2013 Pediatric Position Development Conference

Dual-Energy X-Ray Absorptiometry Interpretation and Reporting in Children and Adolescents: The Revised 2013 ISCD Pediatric Official Positions

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Abstract

The International Society for Clinical Densitometry Official Revised Positions on reporting of densitometry results in children represent current expert recommendations to assist health care providers determine which skeletal sites should be measured, which, if any, adjustments should be made, reference databases to be used, and the elements to include in a dual-energy X-ray absorptiometry report. The recommended scanning sites remain the total body less head and the posterior-anterior spine. Other sites such as the proximal femur, lateral distal femur, lateral vertebral assessment, and forearm are discussed but are only recommended for specific pediatric populations. Different methods of interpreting bone density scans in children with short stature or growth delay are presented. The use of bone mineral apparent density and height-adjusted Z-scores are recommended as suitable size adjustment techniques. The validity of appropriate reference databases and technical considerations to consider when upgrading software and hardware remain unchanged. Updated reference data sets for all contemporary bone densitometers are listed. The inclusion of relevant demographic and health information, technical details of the scan, Z-scores, and the wording "low bone mass or bone density" for Z-scores less than or equal to −2.0 standard deviation are still recommended for clinical practice. The rationale and evidence for the development of the Official Positions are provided. Changes in the grading of quality of evidence, strength of recommendation, and worldwide applicability represent a change in current evidence and/or differences in opinion of the expert panelists used to validate the position statements for the 2013 Position Development Conference.

Key Words: Bone mineral content; bone mineral density; children; dual-energy X-ray absorptiometry; guidelines.

Introduction

Assessment of pediatric bone density is an evolving specialty. Although there have been many advances over the last 6 yr since the publication of the original International Society for Clinical Densitometry (ISCD) recommendations for children and adolescents *(1)*, there are still many areas where significant uncertainties exist. These revised recommendations reflect developments in the pediatric bone field related

to the assessment of bone health and their impact on the issues related to reporting and interpreting pediatric densitometry results.

It has been clearly established that the foundation of adult bone health is built during the childhood and teenage years *(2—5)*. Peak bone mass is established by the third decade *(4,6—9)*, a compromise of which may be associated with an increased lifetime risk of osteoporosis and fractures *(10,11)*. A variety of childhood diseases and pharmaceutical interventions can result in bone loss, suboptimal accrual of bone mass, or a combination of both *(12—17)*. Therefore, clinicians have sought to identify tests that best evaluate bone health in young children and adolescents. The goal of bone densitometry is to identify individuals at risk for skeletal fragility, determine the magnitude of compromised bone mass in children with established bone fragility, and guide and monitor treatment. Although the rationale for densitometry is the same in children as adults, performing and interpreting bone density results is much more complex in young growing patients *(4,5,18—20)*.

Dual-energy X-ray absorptiometry (DXA) is the most commonly used densitometric technique for children throughout the world, preferred over other techniques because of its speed, precision, safety, low cost, and widespread availability *(4,5,20—22)*. However, for a given patient, the clinician must consider the need for a bone density evaluation, including both the duration and severity of the chronic illness and/or frequency and nature of fractures *(20)*. There are significant knowledge gaps in this area, such as the paucity of large representative normative databases from healthy youth, especially for certain ethnic groups, and the need for validated adjustment techniques that may be needed to interpret densitometric tests in children with altered growth or maturity patterns. There is also debate around the issue of whether it is appropriate to compare the bone density of a child with chronic disease with data obtained from healthy youth; the need for disease-specific reference databases has been questioned. Appendicular fractures exhibit a bimodal distribution with an initial peak during puberty (at 11 yr in girls and 14 yr in boys) *(23)*. Such fractures were originally attributed to trauma because of increased activity in this age group, although more recent studies have suggested that such fractures may reflect differential changes in bone mineral content (BMC) and bone geometry during puberty, possibly resulting in transient skeletal fragility *(24)*. Furthermore, a 4-yr follow-up study of children with forearm fractures and low bone mass at study entry demonstrated a low BMC at several skeletal sites, even after adjustment for bone area, height, weight, and pubertal stage, confirming the premise that fractures may indeed represent a marker of skeletal fragility *(25)*. Although still limited, there are increasing data that describe the relationship between DXA measurements and fracture risk in growing children and adolescents. However, all the prospective studies completed to date in this area have examined otherwise healthy children or adolescents with fractures, rather than those with chronic disease *(26—44)*.

The following questions regarding the reporting of pediatric densitometry results were revisited at the 2013 ISCD Pediatric Position Development Conference, in Baltimore, MD, USA:

- What are the most appropriate and reproducible sites for densitometry measures in children and adolescents?
- What is the best method for reporting areal bone mineral density (aBMD) in children?
- What corrections should be made for bone size, height, lean body mass (LBM), skeletal age, or pubertal stage?
- What are the most appropriate normative databases for use in childhood?
- What are the elements that should be included in a DXA report for a child or adolescent?

Methodology

The methods used to develop, and grading system applied to the ISCD Official Positions, are presented in the Executive Summary that accompanies this task force document. In brief, all positions were graded on quality of evidence (good; fair; and poor: where ''good'' is evidence that includes results from well-designed and well-conducted studies in representative populations; ''fair'' is evidence sufficient to determine effects on outcomes, but strength of the evidence is limited by the number, quality, or consistency of the individual studies; and ''poor'' is evidence that is insufficient to assess the effects on outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or information), strength of recommendation (A: B: or C: where ''A'' is strong recommendation supported by the evidence; ''B'' is a recommendation supported by the evidence; and ''C'' is a recommendation supported primarily by expert opinion), and applicability (worldwide = W or variable, according to local requirements = L). Changes to the grading of each of the position statements previously presented in the original 2008 document *(1)* represent a revision in the quality of evidence, the strength of recommendation, and its worldwide applicability. On the other hand, where there has been no change in evidence, the changes may reflect differences in opinions of an alternative group of expert panelists used to validate the position statements.

What Are the Most Appropriate and Reproducible Sites for Densitometry in Children?

ISCD Official Position

- DXA is the preferred method for assessing BMC and aBMD.
  Grade: Good-A-W
- The posterior-anterior spine and total body less head (TBLH) are the preferred skeletal sites for performing BMC and aBMD measurements in most pediatric subjects. Other sites may be useful depending on clinical need.
  Grade: Fair-B-W

- Soft tissue measures in conjunction with whole body (WB) scans may be helpful in evaluating patients with chronic conditions associated with malnutrition or with muscle and skeletal deficits.
  Grade: Fair-B-W
- The hip is not a preferred site in growing children because of variability in skeletal development.
  Grade: Fair-B-W
- If a follow-up scan is indicated, the minimum interval between scans is 6−12 mo.
  Grade: Fair-B-W.

Rationale

Although there are published data describing the relationship between future fracture and bone density in healthy children *(44)*, there is a paucity of prospective data regarding the relationship between a bone density measurement by DXA and fracture risk among youth with chronic illness. There are also limited data relating the optimal bone mass in childhood and risk for the development of future osteoporosis. In the absence of these data, information about a site's reproducibility and the clinical information afforded guide the selection of sites for densitometry in children. The sites selected for DXA measurements are generally intended to provide an evaluation of a child's bone density and insight into overall skeletal health *(19)*.

WB and Spine

If technically feasible, the pediatric DXA examination should include lumbar spine (L1−L4) and total body *(19,20)*. Both sites are highly reproducible, evidenced by a coefficient of variation (CV) documented to be 0.64−1.03 at the spine and 0.66−1.20 at the total body in a study of healthy children aged 6−16 yr *(45)*. Studies of adults have reported similar precision at these sites: 0.7−1.7 at the spine and 0.7 at the total body *(46−48)*. Measurements of the spine and total body provide more information about the status of trabecular and cortical bone, respectively, than standard radiographs *(49)*. The spine is a preferred site in pediatrics because of the speed and precision of measurements, easily identified bony landmarks, and increasing amounts of pediatric normative data *(50)*. The total body is also a recommended site because of excellent precision and fact that this site affords a measurement of total bone mass and evaluation of body composition, including fat mass and its fraction of WB mass and LBM (predominantly muscle mass). However, recent work from a large multicenter study highlighted that machine differences may significantly impact on WB bone density parameters, making the measurement less reliable in multicenter studies *(51)*.

Soft tissue evaluations determined with the WB bone data may be helpful for clinicians caring for children with chronic conditions; DXA scanners generate bone density and body composition measures simultaneously. Growth, chronic illness, and specific interventions may affect both bone and composition *(50)*. Therefore, scans of the total body may be useful for both ongoing clinical assessments and research

purposes as both bone and body composition can be evaluated. Total body measurements have been used in studies of many chronic conditions in pediatrics, including eating disorders (e.g., anorexia nervosa) *(17,52,53)*, inflammatory diseases (e.g., inflammatory bowel disease, celiac disease, systemic lupus erythematosis, etc) *(54−56)*, glucocorticoid therapy related to inflammation or transplantation *(57)*, neuromuscular disorders (e.g., spinal cord injuries *(58)*, paralysis or cerebral palsy (CP) *(59,60)*, Duchenne muscular dystrophy (DMD) *(61−64)*, long-term immobilization after injuries *(65)*, and idiopathic juvenile osteoporosis [IJO]) *(66)*. In fact, muscle development plays an important role in bone mineral accrual, and it has been proposed that insight into the mechanisms of reduced bone mass/density can be obtained through an evaluation of the DXA-based muscle-bone unit *(67−69)*. The relationship between muscle force and mass to bone mass and geometry in the developing skeleton can be considered in the context of the "mechanostat hypothesis" *(70)*. According to this theory, both bone mass and geometry are influenced by growth and muscle development in children and adolescents. Thereby, bone adapts to tissue strain secondary to biomechanical forces. The process is further modified by hormonal signals (i.e., estrogens and androgens), which can be altered by a chronic disease (e.g., low estrogens and androgens in an emaciated adolescent girl with anorexia nervosa who has little body fat and muscle tissue, as well as a low bone mass) *(52,53)*. Increasing amounts of normative data are becoming available to facilitate the use of these measurements in the clinical environment *(71,72)*.

For WB bone assessments, there is growing consensus that TBLH measurements should be obtained. The rationale for excluding the head is that the skull constitutes a large percentage of the skeleton and is not responsive to physical activity or other environmental stimuli *(73)*. Ideally, a clinician would have the choice to evaluate WB scan with head and less head, the latter option especially useful in a young child. A large prospective cohort study examined the relationship between bone mass, assessed as TBLH, and fracture risk in 6213 healthy children (mean age: 9.9 yr) over the subsequent 2 yr *(44)*. There was a weak inverse relationship between areal TBLH BMD and subsequent fracture risk (odds ratio per standard deviation [SD] decrease = 1.12; 95% confidence interval [CI]: 1.02−1.25). Adjustment for bone size and mineral content relative to body size in this cohort improved fracture prediction. Fracture risk was inversely related to BMC adjusted for bone area, height, and weight (odds ratio = 1.89; 95% CI: 1.18−3.04) *(44)*. Of note, however, there are no studies that have examined directly whether fracture risk is improved if the head is excluded.

The relationship between bone mass and fracture risk may differ in children with chronic illness. A recent study of children with chronic disease found lumbar spine and TBLH DXA scans to be relatively sensitive and specific at identifying children with vertebral fractures. Spine and TBLH aBMD were less appropriate when identifying children with long bone fractures. The data suggest that aBMD measurements distant from a long bone fracture site, such as the

lumbar spine or TBLH, may be less sensitive in detecting a localized bone defect responsible for the bone's fragility. Thus, regional DXA measures of long bone sites, such as the distal radius, or the distal and proximal femur, may be more sensitive for the estimation of fracture risk for long bones [74].

Other Skeletal Sites

Proximal Femur and Total Hip. The proximal femur region, commonly assessed by DXA in adults, is more challenging to evaluate in children [50,75,76]. Skeletal landmarks, which guide proper positioning, may not be well developed in young children. This can lead to errors in positioning and placement of the region of interest (ROI) using standard software. However, data from the Bone Mineral Density in Childhood Study (BMDCS) suggest that age-related precision of the total hip and femoral neck is comparable to both that of the spine and TBLH [45]. Currently, normative data for total hip are available for children and adolescents but are more limited than for the spine and WB [21,22,77–79]. Many clinical centers begin to include measures of the hip region during middle to late adolescence (e.g., age 13 and older) as teenagers who possess threats to bone health are approaching the transition to adult providers. The skeletal landmarks are fully formed by late adolescence, and issues related to patient cooperation and positioning approach that seen in adults among this age group.

Lateral Distal Femur. An alternative measurement site for children is the lateral distal femur (LDF). This site can provide a skeletal measure in children for whom standard DXA measures are difficult to obtain because of joint contractures or metal implants [80,81]. Currently, there are no standardized DXA software protocols for the acquisition or analysis of aBMD resident on any DXA machine; however, with training, [82] reliable assessments of the LDF can be performed using the forearm scan software and semistandardized analysis techniques. Recently, data have been published in children with CP, DMD, and congenital spinal syndromes, demonstrating the significant relationship between LDF bone density, fracture history, and ambulatory status [83–85]. At this time, reference data for LDF are only available for Hologic scanners (Hologic Inc.; Bedford, MA) [81,86].

Distal Forearm. The distal forearm is a potential site for assessment in children and adolescents who cannot be scanned at the spine or WB because of obesity or metal implants, for example, patients who exceed the scanner weight limit (300–450 lbs; 135–209 kg) [19,50]. In a study of 90 New Zealand children with repeated forearm fractures, a significant reduction in forearm aBMD and BMC was observed, most markedly at the ultra distal site (i.e., the site with the largest proportion of trabecular bone) [33]. More recently, this site has been shown to be useful when monitoring site-specific changes and appears to correlate well with the strength indices obtained from a peripheral computed tomography scan [87]. However, the distal forearm can be difficult

to position in a young child or child with poor hand control or hand contractures and as such, forearm scans have been shown to have the poorest precision of all the measurement sites [45]. Although reference data exist for this site, they are limited primarily to Hologic scanners [21,88,89].

Vertebral Fracture Assessment. The most common fractures in childhood are forearm fractures. However, often fractures with the greatest clinical consequence are vertebral compression fractures. Frequently, occult (i.e., with no clinical symptoms such as pain or deformity) in nature, they represent a severe failure of bone strength, and in adults, are associated with a significant risk of further vertebral and nonvertebral fractures. Vertebral fractures can occur either at disease presentation or several years after diagnosis. The Canadian Steroid-associated Osteoporosis in the Pediatric Population study has demonstrated the high prevalence of vertebral fractures in many pediatric disease groups [90–92]. In children initiating glucocorticoid therapy for the treatment of rheumatic disorders, 7% of the 134 children studied had either a mild or a moderate vertebral fracture at presentation [90]. Similarly, in children with newly diagnosed acute lymphoblastic leukemia, 16% of the 186 evaluated also presented with vertebral fracture [91]. Although the current gold standard for confirming the presence or absence of a vertebral fracture is a thoracic and lumbar lateral spinal radiograph, vertebral fracture assessment (VFA) by DXA in children is gaining popularity. DXA for VFA in adults has been available for several years and has been shown to have excellent sensitivity for vertebral fracture especially for clinically relevant moderate (grade 2) to severe (grade 3) vertebral fractures [93,94]. Although image resolution from a DXA scanner is lower than that of conventional spinal radiographs, VFA has several advantages. DXA systems are capable of acquiring the whole spine in a single projection in both the posterior-anterior and lateral projections; whereas with conventional radiographs, the thoracic and lumbar spine requires 2 separate exposures/films. VFA with parallel beam geometry results in images without image magnification and artifactual concave vertebral endplates ("bean" can effect) because of the parallax effect of the divergent X-ray beam of conventional spinal radiographs. Most significantly for children, the radiation dose from a DXA VFA scan is approximately 10–100 times lower than the radiation dose from lumbar and thoracic spine radiography [95]. Moreover, the VFA by DXA can be performed at the same time as the routine DXA assessment and negate the need for additional visits to the hospital for further spine imaging.

Earlier studies using this technique in children were not encouraging as the older generations of bone densitometers did not have sufficient image resolution to visualize clearly the vertebrae in children [96]. However, with the introduction of a higher resolution bone densitometer (GE Lunar iDXA, GE Lunar Corp.; Madison, WI), VFA in children has proven to be a useful tool for the diagnosis of moderate and severe fractures [97–100]. Furthermore, VFA has been shown to be superior to conventional radiographs when identifying changes in the thoracic region [97], which in children, as in adults, is

the region where the greatest number of vertebrae fractures occur *(90)*. As such, and in certain situations, VFA by DXA may prove to be a useful practical tool for the assessment in vertebral fractures in children, particularly in the presence of normal bone density, given that both assessments can be done at the same occasion, with minimum radiation exposure.

BMC vs aBMD

For total body measurements, total body BMC has been considered one of the preferred methods of assessment for bone status because of its reproducibility and lack of areal density-related errors *(101)*. Some experts contend that this measurement is the most reliable in pediatric patients, especially during the prepubertal and early adolescent years *(19,101)*. One study found spinal BMC measurements by axial quantitative computed tomography (QCT) and DXA *(102)* to be highly correlated ($R^2 = 0.94$). In a meta-analysis of 10 case-control pediatric fracture studies, Clark et al *(103)* found BMC by DXA to be a reasonable predictor of fracture in healthy children (standardized mean difference: -0.26; 95% CI: -0.40 to -0.11, $p < 0.001$, in those with fractures, compared with controls). Bone area as derived by DXA in centimeters squared can also be monitored separately, in addition to changes in BMC and aBMD. These separate assessments enable one to differentiate the effects of either an intervention and/or disease process on bone mineral accrual and bone size, which is especially useful in the context of a research protocol. However, work from the BMDCS investigators suggests that overall aBMD proved to be a more precise measure than BMC at all sites and across the whole pediatric age range *(45)*.

Accuracy and Precision

Precision is an indicator of the reproducibility of a measurement. Precision error is expressed in terms of the least significant change (LSC), equal to $2.8 \times \%$ CV for the 95% confidence limit *(104,105)* or root mean square SD in g/cm^2 of a set of measurements *(105)*. The root mean square SD is the ISCD-recommended form of expressing precision error. Both long- and short-term precision is important to consider in performing DXA measurements *(19,104)*. Short-term precision may reflect errors in either the acquisition or the analysis of DXA data, or factors directly related to patients *(106)*. Examples include the imprecision of the scanner itself (manufacturers report this to be less than 1%) *(19)* and variation in patient positioning and motion artifacts (typically less than 2%−3% at the spine, up to 5% at the hip, and 1%−2% for the total body) *(107−109)*. Short-term precision also varies with each technologist and should be assessed using a repeated measures procedure *(105,110)*. Long-term precision reflects potential machine drift, which can occur with any scanner. As with short-term precision, this type of precision may reflect errors in the acquisition or analysis of data and patient-related errors. For example, a patient could develop a neurological disease that worsens over time, with motion artifacts introduced on later scans from the inability to remain still. It is important that the technologist regularly review quality control

scans of phantoms daily and graph results over several week periods to monitor for this problem *(111)*. Recent data showed that the DXA precision of adolescents (expressed in CV) is similar to published adult values, but the CV of young children was higher *(45)*. DXA precision also varied by age for scans at multiple sites, including the spine, hip, forearm, and TBLH. In adolescents aged 14−16 yr, the mean CV was 0.64, 0.65, 1.66, and 0.74 at the lumbar spine, total hip, forearm, and TBLH, respectively. In the children studied, ages 6−9 yr, the mean CVs were 1.11, 1.23, 1.56, and 1.25 at these same skeletal regions, respectively *(45)*.

Discussion

Many of the same principles apply for DXA scans obtained in children as those in adults. The clinician interpreting the scans must understand the process by which the numbers were generated and ensure that meticulous scan acquisition and analysis techniques were used. The clinician should also be familiar with the precision and accuracy of this technique including an understanding of LSC. The magnitude of change required to be statistically significant varies with the precision of the measurement technique *(104,105,110)*. To interpret serial measurements accurately, a clinician must know the LSC at the facility in which the aBMD measurements are performed. If the observed change equals or exceeds the LSC, one can be reasonably confident that true bone loss, gain, or a failure to accrue at a normal rate has occurred in a given patient. However, if the LSC has not been equaled or exceeded, the patient can be informed that the changes observed in follow-up measurements are within the error of repeated measurements and may not be significant. These decisions have important implications for clinical care, including dictating whether new therapies are initiated or ongoing ones discontinued. As detailed in the later sections, the application of LSC assessment in children and adolescents is complicated by changes in bone mass because of interval growth. That is, the gain in bone mass may exceed the LSC even if the gain is less than expected given the interval increase in age or height.

The LSC can also be used to guide the timing of follow-up measurements. Children and adolescents, unlike adults, are growing, and the ROIs will change constantly. The mean growth velocity of a healthy child is 5−6 cm/yr until puberty when peak height velocity occurs, averaging 8.3 cm/yr in girls and 9.5 cm/yr in boys *(112)*. The most rapid gains in bone mineral occur during the pubertal growth spurt but lag behind peak growth velocity by several months *(2)*. Chronic illness may significantly inhibit both growth and puberty, thereby compromising the normal building and remodeling of the skeleton, with the potential to compromise peak bone mass *(4,5,113)*. At the present time, as for adults, scans should be repeated in general every 1−2 yr for clinical purposes; scans may be appropriate every 6 mo for patients in a research study and/or those receiving a medical intervention targeting the skeleton *(19,114,115)*. The shorter 6-mo interval may reveal trends in skeletal losses or gains that are not yet clinically significant.

The monitoring time interval (MTI) estimates the duration (years) between 2 aBMD measurements, during which 50%

of the population changes more than the LSC. This concept is important to consider in planning follow-up aBMD measurements. The MTI for children is less well established in children than in adults [116]. In 1554 healthy children, age 6−16 yr, Shepherd et al [45] showed that MTIs were shortest at the anterior−posterior spine (MTI: 0.2−1.1 yr) and were longer at the femoral neck and distal third of the radius (0.6−4.3 yr). A complete understanding of precision and the terminologies LSC and MTI is important for clinicians who order and interpret skeletal assessments by DXA.

What Is the Best Method for Reporting aBMD in Children; What Corrections Should Be Made for Bone Size, Height, Lean Body Mass, Skeletal Age, or Pubertal Stage?

ISCD Official Position

- In children with short stature or growth delay, spine and TBLH BMC and aBMD results should be adjusted. For the spine, adjust using either bone mineral apparent density (BMAD) or the height Z-score. For TBLH, adjust using the height Z-score.
  Grade: Fair-B-W.

Rationale

The current standard for reporting DXA results is the aBMD Z-score, which provides an estimate of the SD(s) away from the mean for chronologic age and sex [4,5,50,106]. A Z-score can also be calculated factoring in other variables such as race/ethnicity and height. The Z-score cannot be used to diagnose ''osteoporosis'' (as a T-score does in adults). Although T-scores may be generated automatically on a DXA report, these should not be used in the interpretation of the aBMD of an individual who has not reached peak bone mass (usually by age 20) [18,19,45,50].

Proposed Size Adjustments

The greatest challenge in the interpretation of pediatric DXA measurements is the optimal method to adjust for the influence of bone size because both BMC and aBMD are highly influenced by skeletal dimensions [117−122]. One study compared bone densitometry results for the spine by DXA and QCT in 200 healthy children and 200 with a chronic disease [123]. DXA aBMD Z-scores predicted QCT Z-scores below −2.0 SD with reasonable sensitivity (72%), specificity (85%), and negative predictive value (98%), but the positive predictive value was low (24%). Among children with DXA aBMD Z-scores less than −2.0, only 24% had QCT Z-scores less than −2.0. Many more subjects were classified as having a low bone density by DXA than QCT, and the apparent overdiagnosis of bone deficits was most pronounced in children with chronic disease [123].

Bone Size. Several mathematical models of estimating volumetric BMD (vBMD) have been proposed to circumvent the confounding effects of bone size on DXA measurements of bone mass. In growing children, debates persist about the validity of their underlying assumptions about bone geometry [118−120]. One of the most commonly used methods is BMAD, which assumes that a vertebral body is shaped like a cube [118]. BMAD is calculated by the following formulae: spine BMAD = BMC $(L_1−L_4) \div Ap^{3/2}$, where Ap is projected area from DXA measurements of aBMD. Femoral neck BMAD = BMC (femoral neck) $\div Ap^2$. BMAD, as generated by Carter et al [118], was correlated with vBMD measured directly by QCT [123], with higher correlations noted among adolescents at Tanner stage 4−5 ($r^2 = 0.56−0.60$) vs Tanner stage 1−3 ($r^2 = 0.13−0.27$). In another study, Jones et al [41] compared measurements of bone mass in 321 subjects with upper extremity fractures vs 321 healthy controls. The only DXA variables that were consistently associated with fracture risk in both boys and girls were spine aBMD and BMAD for total upper limb fractures, and spine and hip BMAD for wrist and forearm fractures.

Kroger et al [119] developed a similar estimate of vBMD based on the assumption that bone is a cylinder or ellipse. Estimated vBMD at the femoral neck is calculated as aBMD × (4/π × [height of measurement area/measurement area of femoral neck]). At the spine, the formula is aBMD × (4/[π × width of lumbar measurement area]), width defined as the mean width of the second to fourth lumbar vertebral body.

Molgaard et al [124] proposed a 3-step approach to adjust for body size, which takes into account multiple measures of growth and development. This method assesses whether bones are the appropriate size for age by looking at height for age (short bones); bone area for height (narrow bones); and whether they are appropriately mineralized for their size, BMC for bone area (light bones) [124]. This approach is provided as an analysis option on some GE Lunar scanners. However, it was subsequently suggested that a drawback of this approach was ignoring the substantial impact of lean mass on bone mass [69], with significant gender differences noted in this parameter [21,68,69,72,125]. Although a few studies have shown that correction for bone size parameters normalizes BMC in children with low bone mass such as children with HIV [126] and other chronic illnesses [127,128], it is not clear that such adjustments prove the structural integrity of bone in these children. There are specific clinical scenarios for which the Molgaard approach could be problematic because the model fails to take height into account. Bone area as generated by DXA is a function of 2 dimensions: width (e.g., periosteal circumference) and length. A tall child with narrow bones will have the same bone area as a short one with broad bones. Thus, it would be inappropriate to expect both children to have the same BMC because they have the same bone area. Data from 2 studies support this point. First, DXA WB BMC-for-bone area Z-score has no correlation with cortical vBMD as measured by pQCT [128]. Second, Leonard et al [129] found that obese children had markedly increased bone area for height ($p < 0.001$). These overweight patients also had a markedly decreased BMC relative to bone area

($p < 0.0001$), which represented an artifact rather than evidence that this group had ''light'' bones. The obese children were compared with controls who had similar bone areas but were significantly taller, thus accounting for the greater BMC in the controls.

The Molgaard model may also be problematic in a child with chronic illness with growth delay. Children with chronic diseases often have a low bone area for height (narrow bones). However, this deficit might be underestimated using the Molgaard method, again because differences in height are not accounted for. When one then assesses BMC in the ill child, compared with a control with the same bone area, one is comparing the child with the chronic illness to a control who is shorter (i.e., same bone area, but secondary to the shorter height). Clark et al *(44)* also showed that BMC adjusted for bone area, as well as height and lean mass, provided the best fracture discrimination. These illustrations support the conclusion that consideration of BMC for bone area has value, but only if corrected for height.

Fewtrell et al *(117)* compared different methods of size adjustment, including BMAD, height, bone area, and both bone area and height, in groups of patients and healthy subjects as predictors of low bone mass for age (defined as a Z-score < -2). All size-adjusted parameters performed similarly and classified fewer patients as having ''abnormal'' bone mass than did aBMD.

Height. Zemel et al *(130)* studied healthy children and demonstrated that spine and WB BMC/aBMD Z-scores adjusted for height for age Z-scores (HAZ) were least biased compared with height age and chronologic age and can be used to evaluate the effect of short or tall stature on BMC/aBMD Z-scores. Thus, adjustment for HAZ is an effective way of removing the effect of height on BMC/aBMD measurements in the healthy population. This adjustment technique is now publicly available as an easy to use web-based analysis tool (http://www.bcmcspublic.com). However, there are currently no data relating height-adjusted bone mass measurements to fracture risk. Furthermore, obtaining a reliable height measurement in the clinic can be difficult, and the proxies for height that are sometimes used in children with disabilities can further distort the adjustments to aBMD based on height. Polgreen *(131)* reported that adjustment for HAZ in children with mucopolysaccharidosis underestimated bone deficits for the total body, but not the spine. However, further study is needed to understand the clinical significance of these findings.

Bone Age. Bone age assessments, in conjunction with measurements by DXA, have been suggested as an approach to adjust for alterations in expected growth and puberty. Bone age is closely linked to pubertal maturation and the adolescent growth spurt, so as to take into account normal biological maturation in the evaluation of BMC or aBMD *(4,5,50)*. In addition, it is noteworthy that there are certain conditions where bone age and height are asynchronous, such as genetic short stature syndromes where children can be extremely short, but bone age is typically normal. Therefore, caution should be used with when substituting bone age for chronologic age in calculating Z-score as bone age may not correct for bone size in this setting. DXA-derived bone age films have also become available *(132,133)*. Evaluating skeletal maturity via this method appears to be less invasive than standard radiographs, with results that appear to be comparable to the standard method.

In the United States, the Greulich and Pyle method continues to be used most frequently for bone age evaluation *(134)*. Outside the United States, the Tanner-Whitehouse II method is commonly used *(135)*. However, there are no published BMC or aBMD reference data adjusted for bone age for either system. One study in 135 healthy children (ages 1−15 yr) demonstrated a significant relationship between bone age and predicted spine aBMD ($r = 0.893$, $p < 0.001$). These results may be misleading because of the large age range of the children and the lack of consideration of the covariation of both chronologic and bone age *(136)*. Using pQCT radial and tibial measurements at baseline and 12 mo, r^2 values for cortical vBMD at the tibia increased from 0.19 to 0.31 for males and from 0.61 to 0.70 for females when bone age was used. The r^2 values for cortical vBMD at the radius increased from 0.37 to 0.40 for males and from 0.70 to 0.78 for females when bone age was used *(137)*.

A delayed bone age was shown in another study to be associated with fracture *(37)*. In some clinical conditions associated with delayed bone age (e.g., multihormonal pituitary deficiency), it may be reasonable to adjust DXA aBMD for bone age instead of chronologic age *(133)*. One study of patients with hypopituitarism who had low aBMD Z-scores (< -1.0) found delayed bone ages in comparison to chronologic age. After adjusting aBMD data for skeletal age, aBMD Z-scores were significantly improved *(133)*. Ideally, the clinician would have the scanner option to adjust DXA data for bone age in those clinical scenarios deemed appropriate. An example is a 15 yr-old adolescent boy with a history of a brain tumor who has received craniospinal irradiation after surgical resection of the lesion. He has deficits of multiple pituitary hormones as well as a low aBMD in the setting of short stature and pubertal delay. Interpretation of aBMD with respect to his delayed bone age in this adolescent avoids an overestimation of skeletal deficits.

Problems that arise using an adjustment for skeletal age must be considered. There are data indicating that the published norms for skeletal maturity may not be valid for current youth from different ethnic or racial groups. Using the Greulich and Pyle method, Mora et al *(138)* showed that the variability between skeletal and chronologic age was significant and varied by ethnic group in a sample of healthy American children. Zemel et al *(139)* noted a significant discrepancy between chronologic age and bone age among a cohort of healthy American boys and girls, concluding that the US standards for bone age are not well matched to maturation rates of contemporary children. These data suggest that the standards need to be revised to incorporate ethnic differences and a pattern of earlier growth and

pubertal development (e.g., earlier pubertal maturation, especially among certain ethnic groups). A clinician must also consider that the distribution of BMC or aBMD values for bone age is unlikely to be the same as that for chronologic age (50), as accounting for skeletal maturation may decrease the variability. Thus, a 1 SD unit change in aBMD when scaled to bone age may be smaller than a 1 SD unit change scaled for chronologic age. This is especially important for children with obesity or a chronic disease, conditions associated with advanced or delayed bone age, respectively (50,140,141). The rising prevalence of overweight and obesity may contribute to the differences that have been recently noted between chronologic and bone age. In contrast, a chronic illness like Crohn disease can delay bone age. In 1 study of children with Crohn disease, when bone age was substituted for chronologic age in the calculation of aBMD Z-score, results were only affected significantly when there was a discrepancy between bone age and chronologic age of greater than 2 yr (141). When deciding whether it is appropriate to adjust an aBMD measurement for bone age, these issues should be carefully considered.

Pubertal Stage. Densitometry data can also be adjusted for pubertal status because puberty influences body size, skeletal maturation, and bone mineral accrual. Few studies have included Tanner stage or gynecologic age as a primary factor in their normative data sets (6,21,142−144). There are no guidelines regarding how to account for pubertal stage in the evaluation of DXA results, although the presence of advanced or delayed puberty is an important consideration in the interpretation, especially in the case of a chronic disease, which can delay both pubertal maturation and bone accretion (54). Although some studies suggest that pubertal staging by a trained clinician is significantly more accurate than self-assessment by teens (145), self-assessments are nonetheless used in many bone density centers, especially when a full examination is not possible (146,147). In clinical practice, it may be important to take evidence of advanced or delayed puberty into account when interpreting measurements of aBMD. Actual correction for pubertal stage is generally reserved for research studies.

Height Age. For clinical purposes, substitution of height age for chronologic age is sometimes used in the calculation of aBMD Z-score. Height age is defined as the age at which the child's height is the median height on the growth chart. This approach is problematic as use of height age may force a comparison with a developmentally inappropriate age group. This practice is especially worrisome if a short pubertal child is compared with a prepubertal child, highlighting the critical role of pubertal development on bone accretion during adolescence (4). This point is underscored in the study of Saland et al (148) who showed that the prevalence of a low bone mass in pediatric renal transplant recipients varied depending on the method of analysis used. When aBMD was interpreted with respect to height age rather than chronologic age, the prevalence of "osteopenia" was significantly lower.

Adjustment for height age improved the aBMD Z-score especially in pubertal patients (1.8 ± 0.9 vs 0.9 ± 0.7 SD, $p < 0.01$) (148)). However, the clinician should be aware that adjusting for absolute height when interpreting the aBMD of 2 adolescents of the same pubertal status, but with different heights, would be inappropriate. The importance of height and puberty adjustment is apparent in children with Hutchinson-Gilford Progeria Syndrome. These patients are profoundly short after age 2 yr but generally remain prepubertal. Adjustment for height age avoids the dramatic overestimation of skeletal deficits as seen in the aBMD Z-score derived for chronologic age alone (149).

Body Composition. There are strong associations between indices of body composition and bone mass measures, with a differential impact in the relative effect of lean mass and fat mass on such measures between sexes (125,150). Several studies have shown that there is a high correlation between muscle mass and bone mass in children (21,50,68,69,125,151,152), consistent with the functional bone-muscle unit theory. There are also sex differences when adjusting for lean mass (21,50,67−69), and lean mass strongly correlates with bone size, height, and pubertal stage.

Several studies support the use of total body BMC to LBM (BMC/LBM) ratio as a relative bone strength index for fracture risk estimation in children (50,66,68,153,154). Crabtree et al (68) proposed a 2-step algorithm to investigate the relation between LBM and BMC in a child with chronic disease. The first step evaluated LBM for height, and stage 2, BMC for LBM. Children studied with spinal muscular atrophy had a low LBM Z-score ($Z = −1.8 \pm 1.4$), but mean BMC/LBM Z-score of 1.2 ± 1.3, indicating that sarcopenia was their primary abnormality. In contrast, children with osteogenesis imperfecta had a normal LBM Z-score of $+0.4 \pm 1.7$, but mean BMC/LBM Z-score of $−2.5 \pm 1.8$, confirming a primary bone abnormality. The data reported by both Crabtree et al (68) and Pludowski et al (66) support the concept that reduced amounts of BMC for a normal LBM may be associated with increased fracture risk for fracture, at least in children. Crabtree et al (68) studied a third group of British children with fragility fractures and found that BMC by DXA was lower than expected for the normal LBM noted in this group. It was found that British children with fractures of mixed etiology had Z-scores of $−1.9 \pm 1.5$ for the TBBMC/LBM ratio. Likewise, Pludowski et al (66) noted aBMD Z-scores below $−2.0$ for the TBBMC/LBM ratio in both boys and girls in a study of children suffering from acute stage of IJO. The magnitude of disturbance between bone and muscle tissue was suggested by the correlation between bone pain as well as both metaphyseal and vertebral fractures. In contrast, during recovery from IJO, the muscle-bone relationship tended to normalize, yielding improved Z-scores of $−1.07 \pm 0.99$ and $−1.15 \pm 1.40$ for TBBMC/LBM ratio in girls and boys, respectively. The marked increase in TBBMC/LBM ratio observed during recovery from IJO coincided with lack of bone pain and no new fractures. In contrast, in another study comparing WB measurements by

DXA and tibial strength surrogates by pQCT *(128)* in healthy children, neither DXA bone area for lean mass nor BMC for lean mass correlated with pQCT cross-sectional area for length or strength-strain index for length. DXA BMC for bone area was weakly associated with pQCT strength-strain index for length, but in females only. DXA BMC normalized for bone area and lean mass were identified as poor indicators of bone strength.

Regression of BMC against lean mass can be carried out in contrast to calculation of the BMC/LBM ratio. Ratios can be problematic especially when comparing variables in which the slope is not 1.0 and the intercept is not 0. A useful approach, especially in studies of children with chronic illness, is to regress BMC against LBM. This maneuver is accurate as long as height is also included in the regression. A study of patients with Crohn disease used this approach *(14)*.

Discussion

When considering adjustments of DXA measurements for bone size, height, LBM, skeletal age, or pubertal stage in growing children, it is relevant to consider the goal of the exercise. Aims might include avoiding overdiagnosis (and hence inappropriate treatment) of osteoporosis in children who are small for their age; understanding the etiology of low bone mass (short stature, narrow bones, low bone area, low lean mass); or predicting fracture risk. There is no single adjustment paradigm proven to be optimal to achieve these aims, and the selected adjustment will also depend on reference data available *(68,69,124,130)*. The type and/or number of adjustments used will vary depending on the specific clinical profile of the child. Another consideration is whether the growing child or adolescent is undergoing the evaluation for clinical or research purposes. Last, it must be considered whether the adjustment tools are being applied in a chronically ill vs healthy child, and/or whether the tools may afford information on disease-specific factors, as was suggested by a published algorithm *(155)*.

If the primary aim is to prevent overdiagnosis (and hence inappropriate treatment) of low bone mass in children who are small for their age, or to understand the etiology of low bone mass, in general, results must be interpreted in terms of relevant clinical factors. These variables include sex, ethnicity, height, weight, body composition, and pubertal development *(20,50,125)*. There is a lack of consensus regarding which combination of these factors provides the most accurate assessment of skeletal status. Whatever combination is chosen, a diagnosis of osteoporosis in children should not be made on DXA results alone without clinical evidence of bone fragility *(49,106)*. As is increasingly becoming apparent, fracture is also highly dependent on bone size, geometry, architecture, quality, factors that affects bone strength, and anthropometic variables, which may be independent of an aBMD measurement by DXA. It is also important to note that low BMC or aBMD may be "appropriate" for individuals with smaller, thinner bones, whereas reduced bone size per se may be a risk factor for fracture at least in older individuals *(155)*.

Although in clinical practice, it would be desirable to use DXA-derived measurements to predict fracture risk, in practice, few studies have validated size adjustments against this outcome, and it is therefore not possible to conclude which adjustments are the most appropriate. Indeed, studies that have measured bone mass in otherwise healthy children with fractures have not implemented such adjustments *(27−30,33,34,44,156−158)*. Furthermore, Henderson *(83)* studied 619 children aged 6−19 yr with CP or DMD and observed a strong correlation between fracture history and unadjusted aBMD Z-scores in the distal femur; 35%−42% of those with aBMD Z-scores less than −5.0 had fractured compared with 13%−15% of those with aBMD Z-scores greater than −1.0. Risk ratios were 1.06−1.15 (95% CI: 1.04−1.22), meaning a 6%−15% increased risk of fracture with each 1.0 decrease in aBMD Z-score. More recently, Crabtree et al *(74)* investigated whether size adjustment techniques improve the diagnostic ability of DXA in a cohort of children with chronic diseases. Lumbar spine (L2−L4) and TBLH Z-scores were calculated using different size adjustment techniques, namely aBMD for age and vBMD for age (BMAD); BMC and bone area for height; BMC for bone area; BMC for lean mass (adjusted for height); and BMC for bone and body size. Fractures in the 12 mo before the DXA scans were documented. All size adjustment techniques improved the predictive ability of DXA for fracture. The most accurate method for assessing vertebral fracture was spine BMAD for age, whereas the most accurate method for assessing long bone fracture was TBLH for LBM adjusted for height.

The only prospective study to examine the predictive value of size-adjusted DXA measurements for *subsequent* fracture risk was conducted in healthy children aged 9 yr at baseline. Clark et al *(44)* reported that 2 DXA measurements were lower in children who had a fracture in the next 2 yr: Humeral vBMD (calculated from regional analysis of the area of the humerus, length, and width from a WB scan) and TBLH area adjusted for height and weight.

There is need for more research regarding the interactions between body composition and bone, and how these interactions differ in an ill vs healthy child. Contradictory conclusions of studies in this area must be resolved before a recommendation regarding use of TBBMC/LBM can be endorsed. As discussed, inclusion of LBM in regression models can be a useful technique as long as height is also considered. In general, an adjustment for LBM may help a clinician understand the etiology of skeletal deficits. For example, if a child has both low muscle and bone mass, the skeletal deficits may be secondary to the compromised muscle mass and/or tone. If one adjusts for muscle, the bones will look "normal" but in reality are not. One should report the unadjusted bone result to show that the bones are weak; then use the adjusted result to suggest that the deficit may be related to the muscle deficits. However, it is important to underscore that there remain gaps in knowledge as to whether these adjustments assist in fracture risk prediction.

What Are the Most Appropriate Normative Databases for Use in Childhood?

ISCD Official Position

- An appropriate reference data set must include a sample of healthy representatives of the general population sufficiently large to capture variability in bone measures that takes into consideration gender, age, and race/ethnicity. Grade: Good-A-W
- When upgrading densitometer instrumentation or software, it is essential to use reference data valid for the hardware and software technological updates. Grade: Good-B-W.

Rationale

There is a lack of consensus regarding the demographic and physiologic factors that should be incorporated into normative databases. "Ideal" characteristics of reference data were considered, including what constitutes an ideal sample and how the data would be modeled in the statistical analysis *(159)*. Characteristics of the ideal sample would include sample of healthy youth (normal growth and development, and free of illness, medication, or lifestyle limitations); representative of the general population; multiregional (to address local differences in ethnicity and lifestyle); and sufficiently large to capture variability because of gender, age, and race/ethnicity.

How reference data are modeled mathematically is important to capture the nonlinearity of gains and the increased variability with advancing age *(50)*. The most common approach to the use of reference data is to define the mean and an SD. However, when the distribution of values for a given age is skewed, it is inappropriate to use the SD to characterize the variability. Furthermore, variability is not fixed and increases with age and puberty. Some statisticians recommend transforming bone mineral data using parametric regression modeling *(101,160)* as has been used previously *(161)*. This technique becomes particularly important when a large data set is not available, as smaller sample sizes are more vulnerable to skewing. The LMS method *(162)* has also been proposed and is more appropriate when data are both skewed and heteroskedastic. The LMS method uses a power transformation to normalize data. The optimal power to obtain normality is calculated, and the trend is summarized by a smooth curve (L). Smoothed curves for the mean (M) and CV (S) by age are acquired, and these 3 measures are used to describe the data distribution *(163)*.

At the present time, there are few reference data sets for bone density measurements in children, which capture all the aforementioned characteristics. The BMDCS funded by the US National Institutes of Health was designed to meet most of these "ideal" characteristics and has obtained longitudinal data on a multiethnic cohort of 2014 children in the United States *(88,89)*. Reference data for African American and Non-African American children, 5–20 yr of age, are available for several skeletal sites. The sample was selected to include a large number of healthy children using a common protocol *(89)*. Results from this study represent an enormous contribution to the densitometry field; however, its applicability to children and adolescents outside the United States is yet to be determined. Another limitation is that these data were derived solely using Hologic scanners. These data show the age-related changes in BMC and aBMD, especially variability and skewness that will be critical for designing studies on other models of DXA machines. More recently, these data sets have been converted to "GE equivalents" using the transformation equations developed by Shepherd et al *(164)* and are currently available as an optional reference database with the latest versions of GE Lunar Encore (GE Lunar Corp.; Madison, WI). Currently, in preparation is a large UK data set with more than 3330 children (The ALPHABET Study). This data set consists of data mainly from GE Lunar scanners and also incorporates Hologic scan data. The overriding motivation of this study was to collate all available UK normative data into 1 unified reporting package, which was maximally compatible with both past and future software versions *(165)*.

When choosing a reference database, it is critical to select normative data collected with the same model and software version as that being used for the patient because of systematic differences between scanners *(19,159,166,167)*. Furthermore, it is important to use the same norms when doing serial studies. Sex-specific norms are essential because the BMC and aBMD of girls and boys differ, especially at different ages and stages of puberty *(137)*. Because the absolute value for aBMD is lower in young children compared with that of a healthy adult, software analysis has been modified for children to improve edge detection of lower density bone at some sites *(19,117,159)*. The ability to measure these parameters using standard adult analysis software may be problematic. As such, the manufacturers have developed specific analysis algorithms for edge detection in patients, specifically children with low aBMD. These algorithms have been validated in healthy, obese, and chronically ill children for assessment of spinal aBMD *(168)*. It has been suggested that normative pediatric data be collected using the low-density analysis routinely in children. As such, this is now an automatic feature on all modern Hologic bone densitometers (Hologic Inc.; Bedford, MA) *(106)*. Auto-Low software (Hologic Inc.; Bedford, MA) for the WB uses a different algorithm for the detection of bone based on the subject's weight. As shown by Shypailo and Ellis *(169)*, if the child's weight is greater than 40 kg, results are not significantly different from those generated using adult software. However, this group illustrated the large magnitude of the effect in smaller children who are below this weight threshold: among children weighing 10 kg, the new software resulted in a 25% lower WB BMC compared with the prior version *(169)*.

Discussion

The ISCD Official Positions regarding appropriate reference databases for children and adolescents include new criteria and expand on other concepts considered in prior positions for adults. Most important is the need to recognize differences and changes in machine-specific software used to

analyze pediatric DXA scans. This issue is critically important for pediatrics as the range of BMC and aBMD result is large. Different thresholds historically have been used to detect the bone edge in pediatric scans to ensure that all the bone is included. However, this has caused problems in situations when scans analyzed with 1 software version have been compared with reference databases that have used scans analyzed with a different software version. Clinicians interpreting scans must be cognizant of the software version used and monitor the impact of future changes on BMC and aBMD results.

Use of locally collected norms that reflect genetic potential and environmental exposure of patients is thought to be ideal. However, collecting data from sufficient numbers of children adequately characterize the variability in bone mass, and density is difficult and costly. Thus, many clinicians depend on normative data collected by others. There are several existing databases that include children and adolescents from differing geographic regions and of varying ethnicities. When choosing reference data, one should consider the sample size, gender, age, and ethnicity of the reference population, and the equipment used is comparable to the hardware and software of the end user. Otherwise significant errors can occur in estimated Z-scores *(170)*). Table 1 represents a compilation of pediatric reference data sets available from the literature and the 3 primary DXA manufacturers *(21,22,86,88,89,125,165,171−184)*. To identify recent articles relevant to normative databases (published since the publication of the last PDC guidelines) for aBMD in pediatric populations, we used key words in combination with explode and with AND as Boolean functions. The key words were bone density, reference standards, reference values, assessment, limited to guidelines, practice guidelines, English language, and Humans. The search identified 744 abstracts from 1996 until 2013, after excluding those for the years before 2007, 304 abstracts remained, of which 60 abstracts were identified as relevant. These were further narrowed to 39 articles, all of which were reviewed and the relevant publications addressing the main goal of our review were summarized in Table 1. Table 1 is limited to data collected on contemporary bone densitometers.

What Are the Elements That Should Be Included in a DXA Report for a Child or Adolescent?

ISCD Official Position

Baseline DXA Testing

- A baseline DXA report should contain the following information:
  - DXA manufacturer, model, and software version,
  - Referring physician
  - Patient age, gender, race/ethnicity, weight, and height
  - Relevant medical history, including previous fractures
  - Indication for study
  - Tanner stage or bone age results, if available
  - Technical quality
  - BMC and aBMD
  - BMC and/or aBMD Z-score
  - Source of reference data for Z-score calculation
  - Adjustments made for growth and maturation
  - Interpretation
  - Recommendations for the necessity and timing of the next DXA study are optional

  Grade: Fair-C-L.

Serial DXA Testing

- Serial reports should include the same information as for baseline testing. Additionally, indicators for follow-up scan; technical comparability of studies; changes in height and weight; and change in BMC and area Z-scores should be reported.
  Grade: Fair-C-W.

Terminology

- T-scores should not appear in pediatric DXA reports.
  Grade: Good-A-W
- The term "osteopenia" should not appear in pediatric DXA reports.
  Grade: Fair/Poor-C-W
- The term "osteoporosis" should not appear in pediatric DXA reports without knowledge of clinically significant fracture history.
  Grade: Good-B-W
- "Low bone mass or bone mineral density" is the preferred term for pediatric DXA reports when BMC or aBMD Z-score are less than or equal to −2.0 SD.
  Grade: Poor-C-W.

Rationale

An appropriate pediatric DXA report should include information that identifies the patient, assists the interpreter in evaluating the scan, conveys the validity of the scan, and provides both clear scan interpretation and recommendations, where appropriate *(185)*. Questionnaires administered to patients at the time of scanning can provide valuable clinical information that will allow for a more accurate BMD interpretation.

As there are sparse data regarding the relationship between a given aBMD measurement by DXA and fracture risk in pediatric patients, caution should be used in making recommendations. Longitudinal changes in both bone measures (e.g., aBMD and BMC) and Z-scores are important to highlight.

Items That Should Not Be Included in a Pediatric DXA Report

- Wording such as the "patient has osteoporosis." The term "osteopenia" must also not be used as these 2 terms generate confusion when used in children, and the World Health Organization criteria based on T-scores apply only

Table 1
Normative Data for DXA in Pediatric Subjects on Contemporary Bone Densitometers

Year of publication (ref.)	DXA	Number	Age	Ethnicity	Sites
2002 (171)	Hologic 4500A	231	5−22	White (American)	Total body
2004[a] (21,125)	Hologic 4500A	363	10−17	Arab (Lebanese)	Spine, femoral neck, total body, forearm
2004[b] (79)	Hologic 4500W	422	12−18	White, black (American)	Spine, femoral neck
2007[a] (22)	Hologic 4500A	442	6−17	White (British)	Spine, femoral neck, total body
2007 (88)	Hologic 4500A	1554	7−17	White, black, Hispanic (American)	Spine, femoral neck, total body, forearm
2007 (172)	Hologic 4500A	179	3−18	White (Canadian)	Spine, femoral neck, total body
2007[c] (173)	Hologic 4500W	1155	15−39	Chinese	Spine, femoral neck, total femur
2009[a] (175)	Hologic 4500A	7398	8−20	White, black, Hispanic (American)	Total body
2009 (86)	Hologic 4500A	821	5−18	White, black (American)	Distal lateral femur
2010 (175)	Hologic 4500A/GE Lunar DPX/Prodigy	439	16−24	White (Canadian)	Spine, femoral neck, total hip
2010[d] (176)	Hologic 4500A	5173	8−25	White, black, Asian, Hispanic (American & Canadian)	Spine, femoral neck, whole body
2010[a] (89)	Hologic 4500A	2014	5−23	Black, nonblack (American)	Spine, femoral neck, total body, forearm
2013 (177)	Hologic 4500A	307	1−36 mo	White, black, Asian (American)	Spine
2011[a] (178)	GE Lunar Pro	920	5−17	Asian (Indian)	Spine, femoral neck, total body
2013[a] (165)	GE Lunar Prodigy & iDXA	3300	5−18	White, black, Asian	Spine, femoral neck, total body
2007 (179)	GE Lunar Prodigy	877	5−13	Asian (Chinese)	Total body
2007 (180)	GE Lunar Pixi	664	7−17	Asian (Indian)	Forearm, calcaneum
2010 (181)	GE Lunar Pixi	1115	9−29	Asian (Korean)	Forearm, calcaneum
1995 (182)	Norland XR-26	778	2−20	White (Argentinean)	Spine, femoral neck, total body, forearm
1998 (183)	Norland XR-26	179	12−13	Asian (Chinese)	Spine, forearm
2004 (184)	Norland XR-35	102	3−15	Turkish	Spine, femoral neck

Abbr: DXA, dual-energy X-ray absorptiometry.

Notes: For reference data on older generation bone densitometers, please refer to the previous International Society for Clinical Densitometry pediatric guidelines publication (1).

Hologic 4500A,4500W (Hologic Inc.; Bedford, MA); GE Lunar DPX/Prodigy, Pro, Prodigy & iDXA, Pixi (GE Lunar Corp.; Madison, WI); Norland XR-26, XR-35 (Norland Corp.; Norland Corporation, White Plains, NY).

[a]Size adjustment data available.
[b]Females only.
[c]Males only.
[d]Includes longitudinal "x".

to postmenopausal women. "Low bone mass" (defined as BMD Z-score less than or equal to −2.0 SD) is a more appropriate term until more information is available. Never use T-scores in children and adolescents.

Discussion

The recommended elements of the DXA report represent a significant change from the standard reports generated by DXA machines historically. Importantly, inclusion of these elements better enables a clinician to interpret the results appropriately. Information on the technical aspects of the DXA scan is generally the same for adults and children. However, information on growth and maturation, processes unique to the pediatric age group, need to be considered to prevent erroneous interpretation that may result from either growth or maturational delay. The terms "T-scores," "osteopenia," and "osteoporosis" (based on densitometry findings) cannot be used for children or adolescents because the diagnostic classification of the World Health Organization was based on studies done on postmenopausal women. The use of

T-scores in children, which compares the aBMD of a child to that of a young adult, is particularly problematic and may result in severe clinical mismanagement. Thus, they should never be used in a pediatric DXA report.

Additional Questions for Future Research

- Which ROIs and adjustments of DXA data for body size, height, pubertal stage, and lean mass best predict fracture in healthy children and those with chronic disease?
- More observational data (fracture registries) are needed in healthy children and those with chronic illnesses to determine which DXA parameters most predict bone fragility.
- How can available databases be kept up to date? How often should they be updated? What adjustments can be made when newer software versions become available? How can these data be shared most effectively as through a Web site?
- Is there a need to consider "universal DXA units," considering the variability among scanners from differing manufacturers and that normative data are generally derived from 1 scanner type? How well have the adjustment for Hologic vs GE Lunar been validated in pediatric populations?
- What are the relationships between DXA measures of BMC and aBMD in children and adolescents and size-adjusted measures, peak bone mass, and the future risk of osteoporosis?
- Will revised bone age standards that incorporate ethnic differences and contemporary patterns of growth and pubertal development improve the interpretation of DXA results in children?
- Will the development of longitudinal pediatric DXA reference data improve the identification of children with impaired bone mineral accrual rates and risk of fracture?

Overall Summary

The ISCD Official Positions on reporting of densitometry positions in children consolidates opinions on which skeletal sites should be assessed, which corrections should be made in these assessments, appropriate pediatric reference databases, and the important elements to include in a DXA report. Opinions from pediatric bone health experts from around the world were elicited, and a systematic literature search was performed. The level of certainty for some positions differs from that reported in 2008 (positions stemming from the 2007 Pediatric PDC) *(1)*. These differences likely reflect consideration of new evidence that has been published since the last PDC, as well as differences in the opinions of experts who participated in the most recent conference. Given the sparse data that are currently available in many of these areas, it is likely that these positions will further evolve and change over time as new data become available. Further research is needed to expand on and confirm many of the opinions cited in this position statement.

Acknowledgments

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