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# AMALGAMATED REFERENCE DATA FOR SIZE-ADJUSTED BONE DENSITOMETRY MEASUREMENTS IN 3598 CHILDREN AND YOUNG ADULTS – THE ALPHABET STUDY

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## Abstract

The increasing use of dual energy X-ray absorptiometry (DXA) in children has led to the need for robust reference data for interpretation of scans in daily clinical practice. Such data need to be representative of the population being studied and be 'future-proofed' to software and hardware upgrades. The aim was to combine all available paediatric DXA reference data from seven UK centres to create reference curves adjusted for age, sex, ethnicity and body size to enable clinical application, using in-vivo cross calibration and making data back- and forward- compatible.

Seven UK sites collected data on GE-Lunar or Hologic Scanners between 1996 and 2012. Males and females aged 4 to 20 years were recruited (n=3598). The split by ethnic group was: White Caucasian 2887; South Asian 385; Black Afro-Caribbean 286; mixed heritage 40. Scans of the total body and lumbar spine (L1-L4) were obtained. The European Spine Phantom was used to cross-calibrate the 7 centres and 11 scanners. Reference curves were produced for L1-L4 bone mineral apparent density (BMAD) and total body less head (TBLH) and L1-L4 areal bone mineral density (aBMD) for GE Lunar Prodigy and iDXA (sex-and ethnic-specific) and for Hologic (sex-specific). Regression equations for TBLH BMC were produced using stepwise linear regression. Scans of 100 children were randomly selected to test backwards and forwards compatibility of software versions, up to version 15.0 for GE Lunar, and Apex 4.1 for Hologic.

For the first time, sex and ethnic- specific reference curves for lumbar spine BMAD, aBMD and TBLH aBMD are provided for both GE-Lunar and Hologic scanners. These curves will facilitate interpretation of DXA data in children using methods recommended in ISCD guidelines. The databases have been created to allow future updates and analysis when more

definitive evidence for the best method of fracture prediction in children is agreed.

**Keywords: DXA; paediatric; BMD; BMC; reference; lean mass**

## Introduction

The increasing availability and use of dual energy X-ray absorptiometry (DXA) technology in children has brought to the fore the need for robust reference data for all DXA manufacturers. Although manufacturer reference databases are available, they are often not population based nor representative of the individual population being studied (1). Such databases may also have wide variability due to small numbers, with limited power to model rapid skeletal changes during different phases of growth. A further limitation for their use in daily practice is the widespread use of multiple generations of hardware and acquisition and analysis software that may distort the output. There is a need to enable transition between them when monitoring skeletal health in individual patients or undertaking longitudinal research studies.

In 2013 the International Society for Clinical Densitometry (ISCD) updated their 2007 Pediatric Bone Densitometry Guidelines for bone assessment in children (1-3). The committee concluded that DXA is the preferred method for assessment of areal bone mineral content (BMC) and density (aBMD) and that estimating aBMD should be part of the overall assessment for children at elevated risk of a clinically significant fracture (1-3). Measurements of total body less head (TBLH) and/ or posterior-anterior lumbar spine aBMD or BMC are recommended; in conjunction with a history of clinically significant fractures, these can be used to indicate the diagnosis of osteoporosis in children and adolescents (1-3). In children with short stature or growth delay, the measurements should be size-corrected using appropriate methods (4-7). The guidelines also acknowledge that adjustment for soft-tissue measurements may be useful in children with malnutrition or in those with muscle and/ or skeletal deficits, as has been shown previously (8-11).Despite these guidelines, there are still inconsistencies in the management of children with low BMD and bone fragility around

the world. The lack of robust reference data in a format that permits the diagnostic application of ISCD recommendations is a source of inconsistency. .

The primary aim of the current study was to combine all available paediatric DXA reference data from seven UK centres to create age-, sex-, ethnic- and size-corrected reference curves for use in clinical practice and prediction equations for the assessment of the muscle and bone relationship, and a database which is in-vivo cross calibrated and back- and forward-compatible.

## Methods

Subjects

Three thousand five hundred and ninety eight healthy, community dwelling children aged 4 to 20 years were recruited from 7 UK centres (Birmingham, Leeds, London, Glasgow, Sheffield, Middlesbrough, Manchester) using centre-specific protocols, from 1996 to 2012**(Supplementary Table 1)**. Participants were a self-selected convenience sample from across each study region, recruited through advertisement in local schools and colleges, general practice surgeries and youth groups. Children of White Caucasian, South-Asian and Black Afro-Caribbean /African descent were included in the study, depending on centre-specific inclusion and exclusion criteria. Ethnicity was defined by participants' self-reporting both parents being of identical ethnic origin; where this was not the case, data were excluded. All centres recruited healthy children without known metabolic bone disease, confirmed through centre-specific screening questionnaires (**Supplementary Table 1**); abnormal results were followed-up and excluded if metabolic bone disease was suspected. Children were included who had had one or more moderate or high trauma fractures (12). At all centres, local research Ethics Committees approved the studies. All research was carried out in accordance with the Declaration of Helsinki.

77

78 Anthropometric measurements

79 Height and weight were measured according to centre specific protocols and body mass index
80 (BMI) calculated as weight/height$^2$ (kg/m$^2$). To describe the population at each centre,
81 height, weight and BMI measurements were transformed to standard deviation scores (Z-
82 Scores) using the 1990 British growth reference data (13-15).

83

84 Scan acquisition

85 Children were scanned at each centre on either a GE Lunar™ DPX-L, Prodigy or iDXA
86 scanner (GE Medical Systems, Madison, Wisconsin, US) in Birmingham, Leeds, London,
87 Glasgow, Sheffield, Middlesbrough or on a QDR Discovery Hologic™ scanner (Hologic,
88 Bedford, MA, US) in Manchester. Total body, lumbar spine and proximal femur scans were
89 obtained; since the femur is not currently a recommended site according to the current ISCD
90 guidelines (2) only total body and lumbar spine are reported. Standard operating procedures
91 were followed in each centre. All scans were analysed centrally in Birmingham by two
92 Clinical Scientists and were scored for quality of scan acquisition and analysis. DPX-L scans
93 were analysed using software version 4.6c, Prodigy and iDXA scans using Encore version
94 15.0 (Basic and Enhanced) and Hologic scans using Apex 4.1. Spine bone mineral apparent
95 density (BMAD) was calculated using an adapted method of Carter et al. (g/cm$^3$) (4, 16, 17).

96 $$\text{Lumbar spine BMAD (g/cm}^3\text{)} = \frac{(BMC_1 + BMC_2 + BMC_3 + BMC_4)}{(V_1 + V_2 + V_3 + V_4)}$$

97 Where $V_n$ is the volume of the n$^{th}$ individual vertebra = $AP_n^{1.5}$ ($AP_n$ = Projected vertebral
98 area of the n$^{th}$ vertebra)

99 $BMC_n$ is the bone mineral content of the n$^{th}$ vertebrae

100

Prediction equations were generated for GE Lunar (Prodigy, iDXA) and Hologic (Discovery) for predicted total body less head bone mineral content (TBLH-BMC) by linear regression analysis of log transformed, lean mass, fat mass, height and age (9, 18).

Centre cross-calibration:

The European Spine Phantom (ESP) was used to cross-calibrate bone measurements at 7 centres and 11 scanners. (19, 20). The phantom was measured once at each centre 10 times without repositioning. For practical purposes this process was not repeated and therefore we relied on local monitoring of scanner operation to verify machine stability. Birmingham was used as the reference centre and all sites cross-calibrated to these measurements. Additional measurements were taken on the iDXA and Hologic scanners using the Leeds Paediatric Spine Phantom, developed by The University of Leeds (in-house).

In-vivo cross calibration:

In-vivo cross calibration was performed in Birmingham, firstly for DPX-L to Prodigy in healthy children (n=105) and then for Prodigy to iDXA in children undergoing scans for clinical purposes (n=70) . Both studies were approved by South Birmingham Ethics Committees. Cross-calibration equations were produced using linear regression analysis of absolute values. Machine differences were tested using paired t-test and machine bias with Bland and Altman (**Supplementary table 2**). The equations were used to transform data from the other GE-Lunar centres to Birmingham for lumbar spine DPX-L to Prodigy Basic and iDXA; and for total body DPX-L to Prodigy basic, Prodigy enhanced and iDXA [1]. In-vivo cross-calibration was not performed between Hologic and GE-scanners for bone or soft tissue measurements.

[a] Prodigy Enhanced is an option only available for total body scans.

## Back- and forward compatibility

Scans of 100 children were selected from each of the GE Lunar and Hologic databases to create equations for back- and forwards-compatibility of the reference curves. Within each cohort of 100 children, 20 children per age-band (5-7, 8-10, 11-13, 14-16, 17-19 years) were selected at random (10 male, 10 female) from each of the manufacturer specific datasets. Total body and lumbar spine scans were analysed on software versions: GE-Lunar 10, 11, 13, 14, 15; Hologic 12.4, Apex 2.4, 3.1, 4.1. This sub-set of scans remains available for analysis for future software versions.

## Statistical analysis

The Lambda-Mu-Sigma (LMS) method was used to produce age reference curves for Lumbar Spine BMAD, L1-L4 aBMD and TBLH BMD. The LMS curves were generated using the method described by Cole and Green (21) (LMSchartmaker Pro version 2.54 © 1997-2011 Medical Research Council, UK). In brief, reference centile curves describe the distribution of the dependent variable as it varies with the independent predictor covariate, here being age. The curves are fitted using the parametric approach of the penalised log likelihood method as cubic splines by non-linear regression. The degree of smoothing required for the curves is expressed in terms of the equivalent degrees of freedom (edf) (21). The resulting model for the dependent variable, generated from the raw data, is summarised by three parameters, namely: L the Box-Cox power transformation needed to remove any skewness from the distribution, M the median, and S the coefficient of variation. The LMS models were fitted using the "Loop" analysis function in the software, setting the maximum edf's for the cubic

splines at 3, 6 and 3 and the minimum edf's at 0,1and 1, for L, M and S respectively. The reference model choice was guided by the Schwarz Bayesian Criterion and visual inspection of the curves, resulting in a parsimonious model. Goodness of fit was investigated using the detrended Q-Q plots and ensuring the Q-test statistic was less than 2 (22-24). Standardized residuals were tested for normality and the distribution of subjects within the expected centiles was calculated.

Figures 1-3 and Supplemental Figures 3-5 highlight the age-related mean with the 5$^{th}$ and 95$^{th}$ confidence intervals with each sex and ethnic group fitted separately. Standard deviation scores (Z-scores) are calculated from the LMS parameters using the equation;

$$Z = ((\frac{y}{M})^{L} - 1)/L * S$$

Z = Z- score, y = measured value, M = estimated mean, L = skewness, S = distribution

The need for ethnic specific curves was tested using a one-sided t-test of the Z-scores calculated from the gender specific white data. Where, a significant difference from zero was observed, ethnic specific curves were generated. The goodness of fit of the curves is described by comparing expected versus observed Z -score centile distributions in **Supplemental Tables 7a-j**.

Regression equations for TBLH-BMC were produced using stepwise linear regression; covariates in the initial model were log-transformed total body lean, total body fat, height and age, only significant covariates were used. Residual plots were inspected for normality to check for skewness and bias in the prediction models.

## Results

A total of 3598 scans from children and young adults aged 4 to 20 years-old were included in this study (1820 female, 1778 male). The split by ethnic group was: White Caucasian 2887;

South Asian 385; Black African/ Afro Caribbean 286 and 40 mixed heritage. One hundred and one subjects were excluded (61 extreme body size [either height, weight or BMI SDS < -3.5 or > 3.5SD]; 40 mixed heritage), leaving a total of 3497 subjects for the generation of reference data (Table 1). Descriptive data by centre are shown in Table 2. There were small, significant centre differences in height, weight and BMI SDS. Subjects were generally taller, heavier with greater BMI than the 1990 UK-reference population (13-15).

Manufacturer differences

Phantom cross calibration: Using the ESP and with Birmingham as the reference centre there were no significant differences between all 11 scanners in phantom BMC and aBMD (including Hologic). In contrast, BA was more variable between the centres but the only significant difference was observed between the Hologic scanner and all GE scanners ($p=0.010$) (Supplemental Figure 1).

We explored these differences further using the Leeds Paediatric Spine Phantom scanned on a Hologic Discovery and GE-Lunar iDXA scanners. There were no significant differences in aBMD however BMC and BA were significantly different between the two ($p<0.001$), with Hologic giving increasingly higher values compared to the iDXA with increasing BMC and BA. Therefore, transformation equations were produced. However, when we applied these to the in-vivo data there were still systematic differences between the Hologic and GE-Lunar datasets. Consequently, we could not combine different manufacturer scan data and thus needed to generate brand-specific reference data for use in clinical practice.

In-vivo cross-calibration: In-vivo cross-calibration data were only available for the GE-Lunar scanners (25, 26). The strong linear relationships between scanners from a single manufacturer enabled successful transformation of the in-vivo reference datasets collected from three generations of GE-Lunar scanners. Once successfully transformed, the Bland

196 Altman tests showed no residual bias. Consequently, this allowed the pooling of all the GE-
197 Lunar data.
198
199 Software differences – backwards and forwards compatibility
200
201 For GE Lunar, there were no differences in any parameter measured using the basic analysis
202 from version 10 onwards (Prodigy). Version 14.0 included an enhanced total body analysis
203 to try and make Prodigy total body results comparable with the newly introduced iDXA.
204 Whilst there were no differences between the basic analysis, it is not surprising that there
205 were differences between the basic and enhanced total body analyses for all measured
206 parameters (aBMD, BMC, BA, lean and fat) (**Supplemental Figure 2**).
207 For Hologic there were no differences between software versions 12.4 through Apex 4.1. It is
208 important to note that this is only true if the same analysis option is used; for this study
209 NHANES BCA was selected throughout.
210
211 Reference curve generation (Figures 1-3, Supplementary data S3-5)
212 Because of the known differences in development between boys and girls their data were
213 separately analysed for BMAD , aBMD and TBLH-BMC.
214
215 Size-adjusted lumbar spine (Supplemental tables 4a-c)
216 Small, but significant differences were found for BMAD between White and Asian, and
217 White and Black children, (Figure 1). In girls, the mean difference in Z-score, calculated
218 using White as the referent group, was 0.25 (0.88), $p<0.0001$ and 0.62 (1.18) $p<0.0001$ for
219 South Asian and Black Caribbean girls respectively (Supplemental Table 7a-b).In boys, the
220 mean difference in Z-score, again calculated using White as referent group, was 0.24 (0.96),

p=0.001 and 0.46 (0.98) p<0.0001 for South Asian and Black Caribbean's respectively (Supplemental Table 7a-b). When Z-scores were recalculated using ethnic-specific LMS data they were no longer significantly different from 0. LMS data were therefore generated for each ethnic group separately.

Figure 3 shows inter-scanner curve comparisons for males and females separately. Despite cross-calibrating the Hologic BMC and BA values to GE Lunar using the ESP, highly significant differences between the scanners remained confirming the differences described earlier. The result of these differences was that calculated BMAD was lower from the Hologic scanner. We explored whether this was due aBMD, BMC or BA. BMC and aBMD were not different but BA was greater in Hologic. Using log-log transformation, (27) the relationship between BA and BMC differed between scanners: for Prodigy, iDXA and DPX-L this was $BA^{1.7}$ (expected $BA^{1.5}$ (4)), whereas for the QDR Discovery it was $BA^{1.9}$.

Lumbar spine and total body less head areal BMD (Supplemental Tables S5-6)

In contrast to the BMAD findings there were no significant differences in South Asian children when compared to the white group. Differences remained for black compared to white girls (lumbar spine 0.69 (1.14) p<0.001; TBLH 1.04 (1.08), p<0.0001) and boys (lumbar spine 0.56 (0.97) p<0.0001; TBLH 0.93 (1.06), p<0.0001) (Supplemental Tables S7d,e, 7e, h). We therefore combined the data for White and South Asian children, and re-checked the distribution of Z-scores to check for normality and to ensure differences were not significantly different from 0, they were not confirming the appropriateness of combining data.

Total body less head BMC (Tables 3-6)

ANOVA was performed with TBLH-BMC as the dependent variable and lean body mass, fat body mass, height, age, gender and ethnicity as co-variates or factors in the model. Significant effects were noted for all covariates and factors. Total body lean mass was the greatest predictor of TBLH-BMC, closely followed by total body fat mass, age and height. Significant interactions were noted for all covariates between genders and ethnic groups ($p<0.001$). Girls had greater TBLH-BMC than males for the same lean mass, fat mass, height and age. For the same gender, Afro-Caribbean children had greater TBLH-BMC for the same covariate values (data not shown). Consequently, using stepwise linear regression analysis with parsimonious variable selection of the log-transformed parameters, individual predictor models were generated for each manufacturer, each ethnic group and each gender (Table 3a-d). Individual Z-scores can be produced from by inputting age, height, lean and fat mass in to the prediction equation. The predicted value can then be used to calculate the Z-score by using the following equation:

$$Z - score = \frac{Measured\ value - Predicted\ value}{Predicted\ value\ x\ SEE}$$

**Discussion**

For the first time, DXA measurements in children and young adults aged 4-20 years combining data collected across multiple generations of GE-Lunar and Hologic DXA scanners and software have been collated. Reference data are presented using some of the recently recommended methods by ISCD for clinical use. We provide reference curves for age- and size-adjusted lumbar spine and total body bone densitometry up to the age of 20 years. We also give prediction equations for size- and body composition-adjusted TBLH-BMC measurements. These data enable calculation of sex-specific Z-scores for three ethnic

groups from 4 years-of-age through to the children switching to adult transition services. Looking ahead, our random dataset of 100 healthy children provides forwards compatibility of software, which allows us testing of future software updates.

Scanner differences

The strong linear relationships between the in-vivo cross-calibration of the reference datasets enabled pooling of all of the GE-Lunar scanners after applying machine specific (i.e. Prodigy, i-DXA) in-vivo transformation equations (**Supplementary Table 2a-b**). Unfortunately, only data from in-vitro phantoms were available for cross-calibration between the two scanner manufacturers. The observed BA differences were due to varying projectional errors of the fan-beam (Hologic) versus narrow-fan (GE-Lunar) technology. Since the phantom consists of an anthropomorphic spine set in a fixed position it cannot account for differences in body thickness or spine depth which introduces significant errors in measurement when scanning in-vivo. For this reason we were unable to cross-calibrate Hologic to GE-Lunar data. Our findings confirm the inappropriate nature of using phantoms to cross-calibrate between hardware with different properties, i.e. pencil →narrow-fan → fan beam (28,29).

Software differences

The data presented here are for the latest software version of each manufacturer; Encore 15.0 (GE Lunar) and Apex 4.1 (Hologic). With simple transformations it is possible to interpret the DXA results using any version of software going back to GE Lunar Encore 10.0 and Hologic 12.4. Our findings confirm that for both manufacturers it is necessary to always use software specific reference data. It should be noted that for both, it is essential to ensure that when comparing results from different software versions the same analysis options are selected. For GE-Lunar this means selecting enhanced or basic analysis, and for Hologic

Apex software the NHANES BCA analysis should be switched on (30). For older, pre-Apex versions of Hologic, the 'auto whole body analysis' should be used.

Reference data and their use in fracture prediction

Our study presents age- (TBLH-aBMD, spine aBMD) and size-adjusted data for bone densitometric variables (BMAD, TBLH-BMC) previously shown to best predict fractures in healthy or chronically ill children (31); these also represent some of the methods currently recommended by ISCD (1, 2). In over 450 children with chronic disease the diagnostic odds ratio for predicting vertebral fractures was 9.3 (5.3-14.9) for lumbar spine BMAD; for predicting long bone fractures the odds ratio was 6.5 (4.1-10.2) for TBLH-BMC for lean mass (31). BMAD has also been shown to be the best size-adjustment method for prediction of fractures in healthy children (32). Current understanding is that when interpreting paediatric bone density results it is preferable to use a size-adjustment method, such as BMAD or a height-adjusted Z-score(1), however a firm consensus regarding the most appropriate size-adjustment technique has yet to be established and for this reason the use of age-adjusted aBMD is still recommended by ISCD (2). Unlike previous studies, some of which are described below, that present reference data from a single manufacturer and using one software version (7, 16, 33, 34 ) the data presented here can easily be applied to different software versions and manufacturers. If necessary, data can be regenerated using newer size-adjustment methodology.

The Bone Mineral Density Childhood Study (BMDCS) multi-center study generated robust US-population-derived reference data for Hologic scanners (software version 12.3 for baseline and Apex 2.1 for follow-up scans) from over 10 000 measurements in over 2000 individuals of TBLH and lumbar spine BMC and aBMD measurements in 5 to 20-year olds (6, 6). Size-adjusted prediction equations using height for age Z-scores were also generated

and verified using an independent dataset. No data have yet been published to show whether this method of adjustment significantly improves fracture prediction. Reference data were also generated from the NHANES study; to date only LMS data for total body composition have been published (33). It should be noted that both the NHANES and the BMDCS studies generate Hologic reference data and are from much larger population samples than the UK database presented here.

In contrast to the current study, NHANES data have been cross-calibrated from Hologic to GE-Lunar. Data generated on Hologic 4500 scanners (software version Apex 3.0) were cross calibrated to GE Lunar iDXA values (Software version 14.0) (29, 34). However, despite being the largest published database (approximately 20 000 measurements), only data for total body measurements were presented. Since reductions in TBLH-BMC only predict long bone and not vertebral fracture risk (31), isolated total body data may have limited clinical use. Another possible limitation of the NHANES reference database translation to GE measurements is that pragmatic cross-calibration was performed using data from a native Chinese population and then applied to transform a much larger dataset of a North American US population (34).

## Limitations

There are several limitations to this study. The previously discussed differences in phantom measurements between the scanners due to projection error and table height differences (Figure 3) and subsequent lack of in-vivo data for cross-calibration meant that we were unable to create a single combined dataset, applicable to both manufacturers' scanners. The data were all collected in UK centres, but are applicable for use worldwide provided the same software and scan protocols are used. Caution should be applied when using the data in

populations in which there may be differences in growth rates or body habitus and robust testing should be employed. In our study the sample size for the South Asian and Afro-Carribean populations were considerably smaller than the White population and recruited mostly from one centre and as such we cannot be certain that this is fully representative of the population. We cannot rule out recruitment bias in any of the centres but as can be seen from **Supplementary Table 1** protocols and sampling strategies were broadly the same. Although we cannot confirm that the differences between GE Lunar and Hologic reference data were not due to population differences, it is likely that the differences are due to differences in scanner technology. We believe the cross-calibration procedure is as robust as it can be, since collecting repeated measurements on scanners across the country is neither ethical nor feasible. Because only one centre collected Hologic data, in one ethnic group, there are fewer subjects and the Hologic dataset did not include different ethnic groups. Despite this, we have made this Hologic dataset robust to software updates and increased the utility of the data previously published in 2007 (16). Finally, we have focussed on testing the data based on bone measurements only, clearly repeating this work for body composition would be an advantage (29, 34).

## Conclusion

In conclusion, we present backwards- and forward- compatible ethnic- and sex specific reference data for size-adjusted bone density in children and young adults, generated from measurements in over 3500 individuals using GE and Hologic scanners. These data have been produced using methods included in the most recent ISCD guidelines and for the first time present curves for lumbar spine BMAD and prediction equations for TBLH-BMC taking into account lean mass and body size, together with age-and gender- specific curves for

lumbar spine and TBLH aBMD. This reference database data has been specifically designed to allow future updates and analysis when more definitive evidence for the best method of fracture prediction in children is agreed.

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## Figure legends

**Figure 1** Comparison of GE Lunar iDXA™ lumbar spine BMAD LMS reference curves between the three different ethnic groups. (A) BMAD ($g/cm^3$) for girls; (B) BMAD ($g/cm^3$) for boys. Solid black line represents the mean for White Caucasian Children (± 95% Confidence interval -dotted black line). Dark grey dashed line represents the mean for Black Afro-Caribbean Children; Dashed light grey line represents the mean for South Asian Children.

**Figure 2** Comparison of lumbar spine BMAD LMS reference curves between males and females (A) GE Lunar iDXA; (B) Hologic Discovery. Solid black line represents males (mean ± 95% Confidence interval). Dashed line represents females (mean ± 95% Confidence interval).

**Figure 3** Comparison of lumbar spine BMAD LMS reference curves between manufacturers, GE Lunar iDXA™ compared to Transformed Hologic Discovery (Hologic data transformed using cross calibration equations generated from the European Spine Phantom). (A) Females; (B) Males. Solid black line represents GE Lunar iDXA™ (mean ± 95% Confidence interval). Dashed line represents Hologic Discovery (mean ± 95% Confidence interval).

513 TABLES

514 **Table 1** Distribution of subjects used for the generation of reference data

| | | | | | |
|---|---|---|---|---|---|
| **GE Lunar Prodigy** | 2547 | Male | 1245 | White Caucasian | 925 |
| | | | | South Asian | 192 |
| | | | | Black Afro Caribbean | 128 |
| | | Female | 1302 | White Caucasian | 970 |
| | | | | South Asian | 184 |
| | | | | Black Afro Caribbean | 148 |
| **GE Lunar iDXA** (including transformed Prodigy) | 2910 | Male | 1411 | White Caucasian | 1091 |
| | | | | South Asian | 192 |
| | | | | Black Afro Caribbean | 128 |
| | | Female | 1499 | White Caucasian | 1167 |
| | | | | South Asian | 184 |
| | | | | Black Afro Caribbean | 148 |
| **Hologic Discovery** | 587 | Male | 325 | White Caucasian | 325 |
| | | Female | 262 | White Caucasian | 262 |

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517 **Table 2** Patient anthropometric data. Mean (SD)

| Centre | Number | Mean (SD) Height Z-score | Mean (SD) Weight Z-score | Mean (SD) BMI Z-score |
|---|---|---|---|---|
| Birmingham | 935 | 0.20 (1.09) | 0.45 (1.24) | 0.46 (1.25) |
| Middlesbrough | 390 | 0.35 (0.97) | 0.41 (0.96) | 0.31 (1.00) |
| Leeds | 171 | 0.34 (1.00) | 0.42 (1.10) | 0.31 (1.11) |
| Glasgow | 212 | 0.15 (1.02) | 0.34 (1.07) | 0.36 (1.02) |
| London | 372 | 0.11 (1.03) | 0.29 (1.10) | 0.27 (1.12) |
| Sheffield | 830 | 0.40 (1.05) | 0.59 (1.11) | 0.51 (1.15) |
| Manchester | 587 | 0.30 (0.96) | 0.47 (1.01) | 0.41 (1.03) |
| TOTAL | 3497 | 0.28 (1.03) | 0.46 (1.11) | 0.42 (1.14) |
| Centre Differences (p value) | | <0.001 | 0.001 | 0.003 |

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519 Using a one-sided t-test all Z-scores were significantly ($p<0.0001$) greater than zero. Centre
520 differences were compared using ANOVA.

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**Table 3a** Prediction Equations for Total body less head bone mineral content (TBLH-BMC (g)) for lean mass (g), fat mass (g), height (cm) and age (1decimal place) for the GE Lunar Prodigy™- Software version Encore 15.0.

| | | GE Prodigy | $r^2$ | SEE |
|---|---|---|---|---|
| Girls | White Caucasian | $TBLH\text{-}BMC = 3.77x10^{-4} \times LEAN^{0.845} \times FAT^{0.130} \times Height^{0.928} \times Age^{0.179}$ | 0.966 | 0.0988 |
| | South Asian | $TBLH\text{-}BMC = 2.24x10^{-4} \times LEAN^{0.603} \times FAT^{0.122} \times Height^{1.535} \times Age^{0.216}$ | 0.970 | 0.0935 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 1.02x10^{-3} \times LEAN^{0.941} \times FAT^{0.100} \times Height^{0.543} \times Age^{0.311}$ | 0.967 | 0.1002 |
| Boys | White Caucasian | $TBLH\text{-}BMC = 2.93x10^{-4} \times LEAN^{0.939} \times FAT^{0.073} \times Height^{0.930} \times Age^{0.079}$ | 0.972 | 0.0976 |
| | South Asian | $TBLH\text{-}BMC = 1.47x10^{-4} \times LEAN^{0.978} \times FAT^{0.060} \times Height^{1.060}$ | 0.978 | 0.0932 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 1.94x10^{-3} \times LEAN^{0.983} \times FAT^{0.048} \times Height^{1.018}$ | 0.973 | 0.0883 |

Total body less head BMC = TBLH-BMC; Total body lean mass = LEAN; Total body fat mass = FAT; SEE = Standard error estimate

Z-Score = (Measure Value – Predicted Value) / (Predicted Value x SEE)

**Table 3b** Prediction Equations for Total body less head bone mineral content (TBLH-BMC (g)) for lean mass (g), fat mass (g), height (cm) and age (1dp) for the GE Lunar Prodigy™ using the ENHANCED analysis mode - Software version Encore 15.0.

| | | GE Prodigy-Enhanced | $r^2$ | SEE |
|---|---|---|---|---|
| Girls | White Caucasian | $TBLH\text{-}BMC = 4.24 \times 10^{-3} \times LEAN^{0.682} \times FAT^{0.079} \times Height^{0.905} \times Age^{0.122}$ | 0.967 | 0.0818 |
| | South Asian | $TBLH\text{-}BMC = 6.04 \times 10^{-3} \times LEAN^{0.511} \times FAT^{0.106} \times Height^{1.110} \times Age^{0.185}$ | 0.937 | 0.0809 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 9.01 \times 10^{-3} \times LEAN^{0.744} \times FAT^{0.103} \times Height^{0.545} \times Age^{0.234}$ | 0.961 | 0.0910 |
| Boys | White Caucasian | $TBLH\text{-}BMC = 1.47 \times 10^{-3} \times LEAN^{0.813} \times FAT^{0.055} \times Height^{0.949}$ | 0.974 | 0.0839 |
| | South Asian | $TBLH\text{-}BMC = 5.06 \times 10^{-3} \times LEAN^{0.883} \times FAT^{0.044} \times Height^{0.586}$ | 0.979 | 0.0775 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 3.81 \times 10^{-3} \times LEAN^{0.856} \times FAT^{0.047} \times Height^{0.692}$ | 0.974 | 0.0735 |

Total body less head BMC = TBLH-BMC; Total body lean mass = LEAN; Total body fat mass = FAT; SEE = Standard error estimate

Z-Score = (Measure Value – Predicted Value) / (Predicted Value x SEE)

**Table 3c** Prediction Equations for Total body less head bone mineral content (TBLH-BMC (g)) for lean mass (g), fat mass (g), height (cm) and age (1dp) for the GE Lunar iDXA™ - Software version Encore 15.0.

| | | GE Lunar iDXA | $r^2$ | SEE |
|---|---|---|---|---|
| Girls | White Caucasian | $TBLH\text{-}BMC = 1.85 \times 10^{-3} \times LEAN^{0.736} \times FAT^{0.077} \times Height^{0.950} \times Age^{0.135}$ | 0.965 | 0.0843 |
| | South Asian | $TBLH\text{-}BMC = 2.58 \times 10^{-3} \times LEAN^{0.538} \times FAT^{0.110} \times Height^{1.210} \times Age^{0.192}$ | 0.967 | 0.0836 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 4.27 \times 10^{-3} \times LEAN^{0.787} \times FAT^{0.105} \times Height^{0.594} \times Age^{0.239}$ | 0.962 | 0.0931 |
| Boys | White Caucasian | $TBLH\text{-}BMC = 5.88 \times 10^{-4} \times LEAN^{0.827} \times FAT^{0.055} \times Height^{1.095}$ | 0.974 | 0.0849 |
| | South Asian | $TBLH\text{-}BMC = 2.01 \times 10^{-3} \times LEAN^{0.906} \times FAT^{0.047} \times Height^{0.708}$ | 0.980 | 0.0798 |
| | Black Afro-Caribbean | $TBLH\text{-}BMC = 1.78 \times 10^{-3} \times LEAN^{0.887} \times FAT^{0.051} \times Height^{0.765}$ | 0.975 | 0.0754 |

Total body less head BMC = TBLH-BMC; Total body lean mass = LEAN; Total body fat mass = FAT; SEE = Standard error estimate

Z-Score = (Measure Value – Predicted Value) / (Predicted Value x SEE)

**Table 3d** Prediction Equations for Total body less head bone mineral content (TBLH-BMC (g)) for lean mass (g), fat mass (g), height (cm) and age (1dp) for the Hologic Discovery – Software version Apex 4.1.

| | | Hologic Discovery | $r^2$ | SEE |
|---|---|---|---|---|
| Girls | White Caucasian | $TBLH\text{-}BMC = 1.20 \times 10^{-2} \times LEAN^{0.704} \times Height^{0.717} \times Age^{0.235}$ | 0.954 | 0.0871 |
| Boys | White Caucasian | $TBLH\text{-}BMC = 4.77 \times 10^{-3} \times LEAN^{1.041} \times FAT^{-0.046} \times Height^{0.398}$ | 0.960 | 0.0962 |

Total body less head BMC = TBLH-BMC; Total body lean mass = LEAN; Total body fat mass = FAT; SEE = Standard error estimate

Z-Score = (Measure Value – Predicted Value) / (Predicted Value x SEE)