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Original Article

A novel non-invasive method for predicting bone mineral density and fracture risk using demographic and anthropometric measures

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ABSTRACT

Fractures are costly to treat and can significantly increase morbidity. Although dual-energy x-ray absorptiometry (DEXA) is used to screen at risk people with low bone mineral density (BMD), not all areas have access to one. We sought to create a readily accessible, inexpensive, high-throughput prediction tool for BMD that may identify people at risk of fracture for further evaluation. Anthropometric and demographic data were collected from 492 volunteers (♂275, ♀217; [44 ± 20] years; Body Mass Index (BMI) = [27.6 ± 6.0] kg/m^2) in addition to total body bone mineral content (BMC, kg) and BMD measurements of the spine, pelvis, arms, legs and total body. Multiple-linear-regression with step-wise removal was used to develop a two-step prediction model for BMC followed by BMC. Model selection was determined by the highest adjusted R^2, lowest error of estimate, and lowest level of variance inflation ($\alpha = 0.05$). Height (HTcm), age (years), sex$^{m=1,\ f=0}$, %body fat (%fat), fat free mass (FFMkg), fat mass (FMkg), leg length (LLcm), shoulder width (SHWDTHcm), trunk length (TRNKLcm), and pelvis width (PWDTHcm) were observed to be significant predictors in the following two-step model ($p < 0.05$). Step1: BMC (kg) = (0.006 3 × HT) + (−0.002 4 × AGE) + (0.171 2 × SEX$^{m=1,\ f=0}$) + (0.031 4 × FFM) + (0.001 × FM) + (0.008 9 × SHWDTH) + (−0.014 5 × TRNKL) + (−0.027 8 × PWDTH) - 0.507 3; $R^2 = 0.819$, $SE \pm 0.301$. Step2: Total body BMD (g/cm^2) = (−0.002 8 × HT) + (−0.043 7 × SEX$^{m=1,\ f=0}$) + (0.000 8 × %FAT) + (0.297 0 × BMC) + (−0.002 3 × LL) + (0.002 3 × SHWDTH) + (−0.002 5 × TRNKL) + (−0.011 3 × PWDTH) + 1.379; $R^2 = 0.89$, $SE \pm 0.054$. Similar models were also developed to predict leg, arm, spine, and pelvis BMD ($R^2 = 0.796$–0.864, $p < 0.05$). The equations developed here represent promising tools for identifying individuals with low BMD at risk of fracture who would benefit from further evaluation, especially in the resource or time restricted setting.

1. Introduction

Osteopenia and osteoporosis are important modifiable health factors in older adults. With a reported 10.3% prevalence of osteoporosis and 43.9% prevalence of osteopenia, it is estimated

That in 2010, 10.2 million adults had osteoporosis and 43.4 million adults had low bone mass.[1]

Although prevalent, osteoporosis can be clinically silent until the time a fracture occurs.[2] Osteoporosis-related fracture incidence and prevalence cost the United States an estimated $19 billion annually.[3] Furthermore, osteoporosis-induced chronic pain and disability place additional burden on the patient's quality of life.[4] All of these stresses necessitate the use of risk-appropriate screening. For example, identification and treatment of patients at increased risk for fragility fractures with appropriate medical intervention has been shown to decrease incidence of fracture by as much as 50%.[5]

Dual energy x-ray absorptiometry (DEXA) allows accurate diagnosis of osteoporosis, estimation of fragility fracture risk, monitoring of patients undergoing treatment, and is commonly used to evaluate bone mineral density (BMD)/bone health in a clinical setting.[6] The World Health Organization has established DEXA as the best densitometric technique for assessing BMD in postmenopausal women and has based the definitions of osteopenia and osteoporosis on its results.[6] Based on an

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Abbreviations

BMC	total body bone mineral content (kg)
BMD	Bone Mineral Density (g/cm^2)
DEXA	Dual-Energy X-Ray Absorptiometry
FFM	Total body fat free mass, kg
FM	Total body fat mass, kg
%Fat	Percent body fat
HT	Height, cm
WT	Weight, kg
LL	leg length (averaged, cm)
ARML	arm length (averaged, cm)
TRUNKL	trunk length, cm
SHWDTH	shoulder width, cm
PWDTH	pelvis width, cm

individual's age, sex, and race, regional BMD measures are scored against population norms using either age-matched Z-scores or young-adult (30 years-old) T-scores whereby a score of less than −1 indicates low-BMD/osteopenia and less than −2.5 indicates osteoporosis.[6] However, DEXA analysis for bone health may not be readily available to all populations nor practical for large-scale and/or high-volume screening. This may particularly be the case for those who live in rural areas. The provision of a screening tool that may predict an individual's DEXA measures in clinical and non-clinical settings would provide a valuable, non-invasive, inexpensive, and readily-available method to screen and identify at-risk individuals and those who may benefit most from further evaluation and/or intervention.

Recently, Lambert et al.[7] observed that demographic variables such as age, weight, and sex as well as anthropometric measures like fat free mass (FFM), % body fat (%Fat), and fat mass (FM) were predictive of total and regional BMD in elite professional ballet performers using multiple linear regression modeling (R^2: 0.65–0.81). Using the same statistical strategy, Carbuhn et al.[8] found similar predictive accuracy in a two-step BMD prediction model in Division IA collegiate cross-country runners (R^2: 0.64–0.80). Although the regression equations developed demonstrated reasonable accuracy (3.8–8.5% error) for screening tools, the authors of both investigations acknowledged that the models developed were limited to the unique populations studied and may not be appropriate for application outside those unique athletic populations.[7,8] Regardless, the development of similar models for the general population across age ranges would provide a valuable tool for use in various health screening settings. For example, fractures represent 9% of occupational injuries, are responsible for more lost work days than any other injury, and are overall the most costly type of musculoskeletal injury.[9,10] This incidence and resulting cost is further accentuated in professions with high degrees of physical demand, like the military.[10] Therefore, although not for diagnostic use, regression models predicting for BMD may be of great value, quick, and cost-effective in screening/identifying those at-risk for fragility fracture who may benefit from direct assessment via DEXA. In light of previous findings[7] and clinical need, the purpose of the present investigation was to develop novel equations to predict total and regional BMD using common noninvasive anthropometric and demographic measures.

2. Materials and methods

The following procedures have been approved by the Institutional Review Board (IRB) for research involving human subjects with all participants providing informed consent prior to participation (IRB# PRO00024857).

2.1. Study population

Data for 492 (Age: 15–79 years) volunteers who consented to undergo analysis of body composition and BMD in two independent clinical laboratories in Texas using the same DEXA scanner make and model (iDXA, GE®, Boston, MA) between 2016 and 2021 was analyzed for this investigation. All participants were recruited in a clinical setting from one of two communities, one being a large metropolitan area (Texas Medical Center in Houston, TX) and the other being a more rural location (Bryan/College Station, TX) via email, phone, recruitment for other clinical investigations, and word of mouth. Individuals were excluded from the data set if they presented with any of the following conditions: muscular dystrophy, multiple sclerosis, myasthenia gravis, myositis, neuropathy, bony infections, Paget's disease, osteonecrosis, bone tumors, ongoing cancer treatment or treatment within 2-years of measurement. Included study participants were generally considered healthy at the time of their scan.

2.2. DEXA analysis

All scans were performed by a certified technician and all data were analyzed using enCORE analysis software (GE®). Following DEXA scan, total body BMD, total body bone mineral content (BMC, kg), and BMD of the arms, legs, spine, and pelvis were assessed. Measures of height (HT, cm), weight (WT, kg), age (years), body mass index (BMI, kg/m^2), sex, race, fat free mass (FFM, kg), fat mass (FM,kg), and %body fat (%fat) were also collected. In addition, using methods previously reported by Stanelle et al.[11] and Carbuhn et al.,[8] skeletal dimensions (shoulder width, trunk length, pelvis width, arm length, leg length) were also obtained from the total-body DEXA scan and analyzed using ImageJ (National Institutes of Health) analysis software. Briefly, shoulder width (SHWDTH, cm) was measured between the widest point of each shoulder. Trunk length (TRNKL, cm) was measured from the top of the widest point on the pelvis (iliac crest) to the vertical level of the bottom of the jaw bone. Arm length (ARML, cm) was measured as length of the proximal humerus to the distal radius. Leg length (LL, cm) was measured from the top of the greater trochanter of the femur to the bottom the distal tibia. All dimensions were derived from the midsagittal plane where all bony land marks were both easily visible and able to be palpated in a clinical setting. Assessment of skeletal dimensions was completed by 5 independent trained laboratory staff with excellent repeatability ($ICC >$ 0.93). All bilateral measures of the extremities were averaged.

2.3. Statistical analysis

All statistical analyses were completed using SPSS Statistics (Version 26, IBM Statistics, Armonk, N Y). Multiple-linear-regression with stepwise removal was used to predict total body BMC and BMD (total body, legs, arm, spine, pelvis) with each of the collected demographic variables and anthropometric variables. Final prediction model selection was determined by the highest adjusted R^2, lowest error of estimate, and lowest level of variance inflation. Significance for prediction models and individual regression coefficients was set at $\alpha = 0.05$.

3. Results

3.1. Study population demographics are presented in Table 1

Regression analysis results for total body BMC was performed. Stepwise removal identified height, age, sex, fat free mass, fat mass, shoulder width, trunk length, and pelvis width to be significantly predictive of BMC yielding the following prediction model: BMC (kg) = (0.015 8 × HT) + (−0.002 4 × AGE) + (0.171 2 × SEX$^{m=1,\ f=0}$) + (0.031 4 × FFM) + (0.001 × FM) + (0.008 9 × SHWDTH) + (−0.014 5 × TRNKL) + (−0.027 8 × PWDTH) - 0.507 3; $R^2 = 0.819$, $SE \pm 0.301$.

Next, in addition to predicted BMC, the following demographic and

Table 1
Study population demographics.

	All participants (n = 492)	Male (n = 275)	Female (n = 217)
Demographics			
Height, cm	173.09 ± 11.64	181.90 ± 8.34	163.37 ± 7.09
Weight, kg	83.38 ± 20.81	91.124 ± 18.74	73.23 ± 18.98
Age, years	43.76 ± 20.42	42.20 ± 20.50	47.69 ± 19.64
BMI, kg/m^2	27.63 ± 6.02	27.80 ± 5.31	27.40 ± 6.84
Body Composition			
% Body Fat (Total)	31.08 ± 11.67	26.33 ± 9.87	37.29 ± 11.02
Fat Free Mass, kg	56.50 ± 13.50	65.85 ± 9.35	44.26 ± 6.47
Fat Mass, kg	26.47 ± 14.23	24.86 ± 13.48	28.58 ± 14.96
Bone Mineral Content, kg	2.97 ± 0.70	3.44 ± 0.50	2.36 ± 0.38
Bone Mineral Density (g/cm^2)			
Total BMD	1.307 ± 0.162	1.391 ± 0.132	1.201 ± 0.131
Pelvis BMD	1.159 ± 0.218	1.261 ± 0.196	1.031 ± 0.172
Spine BMD	1.257 ± 0.206	1.347 ± 0.195	1.142 ± 0.156
Legs BMD	1.336 ± 0.209	1.464 ± 0.154	1.173 ± 0.148
Arms BMD	1.019 ± 0.185	1.119 ± 0.150	0.892 ± 0.145
Skeletal Dimensions			
Arm Length, cm	53.31 ± 4.77	55.24 ± 4.477	50.87 ± 3.97
Shoulder Width, cm	41.24 ± 3.90	42.93 ± 3.05	39.95 ± 3.82
Trunk Length, cm	46.42 ± 3.83	48.60 ± 3.06	43.67 ± 2.80
Pelvis Width, cm	26.94 ± 1.99	27.35 ± 1.84	26.44 ± 2.07
Leg Length, cm	79.77 ± 5.99	83.00 ± 4.81	75.65 ± 4.76
Race Frequencies			
White	69.92%	72.73%	66.36%
Black	9.35%	6.18%	13.36%
Hispanic	12.20%	15.27%	8.29%
Other	8.53%	5.82%	11.99%

Values are presented as means ± *SD* as well as the race frequency distribution of the sample population. Abbreviations: BMI (Body Mass Index, kg/m^2); BMD (Bone Mineral Density, g/cm^2).

anthropometric measures were observed to be predictive of both total and regional BMD (Fig. 1) depending on the model: height, weight, age, sex, body composition, leg length, shoulder width, trunk length, pelvis width.

All models presented were found to be significant ($p < 0.01$), with the R^2 for the equations indicating that approximately 77%–89% of the variance being explained by the independent variables included in each model. A sample application of the total body BMD prediction is provided in Fig. 2 along with a normative *Z*-score calculation reference data from the National Health Survey.[12]

4. Discussion

The results of this study indicate that noninvasive demographic and anthropometric measures may be utilized to reasonably predict for total and regional BMD. Furthermore, the equations developed here may be best utilized as a high-volume screening tool that can be applied in a number of environments where DEXA is unavailable or impractical. In these settings, those observed to be at risk for low BMD/fragility fractures could be referred for further evaluation, thus resulting in improved targeting for those who stand to benefit from potential intervention.

4.1. Regression coefficients

With regard to the variables included in each of the models, biomechanical factors related to age, sex, and bone/soft tissue interactions have all been previously shown to influence bone metabolism.[13–15] With regards to age, factors such as age-related sarcopenia, reduced physical activity, alterations in hormone output, decline in bone tensile strength, and decreases in osteocyte viability were brought about via oxidative stress.[16] Relatedly, skeletal muscle plays a critical role in bone maintenance through mechanical loading, local and systemic signaling from activity as well as direct interactions, via strain, at the muscle-bone interface.[17,18] Regarding the contribution of sex to our models, differences between males and females have been observed, even when correcting for body mass, supporting the necessity of considering sex as an independent prediction variable in many of the models generated here.[19]

Expectedly, total body mass and variables related to soft tissue distribution were observed to be significant predictors of BMD in all of the models. Importantly, bone is highly responsive to mechanical loading via Wolff's Law.[20] Relatedly, although not assessed here, even in osteopenic/-porotic patients, physical activity has shown to increase BMD.[21] Next, skeletal dimensions were observed to be significantly predictive of BMD for all prediction models. In addition to the contribution to BMD from mechanical loading via aforementioned mechanisms, we find it likely that differences in chronic loading placed across differing lever arm lengths may be related to the contribution of skeletal dimensions and height in our prediction models.[22–24] Information on such skeletal dimensions combined with a metric of bone mass also contributed to explaining variance in BMD in this population in a similar manner to prediction models developed by Carbuhn et al.[8] in cross-country runners.

4.2. Significance/clinical relevance

It is estimated that over 10.2 million Americans have osteoporosis with those numbers projected to increase and a large number of new cases unaware of their problem until they sustain a fracture.[2,25] Healthcare cost is estimated to be well over $30 000 in the 12 months following a fragility fracture.[25] In 2015, there were 2–3 million osteoporotic fractures, with only 9% of those patients subsequently undergoing BMD testing in the following 6 months and over 300 000 experiencing a secondary fracture in the short term.[26] Furthermore, it is conservatively estimated that medical treatment could reduce 20% of these secondary fractures to the benefit of the patient and at least $1 billion saved.[26] On a similar note, there is significant morbidity related to osteoporotic fractures, for example hip fractures have up to a 30% 1-year mortality rate.[27] In this light, the utility of this equation as a screening tool would enable patients, their care-takers, health team and family to better advocate for their health by using this screening tool to narrow the treatment gap between the onset of osteoporosis and medical treatment. The United States Preventative Services Task Force (USPSTF) recommends formal BMD testing in postmenopausal women under 65 years old who are clinically assessed to be at risk of fragility fractures, however its recommendations are inconclusive about the testing of men of any age.[27] Utility of this equation may also give primary care physicians more objective data to better assess patients outside of the USPSTF recommendations that may benefit from formal BMD evaluation/treatment. With today's aging population it will be that much more important to exploit ways to prevent the future preventable burden of osteoporosis. The equations developed here may be utilized as a screening tool that can be applied in a number of environments where DEXA may either be unavailable or impractical (physician's office; wellness centers; geriatric or orthopedic care settings; high school/collegiate screening; military screening; corporate fitness settings; rural areas; community/volunteer clinics). In these settings, those observed to be at risk for low BMD could be referred for further evaluation, thus resulting in improved targeting for those who stand to benefit from potential intervention which would serve to decrease fracture incidence. This may also serve to empower patients and those they interact with to take a more active role in advocating for their

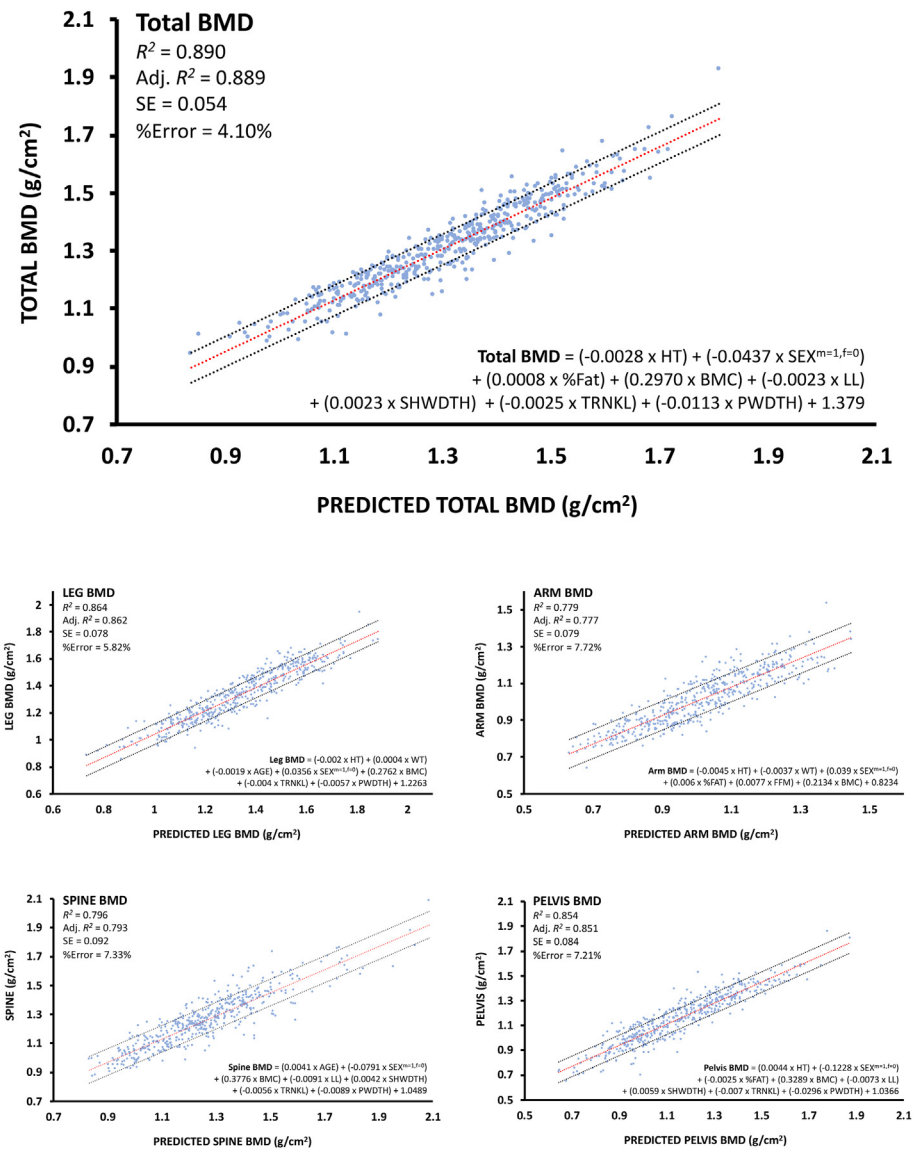

Fig. 1. Prediction of Bone Mineral Density. Data are presented at scatter plots along with R^2, adjusted (Adj.) R^2, standard error of estimate (SE), and %error for the results of multiple linear regression analysis to predict total body regional bone mineral density (BMD, g/cm^2) of the legs, arms, spine, and pelvis. Black dashed lines indicate on either side of the red line of best fit indicate SE. Abbreviations: HT (height, cm), WT (body mass, kg), AGE (age, years), SEX (male = 1, female = 0), %Fat (percent body fat), BMC (bone mineral content, kg), LL (leg length, cm), SHWDTH (shoulder width, cm), TRNKL (trunk length, cm), PWDTH (pelvis width, cm). n = 492.

own health and the health of the ones around them, which in turn may help the clinician and the patient avoid the devastating consequences of osteoporosis related fractures.

4.3. Limitations & considerations

Although the present investigation involved a fairly large pool of participants across a wide age range, the present investigation is not without limitations. First, the population used was taken from the surrounding location of two institutions in a single state. A such, it is important to note that the demographics within our sample (particularly regarding race frequencies) were not completely matched to current national norms on the whole.[28] Validation in other communities is therefore needed. Therefore, while race was not observed to be a significant predictor in any of the current models, we acknowledge that the lack of an appropriate sample size within each respective race cannot rule out any potential impact as BMD differences have been previously observed among different race demographics.[29,30] However, the degree to which these differences are inherent to ethnicity or related to other confounding factors is also unknown. Notably, the majority of participants in this investigation were white. However, in a recent study on bone stress injuries in military populations, Bulathsinhala et al.[31] previously identified whites to be at the greatest risk for such injuries in a cohort of 1.3 million United States Army soldiers. Regardless, future investigations will be required to validate these models among various race demographics. Furthermore, this study utilized participants across the age spectrum and it should be noted that the life cycle differences (i.e. growing/adolescent on hormonal birth control versus retired senior citizen) may have played an unknown effect in the present study. It also cannot be discounted that specific circumstances (i.e. post-partum, post-operative, etc.) may require more individualized models, however this will need to be explored in future validation studies. Importantly, as this was a retrospective investigation, the study did not account/control for modifiable risk factors (i.e. smoking and other lifestyle habits) that have been shown to affect bone metabolism.[2] Further study will be required to determine if the addition of short survey questionnaires regarding lifestyle may add predictive value to the models developed here. Lastly, in practical application and in the absence of DEXA, the models developed here rely on indirect methods of body composition and BMC assessment that undoubtedly add some degree of error propagation similar to other published prediction models of this nature that involve indirect measures.[7,8,11] Therefore, while further investigation remains needed for continued model refinement, we conclude that the models developed here may serve as a useful initial screening tool for BMD (as

EXAMPLE PREDICTION: TOTAL BONE MINERAL DENSITY

Input:		Calculations:
Sex:	Male	Fat Mass = 100kg x 0.30 (30% Fat) = 30kg
Age:	30yr	Fat Free Mass = 100kg – 30kg = 70kg
Height:	160 cm	
Weight:	100 kg	
%Fat:	30%	**Total Bone Mineral Content (BMC)** = (0.0158 x 160cm, height)
Leg Length:	82 cm	+ (-0.0024 x 30yrs, age) + (0.1712 x 1, $SEX^{m=1, f=0}$) + (0.0314 x
Trunk Length:	48 cm	70kg, Fat Free Mass) + (0.001 x 30kg, Fat Mass) + (0.0089 x
Shoulder Width:	42 cm	42cm, Shoulder Width) + (-0.0145 x 48cm, Trunk Length) + (-
Pelvis Width:	27 cm	0.0278 x 27cm, Pelvis Width) – 0.5073 = **3.419 kg**

Total Bone Mineral Density = (-0.0028 x 160cm, height)
+ (-0.0437 x 1, $SEX^{m=1, f=0}$) + (0.0008 x 30, %Fat) + (0.2970 x 3.419kg, BMC)
+ (-0.0023 x 82cm, leg length) + (0.0023 x 42cm, shoulder width)
+ (-0.0025 x 48cm, trunk length) + (-0.0113 x 27cm, pelvis width) + 1.379
= **1.410 g/cm²**

Predicted Z-Score Risk of Osteopenia / Osteoporosis
Z > -1 (Not At Risk), Z < -1 (Osteopenia), Z < -2.5 (Osteoporosis)

BMD Norm: Males 20-30 = 1.212 g/cm² ± 0.109
Predicted Age Matched Z-Score = (1.410 – 1.212) / 0.109 = 1.82 (not at risk)

BMD Norms Reference: Looker, A.C., et al. "Total body bone area, bone mineral content, and bone mineral density for individuals aged 8 years and over: United States, 1999-2006." *Vital Health Statistics. Series 11, Data from the National Health Survey 253* (2013): 1-78

Fig. 2. Example Calculation of Predicted Total BMD and Z-Score Risk. Example reference calculation performed on a 30-year-old male. In addition, an age-matched *Z*-score [(Measure – Reference Population Mean)/*SD* of the Reference Population] was calculated from the resulting BMD prediction using normative population reference data commonly used with DEXA assessments whereby (> 0 = normal, −1 to −2.5 = osteopenia, < −2.5 = osteoporosis).[12] Abbreviations: yr (years of age), %Fat (percent body fat), BMC (bone mineral content, kg), BMD (bone mineral density, g/cm^2).

none currently exist to our knowledge), that may contribute to more regular/focused risk tracking in patients/communities that are at risk of low BMD and associated complications. Importantly, we caution the reader that the models developed here should be considered exclusively for screening and not used for clinical diagnostic purposes. As treatment for low BMD can be multifaceted and heavily individualized, interventions should only be implemented upon physician follow-up with diagnostic imaging. However, as a precaution, it may be advisable for those screened with low BMD to avoid high impact physical activities or activities that may place one at an elevated risk of falls until diagnostic follow-up in a clinical setting.

4.4. Conclusions & future directions

The proposed equations represent a promising, available, commodious tool for identifying individuals with low BMD at risk of fracture who would benefit from further evaluation, especially in the resource or time restricted setting. As previously mentioned, a path for further augmentation of these models would be to evaluate the additional impact of other variables known to influence BMD. As touched on previously, these might include, but are not limited to, nutrition, activity level, smoking status/frequency, alcohol consumption frequency and volume, ethnicity, certain drug consumption (recreational and prescription), certain co-morbidities, and other information that may also be collected quickly and efficiently via survey. Further, it will be necessary to implement these predictions models in various investigational settings among diverse populations to validate its sensitivity and specificity as a screening tool.

Submission statement

All authors have read and agree with the manuscript content. The publication of this work is approved by all authors and tacitly or explicitly by Houston Methodist Hospital. The present work has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis), and is not under consideration for publication elsewhere. Further, while under review, this manuscript will not be submitted elsewhere for review or publication. The submitted manuscript will not be published elsewhere including electronically in the same form, in English or in any other language, without the written consent of the copyright-holder.

Ethical approval statement

The study was approved by the institutional review board for research involving human subjects (IRB# PRO00024857), and all participants provided informed consent for their data to be used for research purposes prior to participating in the experimental procedures.

Authors' contributions

Justin Aflatooni: Primary manuscript writer, Literature review, Data analysis. Steven Martin:Data collection, Study design, Manuscript Review. Adib Edilbi: Literature review, Manuscript Review. Pranav Gadangi, William Singer and Robert Loving: Data analysis, ImageJ Analysis, Manuscript Review. Nandini Solanki and Shreya Domakonda: Data analysis, ImageJ Analysis, Manuscript Review, Generation of tables. Patrick McCulloch: Study Design, Medical Expertise, Manuscript Review. Bradley Lambert: Project director, Data collection, Data analysis, Statistics, Generation of figures, Manuscript development.

Conflict of interest

No funding was received for this research. Therefore, the authors declare no conflict of interest.

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