % Femoral neck: -5.1 %±7.1 % Total hip: -7.8 %±4.8 % Trochanter: -9.3±7.5 % Total body: -1.6±2.0 %	[60]
2 y	17.3±1.9 y	Whole body BMC and BMD Z-score decreased significantly ($P<0.001$) in adolescents who underwent bariatric surgery	Whole body Z-score: 1.5 at baseline 0.1 at follow-up Whole body BMC: -7.4 %	[61]

AN anorexia nervosa, BMC bone mineral content, BMD bone mineral density, BMI body mass index.