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2013 Position Development Conference on Bone Densitometry

The Official Positions of the International Society for Clinical Densitometry: Body Composition Analysis Reporting

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Abstract

Dual-energy x-ray absorptiometry (DXA) measurements of body composition increasingly are used in the evaluation of clinical disorders, but there has been little guidance on how to effectively report these measures. Uniformity in reporting of body composition measures will aid in the diagnosis of clinical disorders such as obesity, sarcopenia, and lipodystrophy. At the 2013 International Society for Clinical Densitometry Position Development Conference on body composition, the reporting section recommended that all DXA body composition reports should contain parameters of body mass index, bone mineral density, BMC, total mass, total lean mass, total fat mass, and percent fat mass. The inclusion of additional measures of adiposity and lean mass are optional, including visceral adipose tissue, appendicular lean mass index, android/gynoid percent fat ratio, trunk to leg fat mass ratio, lean mass index, and fat mass index. Within the United States, we recommend the use of the National Health and Nutrition Examination Survey 1999–2004 body composition dataset as an age-, gender-, and race-specific reference and to calibrate BMC in 4-compartment models. Z-scores and percentiles of body composition measures may be useful for clinical interpretation if methods are used to adjust for non-normality. In particular, DXA body composition measures may be useful for risk-stratification of obese and sarcopenic patients, but there needs to be validation of thresholds to define obesity and sarcopenia. To summarize, these guidelines provide evidence-based standards for the reporting and clinical application of DXA-based measures of body composition.

Key Words: Adipose mass; body composition; bone mineral density; lean mass; whole body.

Background

Task Force 3 was charged with the research and analysis of the published literature covering questions related to the reporting standards for body composition (BC). Literature searches were performed in PubMed by the use of keywords used in the BC literature to help define what parameters are useful in clinical application (Appendix). The search results were distributed to the task force for review and assessment in relation to the questions posed. Recommendations were made on the basis of the evidence presented.

Each section first lists the questions to be addressed, followed by some introductory information, which then leads to the various recommendations. Every recommendation is accompanied with a rationale and a discussion section; where

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appropriate, suggestions for future research also are provided. Explanations as to the process of adopting the various recommendations as well as the grading of the strength and applicability can be found in executive summary.

Introduction

Up to this time, there have been no standards for reporting BC. The rapid evolution of the field has resulted in a proliferation of direct measurements as well as calculated parameters with little guidance on the application of these measures to clinical disorders. In addition, manufacturers have different approaches to reporting that result in difficulties applying information from different machines in a uniform manner for clinical management. The International Society for Clinical Densitometry (ISCD) Position Development Conference section on BC reporting was developed to help provide a foundation for the clinical application of BC data that will aid in the further development of the field. Identification of the gaps in our understanding about the clinical applicability of these measures will also help to direct future research efforts.

The methods used to develop and grade the ISCD official positions are presented in an accompanying article. All positions were rated by the expert panel on the quality of evidence (good, fair, poor), the strength of the recommendation (A, B, C, where A is the strongest recommendation) and the applicability worldwide (W) or locally (L). MEDLINE searches were conducted, and the terms used were documented. The reporting subcommittee analyzed the literature and presented the summary of the evidence for each position to the expert panel at the Position Development Conference held at the 2013 ISCD annual meeting.

What Measures Should Appear on All Reports?

ISCD Official Position

- For adults total body (with head) values of body mass index (BMI), bone mineral density (BMD), bone mineral content (BMC), total mass, total lean mass, total fat mass, and percent fat mass should appear on all reports.
  Grade: Fair-C-W

Rationale

The basic measurement output parameters from DXA machines include whole body and regional BC measurements of BMD, BMC, total mass, total lean soft tissue mass, and total fat mass. Percent fat mass is derived from these basic parameters. BMI (kg/m^2) should also be reported. These measures also all have calculable Z-scores and percentiles from the National Health and Nutrition Examination Survey (NHANES) 1999−2004 reference data for children as young as 8 years and adults to 85 years, men and women, and for white, black, and Hispanic ethnicities.

Discussion

The calculation of BMI requires the technologist to accurately measure and enter information for the patient's current height and weight. The use of scale weight for the calculation of BMI is more accurate and precise than DXA-measured total mass if part of the patient is outside the scan field. The scale weight and the DXA mass may be compared as part of the quality control of the scan.

Additional questions for future research

The utility of reported measures and indices should be assessed using validated survey instruments in both clinician and patient populations.

What Additional Measures and Indices May Be Helpful During Evaluation of Lean Mass and Adiposity?

ISCD Official Position

- DXA measures of adiposity and lean mass include visceral adipose tissue (VAT), appendicular lean mass index (ALMI: appendicular lean mass/ht^2), android/gynoid ratio (A/G ratio), trunk to leg fat mass ratio, lean mass index (LMI: total lean mass/ht^2), and fat mass index (FMI: fat mass/ht^2). The clinical utility of these measures is currently uncertain.
  Grade: Fair-C-W

Rationale

It is important to ensure height is measured by a stadiometer because variability in measurement is more likely with reported height or height measured on other devices.

Measures of Lean Mass. In addition to reporting total lean mass, DXA assessments of soft-tissue lean mass include ALMI and LMI. These measures have been associated with sarcopenia and nutritional status, respectively. Current consensus definition of sarcopenia *(1−6)* includes evaluation of ALM/ht^2 as a criterion for diagnosis of ''low muscle mass'' *(2,5)*. ALMI has proven to be a good predictor for disability and mortality *(7)*. see section on ''Diagnosis of sarcopenia'').

Normalized indices of lean mass initially were proposed for nutritional assessment *(8)* with the use of bioelectrical impedance analysis (BIA) or anthropometry. More recent studies suggest that LMI as assessed by DXA may be a discriminatory marker of under nutrition *(9,10)* and may be associated with socioeconomic status in children *(11)*. In addition, low LMI has been cross-sectionally associated with certain pathologic states, such as low bone density *(12−14)*, polycystic ovarian syndrome *(15)*, chronic kidney disease *(16)*, and pulmonary conditions *(17−20)*. LMI may also be a predictor of increased mortality in hemodialysis patients *(21)*.

Measures of Fat Mass. In addition to measurements of total fat mass and percent fat mass, DXA assessments of adiposity include VAT, A/G ratio, trunk/leg fat mass ratio, and FMI. These additional measures were based on the idea that the pattern of fat distribution may be more important for clinical

health than the total quantity of fat mass (25). VAT carries a greater prediction of mortality than subcutaneous adipose tissue (22–24). Quantification of VAT by DXA represents a precise, low-radiation alternative to computed tomography. CT) and has shorter scan times and easier accessibility than magnetic resonance imaging. MRI) (26,27). The A/G fat mass ratio is an analogue of the anthropomorphic measurement of waist-to-hip ratio. The A/G ratio is correlated with dyslipidemia in both men and women (28) as well as insulin resistance in obese children and adolescents (29). Increased risk of myocardial infarction (30) and mortality (31) has been noted in women but not in men. In some studies, evaluation of abdominal fat and the A/G ratio did not perform any better than waist circumference or CT (32). There are ethnic differences in A/G that require adjustment (33). The trunk-to-leg fat mass ratio has been used to assess fat redistribution in patients with HIV treated with older retroviral therapeutic agents (see discussion in the section "Diagnosis of HIV-Related Complications Such as Lipodystrophy and Lipoatrophy?"). Classification of obesity by FMI measures excess fat rather than excess body weight as compared to BMI. FMI uses gender- and race-specific reference ranges and is corrected by height. The utility of FMI is not clearly established (Table 1 and the section "Diagnosis of obesity?").

Discussion

Dividing the whole body and appendicular BC measurements by height^2 normalizes for variability in subject stature (34) and may therefore provide more informative data than absolute measurements of fat mass and lean mass. Height-normalized indices require current height be accurately measured and entered by the technologist.

Low ALMI is a defining criterion in the definition of sarcopenia, and therefore must be reported when BC is requested for an evaluation for sarcopenia. When optionally reporting an abnormal ALM/ht^2, further recommendations for completing the examination with physical performance tests should be included in the report.

The "lean mass index" terminology is potentially confusing. DXA-derived LMI should be differentiated from skin-fold derived LMI, which is used in assessment of elite athletes (35–37). Skin-fold derived LMI is scaled for body fat mass. as assessed by skin-fold measurements) instead of being scaled for height and is hypothesized to be a measure of muscle hypertrophy (38). In addition, distinction should be made between fat-free mass index, which includes lean mass and bone mass, and LMI, which includes only lean mass measures. A LMI more than 2 Z-scores below normal for young adult has been used to define low muscle mass but has lower predictive value.

VAT will likely replace the A/G ratio as a risk factor for assessment of cardiometabolic risk factor. FMI may be more useful than BMI to assess obesity in individuals with high muscle mass. BMI cutoffs identify individuals with excess mass. In physically active individuals, excess mass may be attributable to high lean mass or a combination of high lean and high fat mass. The Centers for Disease Control and Prevention warns against the use of BMI in individuals with high musculature. Where high BMI may be confounded by high lean mass, FMI, which is a classification based only on fat mass, may be helpful in determining the level of obesity. Table 1 classifies FMI to have the same prevalence as BMI in a young population and seems to be largely ethnicity independent (39–40).

Table 1
Fat Mass Index: Classifications for Obesity Categories for Male and Female Subjects

FMI class	Normal	Excess fat	Obese class I	Obese class II	Obese class III
Male	3–6	>6 to 9	>9 to 12	>12 to 15	>15
Female	5–9	>9 to 13	>13 to 17	>17 to 21	>21

Data from Kelly TL, Wilson KE, Heymsfield SB. 2009 Dual energy X-Ray absorptiometry body composition reference values from NHANES. PLoS One 4:e7038.

Additional Questions for Future Research

The utility of reporting ALMI in every patient referred for DXA BC should be assessed. Universal reporting of ALMI would permit screening for "low muscle mass" in all patients referred for BC. Most studies have used LMI as a descriptive end point. Large prospective studies are needed to validate the utility of this measure as a predictor of disease-associated outcomes. The utility of DXA-derived LMI should be assessed in the athletic population. Large prospective studies are needed to assess fat distribution measures as a risk factor for cardiovascular disease, diabetes, and metabolic syndrome. Comparison with CT, MRI, and waist circumference is also needed in subsets of such studies.

What Reference Database Should Be Used to Represent the General Healthy Population According to Age, Health Status, Race, and Physical Activity?

ISCD Official Position

- When comparing to the US population, the NHANES 1999–2004 BC data are most appropriate for different races, both sexes, and for ages 8 to 85 years. (Note: reference to a population does not imply health status.) Grade: Fair-C-L

Rationale

There are few reference databases available for BC. Both the Hologic (Bedford, MA) and GE (Madison, WI) systems have reference data for whole-body scans from pooled studies or from convenience samples. The GE data were derived from several sources: 270 subjects. The Monarch Foundation), 169 subjects. Ohio State University), and 1468 other subjects obtained from the literature. A total of 1905 subjects are pooled

to make the GE whole body reference data. The subjects ranged in age from 20 to 89 yr, were ''healthy'' and excluded for chronic disease or medications known to affect bone. Other smaller healthy reference datasets were found for GE systems *(42,43)*.

NHANES is a survey that periodically samples the US population on various health and nutrition indicators. Whole-body DXA data were acquired and made publically available for the survey that ran from 1999 to 2004. These data comprised 10,560 male and 9993 female subjects aged 8 to 85 yr of3 races: white, black, and Hispanic. The scans were acquired on Hologic QDR 4500 A systems in 3 mobile centers. The raw data are available for download. http://www.cdc.gov/nchs/about/major/nhanes/dxx/dxa.htm).

We found that NHANES 1999−2004 is the most representative database for BC in the United States for whole-body DXA measures. Z-scores and percentiles are derivable for a variety of measures are shown in Table 2 *(39)* The Z-scores and percentiles for these measures are available in the DXA software for both GE and Hologic systems. The NHANES measures for percent fat also were validated against other models, including total body water studies and 4-compartment studies summarized in Schoeller et al *(44)*. Virtually all other databases available are samples of convenience. Because NHANES is only representative of the US population, other datasets may be more representative of other nationalities. For example, several countries have similar studies to the NHANES survey, including South Korea *(45)*.

Discussion

There are some pediatric reference datasets available, including van der Sluis *(46)*. However, we deferred all things pediatric to another Position Development Conference (PDC). However, the NHANES 1999−2004 does contain reference values for subjects as young as 8 yr of age. Furthermore, NHANES is a population-based cohort and therefore is considered a representative database, not an exclusively healthy cohort. The only exclusions in the NHANES cohort were made for reasons of DXA scan accuracy, and average values from a population-based sample may not reflect healthy individuals. Therefore, the use of NHANES for reference data may not be appropriate for all uses of DXA BC. For example, it does an athlete little good to compare with him or her with the population average.

Table 2
List of Reference Curves Generated From the 1999−2004 NHANES DXA Whole-Body Data Set

DXA measure	Independent variable	Age group	Supplemental table and figure
Fat mass/height^2 (FMI)	Age	Adult only	S1
Total body % fat	Age	Adult and pediatric	S2 and S9
% Fat trunk/% fat legs	Age	Adult only	S3
Trunk/limb fat mass ratio	Age	Adult only	S4
Lean mass/height^2	Age	Adult and pediatric	S5 and S10
Appendicular lean mass/ height^2	Age	Adult only	S6
Total body BMD	Age	Adult and pediatric	S7 and S11
Total body BMC	Age	Adult and pediatric	S8 and S12
Subtotal body BMD (excludes head)	Age	Pediatric only	S13
Subtotal body BMC (excludes head)	Age	Pediatric only	S14
Total body BMD	Height	Pediatric only	S15
Total body BMC	Height	Pediatric only	S16
Subtotal BMD (excludes head)	Height	Pediatric only	S17
Subtotal body BMC (excludes head)	Height	Pediatric only	S18
Total lean mass	Height	Pediatric only	S19
Subtotal body BMC (excludes head)	Total Lean Mass	Pediatric only	S20

Note: For each whole body DXA measure in column 1, male and female reference curves for white, black, and Mexican-American subjects were modeled against the independent variable in column 2. Adult age range is 20−85 yr; Pediatric age range is 8−20 yr.

Abbr: BMC, bone mineral content; BMD, bone mineral density; DXA, dual-energy x-ray absorptiometry; FMI, fat mass index.

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Data from Kelly TL, Wilson KE, Heymsfield SB. 2009 Dual energy X-Ray absorptiometry body composition reference values from NHANES. PLoS One 4:e7038.

Additional Questions for Future Research

There are no NHANES reference values available for many ethnic minorities. In addition, more country-specific reference datasets should be developed.

What Reference Database Should Be Used to Report DXA BMC for 4-Compartment BC Analyses?

ISCD Official Position

- Total body BMC as represented in the NHANES 1999−2004 reference data should be used when incorporating DXA in 4-compartment models.
  Grade: Fair-B-W

Rationale

The use of a standardized calibration value for BMC would provide consistency in reporting percent fat from 4-compartment model measures. Use of the Hologic calibration for BMC would provide comparability back to the NHANES reference data.

Whole-body BMC is not often used as a stand-alone bone health marker. The exception is the reporting of whole-body BMC as a relative Z-score value in pediatrics *(47)*. However, in BC studies, whole-body BMC is a necessary measure for the 4-compartment model. The 4-compartment model as described by Lohman and Going *(48)* decouples BMC, water, and a residual compartment from fat-free mass and is considered a gold-standard model for fat mass measures. The complete model solves for fat mass with the use of a dual-energy DXA scan for the BMC, total body water by deuterium dilution, and body volume by air displacement plethysmography or underwater weighing.

Significant differences exist between different makes of DXA systems. Average differences as high as 8% were pointed out by Tothill et al *(49)* in previous generation systems of GE (Lunar DPX), Hologic (QDR-1000 W), and XR-26 (Norland Corporation, Fort Atkinson, WI) Fig. 1. Ellis et al *(50)* found that the BMC measures on Hologic were approximately 25% lower than the total ash carcass mass for piglets weighing from 5 to 35 kg. In fan-beam systems, BMC is impacted by fan beam magnification. In a recent cross-calibration study, Shepherd et al *(51)* found that differences in BMC still exists between the most current versions of the Hologic and GE systems, and that the relationship between these 2 systems for BMC differed for pediatric vs adult values and had significant covariates of lean soft tissue and fat masses.

Given this, can we claim to know the absolute accuracy of BMC well enough to improve the accuracy of the 4-compartment model over 3-compartment or 2 compartment models where an estimated BMC value is used in the model? Lohman's original derivation assumed both constants for bone's physical density and that the measure of BMC would be accurately made by DXA. Tothill did find that the changes in adult BMC were linearly correlated between later generation of GE, Hologic, and Norland systems *(52)*.

In summary, there is little evidence that any of the DXA systems work with absolute accuracy and there is no way to confirm if they are in the field. A standardized measure of BMC will at least provide consistency between research studies and clinical measures. Standardizing to a BMC calibration that was used to report the NHANES reference data is a reasonable choice given that both Hologic and GE use the NHANES 1999−2004 data as the reported reference values for BMC.

Discussion

The lack of knowledge of absolute accuracy in fundamental DXA measures like BMC is surprising 30 years after their introduction. This has as much to do with the low utility of this measure as it does the difficulties and expense to update medical equipment after it has been introduced. A standardized value for BMC in 4-compartment models and the calibration used to report the NHANES tables are reasonable given this environment. Otherwise, inconsistent fat mass and percent fat measures from the 4-compartment model will continue to be a problem.

Additional Questions for Future Research

Studies to provide an accurate calibration for BMC are needed to ensure accurate 4-compartment modeling. These studies would include the measure of BMC in cadavers and reference material phantoms on multiple DXA systems and performing ash mineral mass experiments afterward. These are expensive and laborious studies that are the only way to improve on a standardized but indeterminately accurate measure of BMC.

How Should Reference Data Be Used in Reporting DXA BC?

a. Should T-scores be used in reporting BC measures?
b. Should Z-scores be used in reporting BC measures?
c. Should percentile values be used in reporting BC values?

ISCD Official Position

- Both Z-scores and percentiles are appropriate to report if derived using methods to adjust for non-normality.
  Grade: Fair-C-W

Rationale

Accurate Z-scores are most useful when the BC percentile exceeds the 97th percentile or is less than the 3rd percentile. Percentiles, particularly when expressed as integers, fail to capture the severity of extreme values. However, for typical results (those between the 97th and 3rd percentile) they are preferred over Z-scores because both patients and clinicians more easily understand them. Z-scores and percentile values have been derived for specific NHANES BC values. BC T-scores have been occasionally used, for example, in many of the proposed definitions of sarcopenia, but controversy exists regarding the appropriate age to use for the young reference value, whether T-scores in BC should be ethnicity matched, as well as the ultimate clinical utility of T-scores.

Discussion

Accurate Z-scores and percentiles require statistical methods that account for the non-normal distribution of the data. The LMS method *(53–55)* is one method that can be used for DXA BC reference data to generate appropriate Z-scores and percentiles.

Additional Questions for Future Research

None identified.

How Are DXA BC Values Used for Risk Stratification and Diagnosis of Obesity?

ISCD Official Position

- The use of DXA adiposity measures (percent fat mass or fat mass index) may be useful in risk-stratifying patients for cardiometabolic outcomes. Specific thresholds to define obesity have not been established.
  Grade: Fair-C-W

Rationale

The definition of obesity based on BMI (kg/m^2) is simple and therefore clinically expedient but is not based on a measure of adiposity. The use of a direct adiposity measure to define obesity is physiologically rational, but controversy exists over what thresholds best define obesity.

In cross-sectional studies, percent body fat is correlated with cardiometabolic outcomes independent of BMI, particularly within the indeterminate BMI range *(56–58)*. When percent body fat is used as the gold standard, BMI misclassifies a large segment of the population, particularly those with high muscle mass (overclassification) *(59)* and those with disproportionally high fat mass but normal weight (underclassification, ''normal-weight obesity'') *(60)*. BMI is thought to be a particularly insensitive measure of adiposity within Asian populations *(61)*. In one large meta-analysis in which authors assessed the diagnostic performance of BMI, a sensitivity of 50% and specificity of 90% was found for detecting excess adiposity, although this study was limited by large heterogeneity and variable percent fat thresholds for defining obesity between studies *(62)*. In addition, longitudinal studies of exercise training have demonstrated improvements in adiposity measures even in the absence of change in BMI, demonstrating a higher sensitivity of DXA measures *(63)*.

Discussion

As discussed previously, direct measurements of adiposity may more accurately predict obesity-related outcomes compared with BMI. Although continuous DXA measures of adiposity are strongly correlated with deleterious cardiovascular and metabolic outcomes, no consensus exists regarding categorical cutoffs for the definition of obesity. The optimal thresholds for defining obesity have not been prospectively validated, and considerable variation remains in the reporting of percent body fat thresholds in the scientific literature, with proposed values of 20%–25% for men, 30–35% for women, and up to 45% for the elderly *(62)*. Guidelines published by the American Society for Bariatric Physicians suggest using values of >25% body fat in men and >30% body fat in women *(64)*. These thresholds, however, would lead to an unusually large percentage of the US population as being considered obese (e.g., 58% of men and 85% of women aged 20–49) *(65)*. Percent body fat measurements that correspond with BMI >30. current obesity definition) are approximately >30% in men and >40% in young women aged 19–29 yr *(66)*. Some researchers advocate using age-specific *(67)* or ethnic-specific *(68)* cutoffs for percent body fat definitions. An alternative method to define categories of adiposity is based on the expected prevalence of obesity defined by BMI >30 at age 25; when this definition is used, fat mass index thresholds for obesity are >9 in men and >13 in women *(39)* (see the section ''What Additional Measures and Indices May Be Helpful During Evaluation of Lean Mass and Adiposity?'' for additional discussion of fat mass index).

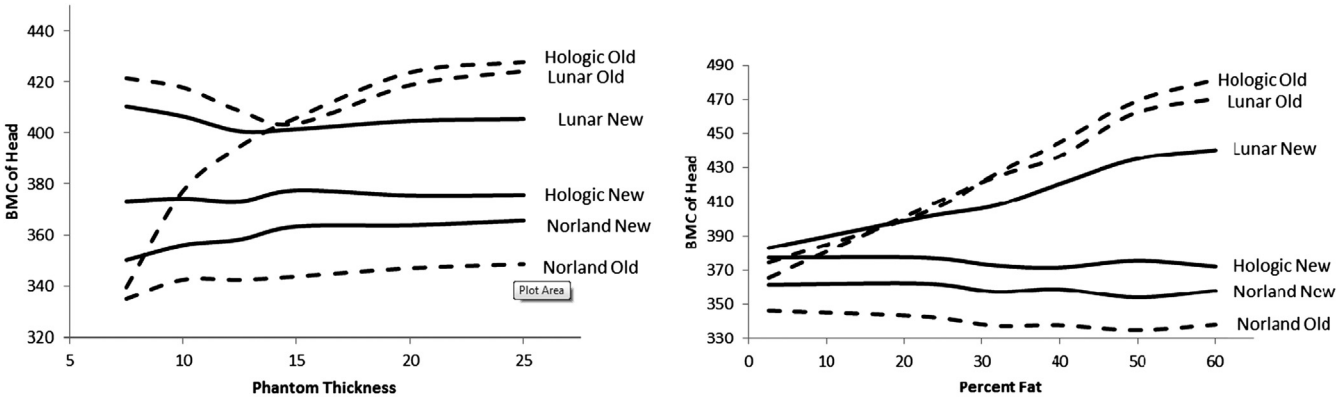

Fig. 1. Phantom difference in BMC across GE, Hologic, and Norland pencil-beam systems. Note the wide differences in absolute BMC as well as how BMC changed as a function of thickness and whole body percentage fat. (Data from Fielding RA, Vellas B, Evans WJ, et al. 2011 Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International Working Group on Sarcopenia. J Am Med Dir Assoc 12:249–256.)

Table 3
Sarcopenia: Models for Defining and Clinical Application

Reference for definition	Parameter	Cut points	Method used	Muscle quality
Baumgartner et al. *(70)* The New Mexico Elder Health Survey, 1993−1995	ALM/h^2	≤5.45 kg/m^2 for women ≤7.26 kg/m^2 for men.	2 standard deviations below younger reference population	No
Newman et al. *(69,76)* Delmonico et al. *(71)* Health Aging and Body Composition study database	ALM/h^2 comparing to ALM adjusted for height and body fat mass (residuals).	<5.67 kg/m^2 for women and <7.25 kg/m^2 for men	The lowest 20th sex specific percentiles. Residuals were calculated from linear regression models predicting ALM from height and total fat mass.	No
Woo et al. *(81)* Four-year prospective study. Chinese community in Hong Kong SAR China	ASM/h^2	U-shaped relationship was observed between physical limitation and ASM/ht^2, with increasing physical limitation below or above a range of 7.25−6.75 kg/m^2 in men and 6.00−6.25 kg/m^2 in women.	ASM/h^2 below 2 standard deviations or more below the young adult mean	No
International Working Group on Sarcopenia Consensus *(2)*	Appendicular fat free mass to height squared. ALM/h^2) or whole body fat free mass to height squared	Women: <5.67 kg/m^2 Men: <7.23 kg/m^2	20 percentile of values for healthy young adults	GS <1.0 m/s
The European Society of Parenteral and Enteral Nutrition Special Interest Groups *(6)*	ALM/h^2	Women: <5.67 kg/m^2 Men: <7.25 kg/m^2	Percentage of muscle mass > 2 standard deviations below mean in individuals aged 18−39 yr in the NHANES III cohort	Walking speed <0.8 m/s in the 4-min test or reduced performance in any functional test used for the comprehensive geriatric assessment
Society of Sarcopenia, Cachexia and Wasting Disorders Consensus Sarcopenia with limited mobility *(3)*	ALM/h^2	Women: <5.45 kg/m^2 Men: <7.26 kg/m^2	more than 2 standard deviations below that of healthy persons between 20 and 30 yr of age in the same ethnic group.	Walking speed is equal to or less than 1 m/s or who walks less than 400 m during a 6-minute walk
EWGSOP *(5)*	ALM/h^2	Women: <5.67 kg/m^2 Men: <7.25 kg/m^2	Reference population of healthy young subjects using cutoff points < 2 standard deviations below mean.	Lowest 25th grip strength OR GS < 0.8 m/s

Abbr: ALM, appendicular lean mass in kilograms; ALM/h^2, appendicular lean mass in kilograms relative to squared height in meters; EWGSOP, The European Working Group on Sarcopenia in Older People *(9)*; GS, gait speed; NHANES, National Health and Nutrition Examination Survey.

Additional Questions for Future Research

Rigorous studies are required to better define and validate adiposity thresholds as predictors of cardiometabolic disease, functionality, or mortality.

How Are DXA BC Values Used for Risk Stratification and Diagnosis of Sarcopenia?

ISCD Official Position

- "Low lean mass" could be defined using appendicular lean mass divided by height squared (ALM/height^2) with Z-scores derived from a young adult, race, and gender-matched population. Thresholds for low lean mass from consensus guidelines for sarcopenia await confirmation. Grade: Fair-C-W

Rationale

Diagnostic thresholds of sarcopenia have evolved over time (Table 3). Thus, starting from the early description of sarcopenia as "low muscle mass," 3 definitions were developed based on the assessment of the muscle mass *(69–71)*. Two of these definitions rely on the ALM/h^2 parameter. Because the relevance of sarcopenia evaluation resides in its predictive value for mortality and disability *(72,73)*, efforts were made to improve the predictive value by assessment of muscle quality. Several studies have shown different parameters of muscle strength and physical performance are independent contributors to sarcopenia related disability and mortality *(74–80)* in addition to a predictor of physical disability *(81)*.

Current definitions of sarcopenia consistently recognize both muscle quantity and quality *(1–6)*. Assessing the amount of muscle mass or any loss of muscle mass *(82)* can be determined by DXA. For qualitative assessment, physical performance evaluation is mandatory to complete the diagnosis of sarcopenia. In the absence of this qualitative evaluation, DXA report should only refer to 'low muscle mass' *(83)*.

Thresholds for Low Muscle Mass. Appendicular skeletal muscle mass/height^2 less than 2 Z-score below the young reference population is the most documented and frequently used parameter for the quantitative assessment of sarcopenia in DXA studies *(84,85)*. An ALM/ht^2 less than a Z-score of 2 below young reference population is a strong predictor of functional disabilities in the elderly and frequently but not exclusively used for the quantitative assessment of sarcopenia in DXA studies *(86,87)*. Having a low amount of appendicular fat-free mass compared to the lowest sex specific quartile has been shown to be a significant predictor of mortality in older people *(7)*.

There are also data indicating that obesity *(88,89)* or fat mass *(69–71)* are also predictors for disability and should be included in the evaluation. Data from Health ABC study using a comparison between ALM/ht^2 cut points and the ALM adjusted for body fat residuals showed that including body fat could increase the predictive value for disability. However, this study showed also a slightly greater influence of ethnicity and gender when using ALM/body fat residuals. Loss of appendicular muscle mass of more than 3% in 3 years was also proposed as threshold for low muscle mass. Subjects ages 18–39 yr in the NHANES III population with ethnicity and gender taken into account would a reasonable choice for a reference population.

Discussion

Sarcopenia is an important risk factor for incident disability and mortality due to age or particular diseases. Despite increasing data on it, there is no consensus on a definition of sarcopenia. Differences among the existing definitions are related to different approaches either in defining the thresholds for low lean mass or for testing designed to evaluate physical performance and muscle strength. DXA evaluation can only reveal data regarding the muscle mass, not physical performance, so it should be used only for this aspect.

LMI Z-score less than 2 below normal for young adult is used for defining low muscle mass based on some expert consensus definitions but has lower predictive value for mobility. The cut point of −2 SD was chosen based on the cut-point for osteopenia. The data linking this value to the risk of disability and mortality is based on cross-sectional studies. The thresholds for defining a low muscle mass should be based on prospective studies. Hence, the clinical relevance of the cut off values for defining low muscle mass based on the ALM/ht^2 has to be confirmed.

Young normal data to be used in evaluating the ALM/ht2 is also subject to debate. The NHANES data provide the Z-score at age 25 for the various gender and ethnicities for the 2 different BC analysis calibrations Hologic supports. The values are represented in Hologic units and use the NHANES calibration *(44)*.There are significant differences among cut points in women compared with men and among women of different ethnicities. There should be gender and ethnically derived reference data. Moreover, data from several studies in Asian populations showed significant differences in the prevalence of sarcopenia compared with white subjects when the same definition was used, highlighting the importance of population specific normal reference database.

Additional Questions for Future Research

More large epidemiological studies are needed to establish a clinically relevant threshold for low muscle mass. The predictive value of DXA BC "low muscle mass" for further physical disability later in life as demonstrated in longitudinal studies could suggest that physical performance evaluation and low muscle mass contributions to predict disability could overlap. In addition, examining the trajectories of the change in lean mass throughout the lifespan may be more predictive of subsequent bad outcomes than a single arbitrary cut-point. Selecting patients for muscle mass evaluation based on physical performance could exclude the contribution of muscle mass independently. A "FRAX"-like model (i.e., Fracture Risk Assessment Tool [FRAX], World Health Organization, University of Sheffield, Sheffield, UK) for risk factor assessment may be worth pursuing.

How Are DXA BC Values Used for Risk Stratification and Diagnosis of HIV-Related Complications Such as Lipodystrophy and Lipoatrophy?

- No position could be agreed upon at this time.

Rationale

At the moment there are no universally accepted values to for reporting or diagnosing HIV lipodystrophy. People with HIV lipodystrophy can have not only peripheral lipoatrophy but also excess central fat accumulation, each with a different pathophysiology. Ratios such as trunk/limb fat, trunk/leg fat, fat mass ratio, and even trunk or limb fat as a percent of total fat do not fully differentiate between peripheral fat loss and central fat gain; although they may be useful, they must be interpreted with caution.

Studies in which authors use DXA to characterize fat distribution in HIV infection have expressed DXA results via a wide assortment of methods, with no widely agreed-upon convention. Different cross-sectional studies report absolute values. grams or kilograms), all of the aforementioned ratios for regional fat, or have put height, height squared, or BMI in the denominator. Typically, longitudinal studies primary report changes in absolute terms (grams or kilograms) or percent changes in total and regional fat. Some of these studies have used arbitrary benchmarks such as net 10% or 20% loss in peripheral fat to define lipoatrophy. Some also report changes in fat ratios.

Carr et al *(90)* conducted a multinational study to develop an objective case-definition for HIV lipodystrophy. The definition encompassed a number of biochemical and anthropometric variables and included DXA measures of trunk/limb fat ratio and leg fat as a percent of total leg mass, as well as the ratio of VAT/subcutaneous adipose tissue by CT. The case definition was further adapted to yield a scoring system *(91)* that was applied in some studies but did not gain widespread use as either a research or clinical tool. Bonnet et al *(91)* proposed the use of the fat mass ratio (described in the section "What Additional Measures and Indices May Be Helpful During Evaluation of Lean Mass and Adiposity?") for diagnosis of HIV lipodystrophy based on a cross-sectional comparison of HIV-infected and uninfected men. This metric has been applied occasionally in other studies but its generalizability to women and other racial and ethnic groups has not been established. In a large randomized survey of fat distribution among HIV infected and uninfected men and women in the United States, Scherzer et al *(92)* defined HIV lipoatrophy as leg fat by DXA in the lower decile of values in seronegative controls of the same sex but warned that this approach yielded a greater prevalence of HIV lipoatrophy than was obtained by MRI. This approach may hold promise if acceptable normative DXA data for regional fat become available. The effects of racial and ethnic variation on fat distribution in healthy populations require further study before cut points to define HIV lipodystrophy can be identified.

Overall Conclusions for DXA Reporting

Standards for the reporting of BC data are necessary to allow a uniform and evidence-based approach to relevant clinical application. As the field advances, changes will need to be made in these standards using the best available evidence. The recommendations made in this document help provide a foundation for addressing basic science and clinical questions that are necessary for helping provide care for many of the most debilitating diseases facing our population.

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Appendix

ISCD TF-3 Search Strategy

Measures and Reporting in General

- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) and reporting

Reference databases

- body composition[mh] AND (((DXA or DEXA) OR photon absorptiometry[mh]) and reference
- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) and NHANES

T-Scores and Z-scores

- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) and z-score
- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) and t-score

Obesity

- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) AND obesity[mh]
- body composition[mh] AND ((DXA or DEXA) OR photon absorptiometry[mh]) AND bariatric surgery[mh]

body composition[mh] AND photon absorptiometry[mh] AND ''humans''[Filter] AND reference

- (DXA or DEXA or ''dual-energy x-ray absorptiometry'') AND (''lean mass index'')
- AND. humans)
- (DXA or DEXA or ''dual-energy x-ray absorptiometry'') AND (''fat mass index'')

AND. humans)

- (DEXA or DXA or ''dual-energy x-ray absorptiometry'') AND (obesity) AND
- ((percent fat) OR (''fat mass index''))

Sarcopenia

- (((DXA[All Fields] OR DEXA[All Fields]) OR (''absorptiometry, photon''[MeSH Terms] OR (''absorptiometry''[All Fields] AND ''photon''[All Fields]) OR ''photon absorptiometry''[All Fields] OR ''dual energy x ray absorptiometry''[All Fields])) AND (normal[All Fields] AND reference[All Fields])) AND (''body composition''[MeSH Terms] OR (''body''[All Fields] AND ''composition''[All Fields]) OR ''body composition''[All Fields]) AND (''humans''[MeSH Terms] AND English[lang])
- (''sarcopenia''[MeSH Terms] OR ''sarcopenia''[All Fields]) AND ((''epidemiology''[Subheading] OR ''epidemiology''[All Fields] OR ''epidemiology''[MeSH Terms]) OR (''epidemiology''[Subheading] OR ''epidemiology''[All Fields] OR ''prevalence''[All Fields] OR ''prevalence''[MeSH Terms]) OR (''diagnosis''[Subheading] OR ''diagnosis''[All Fields] OR ''diagnosis''[MeSH Terms]) OR (''evaluation studies''[Publication Type] OR ''evaluation studies as topic''[MeSH Terms] OR ''evaluation''[All Fields]) OR (cut[All Fields] AND off[All Fields] AND limits[All Fields]) OR (''Assessment''[Journal] OR ''assessment''[All Fields]) OR thresholds[All Fields] OR threshold[All Fields] OR definition[All Fields] OR definitions [All Fields] OR ''standard''[All Fields] OR (''standards'' [Subheading] OR ''standards''[All Fields] OR ''criteria'' [All Fields]) OR (cut[All Fields] AND off[All Fields] AND points[All Fields]) OR (''diagnosis''[MeSH Terms] OR ''diagnosis''[All Fields] OR ''diagnostic''[All Fields]) OR cutpoints[All Fields]) AND (hasabstract[text] AND ''humans''[MeSH Terms] AND English[lang])

Lipodystrophy

- Lipodystrophy and ''body composition'' and (DXA or DEXA)