

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

## Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032268
Article Type:	Research
Date Submitted by the Author:	12-Jun-2019
Complete List of Authors:	Xiao, Zeyu; The first affiliated hospital of Jinan University, Radiology Xu, Hao; The first affiliated hospital of Jinan University, Nuclear medicine
Keywords:	body composition, aging, bone mineral density, fat distribution, appendicular lean mass

SCHOLARONE™  
Manuscripts

1  
2  
3  
4 **Sex- and age-specific characteristics of body composition and its**  
5  
6 **effect on bone mineral density in Chinese adults: a southern China**  
7  
8 **aging study**  
9  
10

11  
12  
13 Zeyu Xiao <sup>a, b, c</sup>, Hao Xu <sup>a, c, \*</sup>  
14  
15

16  
17  
18 <sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University,  
19  
20  
21 Guangzhou, PR China  
22

23 <sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University,  
24  
25  
26 Guangzhou, Guangdong, China

27 <sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University,  
28  
29  
30 Guangzhou, Guangdong, China  
31

32  
33  
34  
35 **Corresponding Author:**

36  
37 Hao Xu, e-mail: [txh@jnu.edu.cn](mailto:txh@jnu.edu.cn);  
38

39  
40  
41 Address: No.613, Huangpu Road West, Tianhe District, Guangzhou, Guangdong  
42  
43 Province, China, 510630.

44  
45  
46 Tel: +86-2038688405.

47  
48  
49 Fax: +86-2038688888.  
50

51  
52 **Keywords:** body composition; aging; bone mineral density; fat distribution;  
53  
54  
55 appendicular lean mass.  
56

57  
58  
59 **Word count:** 4721  
60

## Abstract

**Objectives:** This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD) across a cohort of southern Chinese adults.

**Design:** Cross-sectional study.

**Setting and Participants** A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

**Primary outcome measures:** Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between BC, adipose distribution, and BMD of each skeletal site.

**Results:** Whole-body FM, fat%, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, BMI, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard  $\beta$  0.207 to 0.388,  $P < 0.01$  for all), although not the largest but still a positive predictor of BMD in females (standard  $\beta$  0.123 to 0.227,  $P < 0.001$  for all). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard  $\beta$  -0.052 to -0.236,  $P < 0.01$  for all) but not in males.

**Conclusions:** In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

## Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.
- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

## Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean fat and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different

1  
2  
3  
4 methods or indexes, the findings regarding the relationship of central adipose with BMD are more  
5 controversial. Several studies indicate that central adipose accumulation is negatively related to  
6 BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD  
7 in postmenopausal women [14]. These heterogeneous findings may result from the rather complex  
8 mechanisms underlying the relationship between fat and bone, including mechanical loading as well  
9 as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism  
10 to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the  
11 relationship between BMD with ALM and central FM have not been well studied.

12  
13  
14  
15  
16  
17  
18  
19 To our knowledge, only a few other studies have documented the relationships of ALM and  
20 A/G FMR with BMD at multiple sites in different ages, menopausal status, and in both genders. In  
21 the current study, we aim to investigate the relationship between BMD and body composition,  
22 especially the effect of regional body composition on BMD. We also want to examine whether these  
23 relationships differ by gender, age, and menopausal status in a large population-based sample of  
24 Chinese adults.  
25  
26  
27  
28  
29  
30  
31  
32

## 33 **Methods**

### 34 **Subjects**

35  
36  
37 The present study included healthy Chinese men and women aged 20 to 95 years old. The  
38 participants were recruited from the body composition and osteoporosis study at the First Affiliated  
39 Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study  
40 were Chinese individuals who appeared to be in good health and functionally independent. Subjects  
41 were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication  
42 known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen  
43 drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism,  
44 hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants  
45 (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or  
46 non-natural menopause (natural menopause was designated if there was a complete natural cessation  
47 of menses for more than twelve months). In the end, 1703 men and 4046 women were included in  
48 our study. All subjects provided written informed consent to participate in the study, which was  
49 approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

### **Anthropometry, BMD and body composition measurement**

A research physician obtained information on medical history, medication use, smoking, and alcohol history in a personal interview. Height and body weight were obtained based on standard methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg. Body mass index (BMI) was calculated as body weight divided by height squared ( $\text{kg}/\text{m}^2$ ). Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086; GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android and Gynoid regions were automatically attained using the software provided by the manufacturer. Android region is defined as the portion of the abdomen included between the line joining the two superior iliac crests, extending cranially up to 20% of the distance between this line and the chin. Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter, directed caudally up to twice the height of the android region. The appendicular region is defined as the areas including both the left and right arms and legs. Daily quality assurance scans were performed by scanning the spine phantom according to the manufacturer's instructions; the same trained technologist conducted all DXA measurements throughout the study. The precision error (%CV) was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD, and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was determined by duplicate scans with repositioning between each measurement in 30 volunteer subjects.

### **Statistical analyses**

Subjects were categorized into four groups according to gender, age, and menopausal status (786 men < 50 years, 917 men  $\geq$  50 years, 1534 premenopausal women, and 2512 postmenopausal women). The values of continuous variables were presented as the mean  $\pm$  standard deviation (SD). Unpaired-sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's correlation coefficients (*r*) were conducted to determine the linear relationships among various parameters. We performed linear regressions to assess the association strength between ALM, A/G FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used as dependent variables, and ALM and A/G FMR were treated as independent variables; age, height, and lifestyle factors (smoking and alcohol history) were also included. When we performed linear

1  
2  
3  
4 regression analyses, we chose the stepwise methods and expressed the results as standard  $\beta$  coefficients;  
5 only significant ( $P < 0.05$ ) factors were retained in the models. All tests were two-sided, and  $P < 0.05$   
6 was considered statistically significant. All statistical analyses were performed using the statistical  
7 package for social sciences (Version 19.0) (SPSS Inc., Chicago, IL, USA).  
8  
9

### 10 **Patient and Public Involvement**

11  
12 There was no patient or public involvement in this study.  
13  
14  
15

## 16 **Results**

### 17 **Basal characteristics of subjects**

18  
19 Table 1 details the subject characteristics in each group. Males  $\geq 50$  years had higher BMI, whole-  
20 body FM, fat%, trunk FM, and appendicular FM, but lower weight and lumbar spine BMD than  
21 males  $< 50$  years ( $P < 0.001$ ). Postmenopausal females had higher values for whole-body FM, whole-  
22 body LM, trunk FM, appendicular FM, and A/G FMR, and lower BMD at each site than  
23 premenopausal females ( $P < 0.05$ ).  
24  
25  
26  
27  
28  
29

### 30 **Changes of BMD and body composition with age**

31  
32 To further explore the distribution characteristics of body composition and BMD regarding age, we  
33 divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table  
34 2 and Figure 1, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in  
35 both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip  
36 BMD were observed in the second decade and then decreased slightly with age in males. BMD at  
37 each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in  
38 females, and then decreased dramatically after menopause. Interestingly, appendicular LM started  
39 to decline after 50 years old in both males and females.  
40  
41  
42  
43  
44  
45  
46  
47

### 48 **Associations of BMD with whole and regional body composition in different groups**

49  
50 In Pearson's correlation analyses, significant positive correlations were found between BMD at all  
51 sites with height, weight, BMI, whole-body LM, whole-body FM, FAT%, Android FM, Gynoid  
52 FM, and ALM in all groups ( $r = 0.218-0.616$ ,  $P < 0.05$ ). A/G FMR showed positive correlations with  
53 whole-body, lumbar spine, femoral neck, and total hip BMDs in men  $< 50$  years and  $\geq 50$  years old  
54 ( $r = 0.089-0.318$ ,  $P < 0.001$ ). However, A/G FMR was negatively correlated with whole-body and  
55 femoral neck BMDs in postmenopausal females, though the correlation strengths were weak ( $r = -$   
56  
57  
58  
59  
60



1  
2  
3  
4 0.075,  $P < 0.001$  and  $r = -0.091$ ,  $P < 0.001$ , respectively). A/G FMR was insignificantly correlated with  
5  
6 BMD in premenopausal females (Shown in supplemental table 1-4).

7  
8 To further explore the independent predictive value of A/G FMR and ALM for BMD at all  
9  
10 sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that  
11  
12 associated with BMD were also included in the multiple linear regression analyses (shown in Table  
13  
14 3). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD.

15  
16 The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal site  
17  
18 and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck,  
19  
20 and total hip BMDs in both premenopausal and postmenopausal women (standard  $\beta = -0.236 \sim -0.052$ ),  
21  
22 while men had no significant relationship between A/G FMR and each part of BMD after adjustment.  
23  
24 ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs  
25  
26 in both males and females, and the correlations were higher in males (standard  $\beta = 0.207 \sim 0.388$ ) than  
27  
28 that in females (standard  $\beta = 0.123 \sim 0.227$ ), in both younger adults and older adults after adjustment.  
29  
30

### 31 **Discussion**

32  
33 The global epidemic of obesity has become a significant concern in our daily life as it not only has  
34  
35 a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health  
36  
37 [15]. As a part of body composition, bone density was mainly determined by body weight and BMI.  
38  
39 Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females  
40  
41 [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 90 years old  
42  
43 to further explore the factors that may influence bone health. We divided the participants into  
44  
45 different age groups to investigate the changes in body composition and BMD with age in males  
46  
47 and females. We also performed multivariable regression analyses to confirm that whether A/G  
48  
49 FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and  
50  
51 alcohol consumption. The current report provided more detailed and impressive results which were  
52  
53 different from previous studies performed in America [13] and Australia [1]. We found that ALM  
54  
55 positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR  
56  
57 as an indicator of central adipose accumulation was inversely associated with BMD in females but  
58  
59 not in males. These results, based on a large population of Chinese adults, were convincing.  
60

In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and

1  
2  
3  
4 then decreased gradually in both genders, whereas whole-body FM steadily increased from youth  
5  
6 to older age in both genders. After analyzing the baseline characteristics, we found that the  
7  
8 decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the  
9  
10 increased whole-body FM in older men and women mainly arose from the increase of Trunk FM.  
11  
12 In the meantime, we found that the A/G FMR increased with age in both males and females. Men  
13  
14 had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD  
15  
16 at all sites decreased slightly in older men, but more obviously in postmenopausal women. These  
17  
18 results provided us a healthy bone mass for each age group in both men and women. The BMD at  
19  
20 each region lower than the guidance ranges in the respective age group should alarm the physician  
21  
22 for appropriate intervention.

23  
24 In our study, the results showed that both total LM and total FM are positively associated with  
25  
26 BMD in both genders. The effect size of total LM and total FM to BMD was different according to  
27  
28 gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in  
29  
30 men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in  
31  
32 postmenopausal women. Several potential theories may explain the observed findings. The  
33  
34 influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces  
35  
36 a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted  
37  
38 for a large proportion of body weight in both males and females, would perform a gravitational  
39  
40 loading on the bone. On the other hand, the contraction strength of lean muscle should also be  
41  
42 considered a specific mechanism of action. A previous study reported that the augmentation and  
43  
44 thickening of bone trabecula was an adaption to increased mechanical stress. However, whole-body  
45  
46 FM only accounted for a small proportion of body weight in both males and females, but it still  
47  
48 performed a significant and positive correlation with BMD, especially in postmenopausal women,  
49  
50 in whom a higher standard  $\beta$  value with BMD in all the skeletal sites was shown compared with whole-body LM.  
51  
52 Several mechanisms could explain the association between fat tissue and BMD. The outcomes of  
53  
54 fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight  
55  
56 bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related  
57  
58 mechanism may help to interpret this finding, as the postmenopausal women also had the highest  
59  
60 whole-body FM, more than males and premenopausal women in our study. Several hormones,  
including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from

1  
2  
3  
4 adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the  
5 enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated  
6 estrogen level. These bone protective hormones led to a positive influence on bone formation via  
7 stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption.  
8 This finding further confirmed the results from previous studies that FM should have a positive  
9 relationship with bone mass [8, 17].

10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
Though both whole-body LM and FM were found to be positively associated with BMD in both genders, how regional body compositions and differences in fat distribution influence bone metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which may have close relationships with BMD, were considered in multiple linear regression analyses. In the current study, we found that ALM was positively related to BMD at all sites after adjustment for BMI and age in both genders. ALM is considered one of the most important indexes of the diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7] also found that ALM was most strongly associated with femoral neck BMD independent of nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may explain the observed association between ALM and BMD. The amount of ALM was smaller than trunk LM in this study, suggesting ALM may affect on bone via contraction strength instead of gravitational loading, especially in males younger than 50 years old, in whom the strongest relationships with BMD in all sites were demonstrated, compared with other groups. Systemic factors that simultaneously involve both ALM and bone metabolism may exist as the decline of ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to explore the potential mechanism further.

Depot-specific fat has been known to play a different role in terms of obesity and metabolism. A previous study indicated that different fat depots might have distinct relationships with bone mass [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD

1  
2  
3  
4 in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative  
5 [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with  
6 BMD and regarded as an independent and protective factor on the presence of osteoporosis or  
7 osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with  
8 increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution  
9 difference seems to produce a meaningful but contradicted effect on bone mass based on previous  
10 studies. To further confirm this finding, we performed Pearson's correlation to assess the  
11 relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The  
12 results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males  
13 and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies  
14 reported abdominal fat and android fat measured by CT or DXA had a negative association with  
15 BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for  
16 bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males  
17 and females. The results revealed that A/G FMR was positively correlated with each part of BMD  
18 in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse  
19 association with whole-body ( $r=-0.075$ ,  $P<0.001$ ) and femoral neck BMD ( $r=-0.091$ ,  $P<0.001$ ), and  
20 had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported  
21 that A/G FMR was inversely associated with the trabecular bone score after age adjustment ( $r=-$   
22  $0.288$ ,  $P<0.05$ ), which was similar with our findings. Android fat mainly represents visceral fat in  
23 the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher  
24 A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a  
25 higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to  
26 be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat  
27 storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association  
28 among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu  
29 et al. [17] reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association  
30 with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and  
31 visceral fat had opposite effects on femoral bone structure and strength in healthy young females,  
32 and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a  
33 negative association with bone. These heterogeneous findings may be related to the use of diverse  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 methods for measuring body composition and BMD, disparities in study design, or the different  
5 criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex  
6 mechanisms underlying the relationship between fat and bone. As a result, we subdivided the  
7 Chinese people into different age and gender groups and found that android fat increased with age,  
8 especially in females, whose android fat accounted for a more substantial proportion of body weight  
9 and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included  
10 A/G FMR instead of the total and regional body composition into the same multiple regression  
11 analysis when we explored the associations of regional fat depots with BMD, which provided a  
12 more reliable result.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

### 23 **Limitations**

24  
25 This study had several limitations. First, we did not obtain a blood sample from participants;  
26 thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on  
27 bone mass mainly referenced in previous reports based on our data and the statistical results. Second,  
28 we only collected cross-sectional data and cannot directly conclude the causality limited by its study  
29 design. Third, though we evaluated the relationships of body composition and fat distribution with  
30 BMD by adjusting age, smoking, and alcohol consumption, other confounders such as  
31 socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and  
32 metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a  
33 more substantial amount of visceral fat mass was found in Asians compared with the European  
34 people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when  
35 interpreting the findings.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

### 48 **Conclusions**

49  
50 In summary, in this large cohort of Chinese adults, ALM had a strong positive association with  
51 BMD in both genders and suggesting that low ALM is related to low BMD and may be considered  
52 an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was  
53 inversely associated with BMD in females but not in males.  
54  
55  
56  
57  
58  
59  
60

## Contributors

Xiao participated in collection, analysis, interpretation of data, and the writing of the paper. Xu, Principal Investigator, innovator for the project, participated in the conception, design, and revision of the manuscript.

## Conflict of interest

The authors have no conflicts of interest.

## Funding

This work was supported by the National Natural Science Foundation of China (Grant No. 81871383), and the Medical Scientific Research Foundation of Guangdong Province, China (Grant No. A2018132).

## Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

## Data sharing statement

Data will be made available on request.

## Acknowledgements

The authors would like to express their gratitude to all participating subjects.

## Abbreviations

BMD: bone mineral density; LM; lean mass; FM: fat mass; ALM: appendicular lean mass; DXA: dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.

## Figure legend

Fig.1 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM), percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

## References

1. Zhu K, Hunter M, James A, et al. Associations between body mass index, lean and fat body mass and bone mineral density in middle-aged Australians: The Busselton Healthy Ageing Study. *Bone*. 2015; 74:146-52.

- 1  
2  
3  
4 2. Chen SC, Chung WS, Wu PY, et al. Associations among Geriatric Nutrition Risk Index,  
5 bone mineral density, body composition and handgrip strength in patients receiving  
6 hemodialysis. *Nutrition*. 2019; 65:6-12.  
7
- 8  
9 3. Stroup BM, Hansen KE, Krueger D, et al. Sex differences in body composition and bone  
10 mineral density in phenylketonuria: A cross-sectional study. *Mol Genet Metab Rep*. 2018;  
11 15:30-5.  
12
- 13  
14 4. Heiss CJ, Sanborn CF, Nichols DL, et al. Associations of body fat distribution, circulating  
15 sex hormones, and bone density in postmenopausal women. *J Clin Endocrinol Metab*. 1995;  
16 80:1591-6.  
17
- 18  
19 5. Guo B, Wu Q, Gong J, et al. Gender Difference in Body Fat for Healthy Chinese Children  
20 and Adolescents. *Child Obes*. 2016; 12:144-54.  
21
- 22  
23 6. Guo B, Wu Q, Gong J, et al. Relationships between the lean mass index and bone mass  
24 and reference values of muscular status in healthy Chinese children and adolescents. *J Bone  
25 Miner Metab*. 2016; 34:703-13.  
26
- 27  
28 7. Blain H, Jaussent A, Thomas E, et al. Appendicular skeletal muscle mass is the strongest  
29 independent factor associated with femoral neck bone mineral density in adult and older men.  
30 *Exp Gerontol*. 2010; 45:679-84.  
31
- 32  
33 8. Bogl LH, Latvala A, Kaprio J, et al. An investigation into the relationship between soft  
34 tissue body composition and bone mineral density in a young adult twin sample. *J Bone Miner  
35 Res*. 2011; 26:79-87.  
36
- 37  
38 9. Cui LH, Shin MH, Kweon SS, et al. Relative contribution of body composition to bone  
39 mineral density at different sites in men and women of South Korea. *J Bone Miner Metab*.  
40 2007; 25:165-71.  
41
- 42  
43 10. Walsh CJ, Phan CM, Misra M, et al. Women with anorexia nervosa: finite element and  
44 trabecular structure analysis by using flat-panel volume CT. *Radiology*. 2010; 257:167-74.  
45
- 46  
47 11. Kang SM, Yoon JW, Ahn HY, et al. Android fat depot is more closely associated with  
48 metabolic syndrome than abdominal visceral fat in elderly people. *PLoS One*. 2011; 6:e27694.  
49
- 50  
51 12. Choi HS, Kim KJ, Kim KM, et al. Relationship between visceral adiposity and bone  
52 mineral density in Korean adults. *Calcif Tissue Int*. 2010; 87:218-25.  
53
- 54  
55 13. Katzmarzyk PT, Barreira TV, Harrington DM, et al. Relationship between abdominal fat  
56  
57  
58  
59  
60

- and bone mineral density in white and African American adults. *Bone*. 2012; 50:576-9.
14. Warming L, Ravn P, Christiansen C. Visceral fat is more important than peripheral fat for endometrial thickness and bone mass in healthy postmenopausal women. *Am J Obstet Gynecol*. 2003; 188:349-53.
15. Shapses SA, Pop LC, Wang Y. Obesity is a concern for bone health with aging. *Nutr Res*. 2017; 39:1-13.
16. De Laet C, Kanis JA, Oden A, et al. Body mass index as a predictor of fracture risk: a meta-analysis. *Osteoporos Int*. 2005; 16:1330-8.
17. Zhu K, Briffa K, Smith A, et al. Gender differences in the relationships between lean body mass, fat mass and peak bone mass in young adults. *Osteoporos Int*. 2014; 25:1563-70.
18. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*. 1998; 147:755-63.
19. Melton LJ, 3rd, Khosla S, Crowson CS, et al. Epidemiology of sarcopenia. *J Am Geriatr Soc*. 2000; 48:625-30.
20. Verschueren S, Gielen E, O'Neill TW, et al. Sarcopenia and its relationship with bone mineral density in middle-aged and elderly European men. *Osteoporos Int*. 2013; 24:87-98.
21. Seeman E. Clinical review 137: Sexual dimorphism in skeletal size, density, and strength. *J Clin Endocrinol Metab*. 2001; 86:4576-84.
22. Kim JH, Choi HJ, Ku EJ, et al. Regional body fat depots differently affect bone microarchitecture in postmenopausal Korean women. *Osteoporos Int*. 2016; 27:1161-8.
23. Marques EA, Moreira P, Wanderley F, et al. Appendicular fat mass is positively associated with femoral neck bone mineral density in older women. *Menopause*. 2012; 19:311-8.
24. Kuwahata A, Kawamura Y, Yonehara Y, et al. Non-weight-bearing effect of trunk and peripheral fat mass on bone mineral density in pre- and post-menopausal women. *Maturitas*. 2008; 60:244-7.
25. Yoo HJ, Park MS, Yang SJ, et al. The differential relationship between fat mass and bone mineral density by gender and menopausal status. *J Bone Miner Metab*. 2012; 30:47-53.
26. Freitas P, Garcia Rosa ML, Gomes AM, et al. Central and peripheral fat body mass have a protective effect on osteopenia or osteoporosis in adults and elderly? *Osteoporos Int*. 2016; 27:1659-63.



- 1  
2  
3  
4 27. Sharma A, Flom PL, Rosen CJ, et al. Racial differences in bone loss and relation to  
5 menopause among HIV-infected and uninfected women. *Bone*. 2015; 77:24-30.  
6  
7 28. Tchernof A, Desmeules A, Richard C, et al. Ovarian hormone status and abdominal  
8 visceral adipose tissue metabolism. *J Clin Endocrinol Metab*. 2004; 89:3425-30.  
9  
10 29. Kim CJ, Oh KW, Rhee EJ, et al. Relationship between body composition and bone mineral  
11 density (BMD) in perimenopausal Korean women. *Clin Endocrinol (Oxf)*. 2009; 71:18-26.  
12  
13 30. Gilsanz V, Chalfant J, Mo AO, et al. Reciprocal relations of subcutaneous and visceral fat  
14 to bone structure and strength. *J Clin Endocrinol Metab*. 2009; 94:3387-93.  
15  
16 31. Lesser IA, Gasevic D, Lear SA. The effect of body fat distribution on ethnic differences  
17 in cardiometabolic risk factors of Chinese and Europeans. *Appl Physiol Nutr Metab*. 2013;  
18 38:701-6.  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Table 1** Baseline characteristics of subjects

	Male		Female	
	Age < 50 years	Age ≥ 50 years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0 <sup>c</sup>	37.4±8.7	63.9±9.1 <sup>c</sup>
Weight (kg)	63.9±12.4	63.8±10.8 <sup>c</sup>	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	22.4±3.9	22.9±3.3 <sup>c</sup>	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5 <sup>c</sup>	16.7±6.0	18.9±6.2 <sup>b</sup>
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0 <sup>a</sup>
Fat%	20.2±8.3	23.0±7.3 <sup>c</sup>	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4 <sup>c</sup>	8.7±3.6	10.6±3.7 <sup>b</sup>
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1 <sup>c</sup>	7.3±2.5	7.5±2.6 <sup>c</sup>
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15 <sup>c</sup>
Bone mineral density (g/cm <sup>2</sup> )				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106 <sup>c</sup>
Lumbar spine	1.114±0.162	1.099±0.200 <sup>c</sup>	1.124±0.155	0.950±0.186 <sup>c</sup>
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132 <sup>b</sup>
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144 <sup>b</sup>
Current Smoker (%)	17.9%	13.0%	2.4%	2.8%
Current alcohol user (%)	15.4%	12.8%	2.3%	1.5%

*Note.* Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with the same gender of the different age group (unpaired-sample *t*-tests or chi-squared test).

**Table 2** Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm <sup>2</sup> )	LSBMD (g/cm <sup>2</sup> )	FNBMD (g/cm <sup>2</sup> )	THBMD (g/cm <sup>2</sup> )
<b>Male</b>												
20-29	199	47.3±6.0 <sup>c</sup>	12.1±8.2 <sup>c</sup>	18.1±9.0 <sup>c</sup>	1.2±0.9 <sup>c</sup>	2.4±1.3 <sup>c</sup>	0.47±0.14 <sup>c</sup>	21.6±3.3 <sup>c</sup>	1.102±0.103	1.126±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9 <sup>c</sup>	12.8±7.3 <sup>c</sup>	19.4±8.2 <sup>c</sup>	1.4±0.9 <sup>c</sup>	2.4±1.3 <sup>a</sup>	0.55±0.16 <sup>c</sup>	21.0±3.3 <sup>c</sup>	1.090±0.113 <sup>c</sup>	1.110±0.149	0.909±0.140 <sup>b</sup>	0.922±0.154 <sup>c</sup>
40-49	333	48.3±6.0 <sup>c</sup>	15.4±7.2 <sup>c</sup>	22.1±7.6 <sup>c</sup>	1.7±0.9 <sup>c</sup>	2.6±1.0	0.63±0.17 <sup>c</sup>	21.5±3.2 <sup>c</sup>	1.119±0.108 <sup>b</sup>	1.111±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1 <sup>c</sup>	15.2±6.5	22.2±7.2 <sup>a</sup>	1.7±0.8 <sup>c</sup>	2.5±0.9	0.67±0.18 <sup>c</sup>	21.0±3.2 <sup>c</sup>	1.122±0.110	1.096±0.192	0.895±0.140	0.946±0.154 <sup>a</sup>
60-69	281	46.9±5.4 <sup>c</sup>	15.5±6.5	23.0±7.3 <sup>a</sup>	1.8±0.8 <sup>c</sup>	2.5±0.9	0.71±0.19 <sup>c</sup>	20.4±2.8 <sup>c</sup>	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2 <sup>c</sup>	15.0±6.5	23.8±7.5	1.7±0.9 <sup>b</sup>	2.4±0.9	0.70±0.19 <sup>c</sup>	18.4±2.7 <sup>c</sup>	1.086±0.101	1.086±0.215 <sup>c</sup>	0.783±0.135 <sup>c</sup>	0.863±0.147 <sup>a</sup>
<b>Female</b>												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.103±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.131±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.131±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.008±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	1.0931±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	1.0889±0.177	0.672±0.105	0.732±0.125

*Note.* Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with female of the same age group (unpaired-sample t-tests).

**Table 3** Multiple regression analyses of bone mineral density at different skeletal sites with age, BMI, A/G FMR, and appendicular LM (adjusted smoke and alcohol).

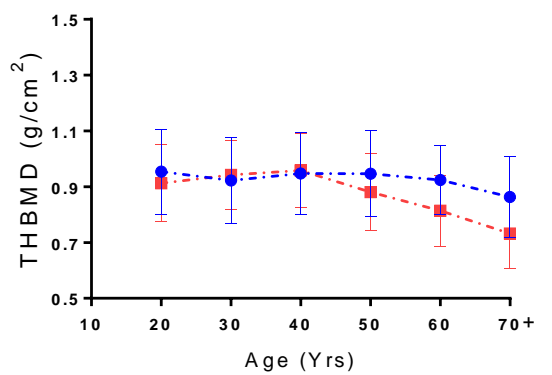
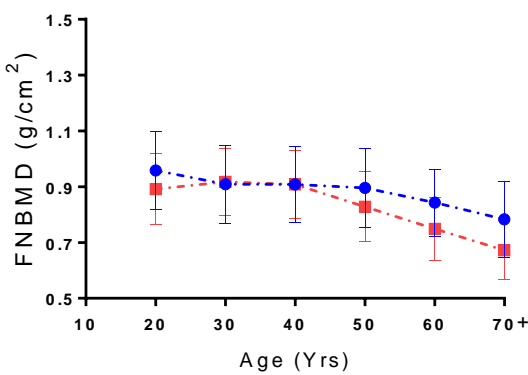
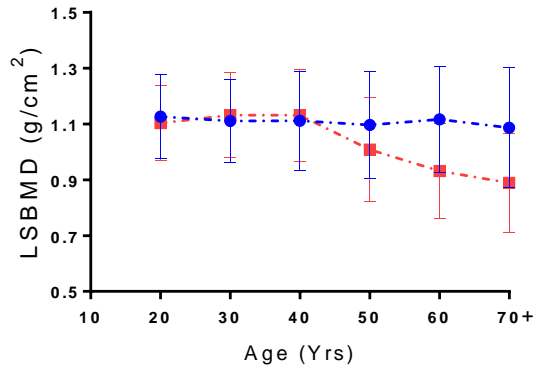
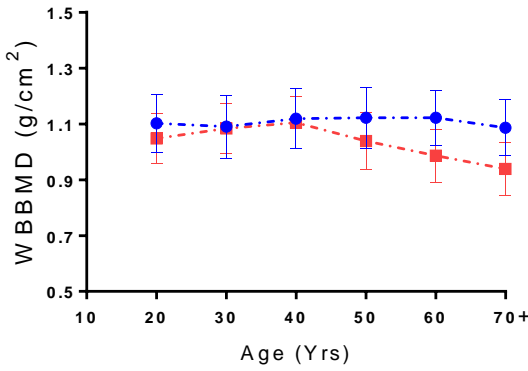
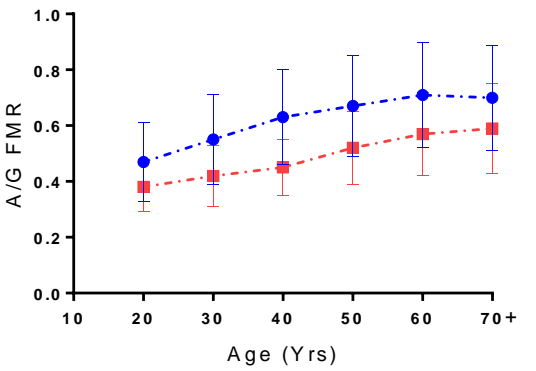
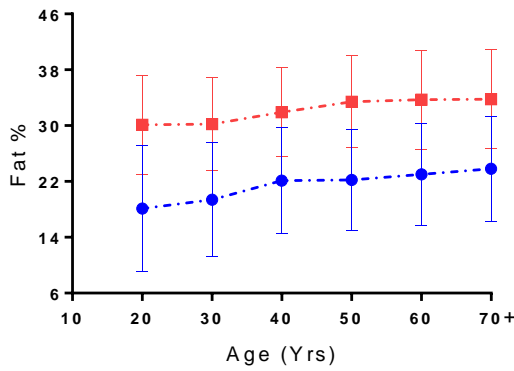
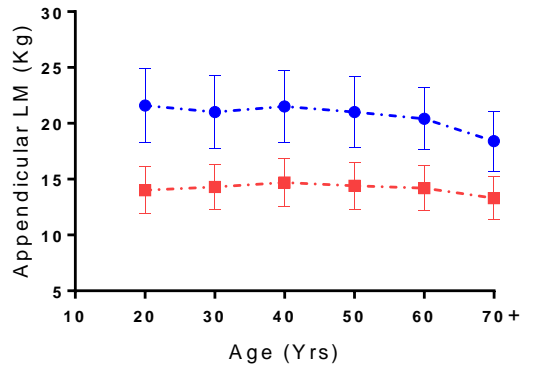
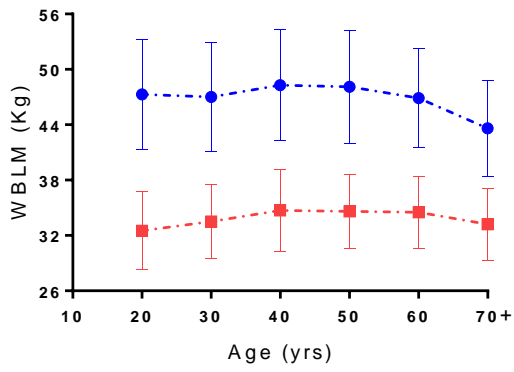
	WBBMD	LSBMD	FNBMD	THBMD
	Standard $\beta$	Standard $\beta$	Standard $\beta$	Standard $\beta$
<b>Male</b>				
<b>&lt;50years</b>	R <sup>2</sup> =0.376	R <sup>2</sup> =0.150	R <sup>2</sup> =0.215	R <sup>2</sup> =0.283
Age	0.034	-0.019	<b>-0.137<sup>c</sup></b>	-0.025
BMI	<b>0.276<sup>c</sup></b>	<b>0.148<sup>a</sup></b>	<b>0.121<sup>a</sup></b>	<b>0.185<sup>c</sup></b>
A/G FMR	0.011	-0.084	-0.048	-0.003
Appendicular LM	<b>0.379<sup>c</sup></b>	<b>0.301<sup>c</sup></b>	<b>0.371<sup>c</sup></b>	<b>0.388<sup>c</sup></b>
<b>≥50years</b>	R <sup>2</sup> =0.290	R <sup>2</sup> =0.190	R <sup>2</sup> =0.269	R <sup>2</sup> =0.263
Age	-0.015	<b>0.087<sup>b</sup></b>	<b>-0.220<sup>c</sup></b>	<b>-0.124<sup>c</sup></b>
BMI	<b>0.260<sup>c</sup></b>	<b>0.268<sup>c</sup></b>	<b>0.190<sup>c</sup></b>	<b>0.261<sup>c</sup></b>
A/G FMR	0.008	0.027	-0.054	-0.035
Appendicular LM	<b>0.321<sup>b</sup></b>	<b>0.207<sup>c</sup></b>	<b>0.264<sup>c</sup></b>	<b>0.256<sup>c</sup></b>
<b>Female</b>				
<b>Premenopausal</b>	R <sup>2</sup> =0.280	R <sup>2</sup> =0.140	R <sup>2</sup> =0.133	R <sup>2</sup> =0.177
Age	<b>0.167<sup>c</sup></b>	-0.001	-0.021	<b>0.062<sup>a</sup></b>
BMI	<b>0.351<sup>c</sup></b>	<b>0.328<sup>c</sup></b>	<b>0.232<sup>c</sup></b>	<b>0.295<sup>c</sup></b>
A/G FMR	<b>-0.236<sup>c</sup></b>	<b>-0.183<sup>c</sup></b>	<b>-0.155<sup>c</sup></b>	<b>-0.153<sup>c</sup></b>
Appendicular LM	<b>0.227<sup>c</sup></b>	<b>0.123<sup>c</sup></b>	<b>0.206<sup>c</sup></b>	<b>0.192<sup>c</sup></b>
<b>Postmenopausal</b>	R <sup>2</sup> =0.348	R <sup>2</sup> =0.209	R <sup>2</sup> =0.344	R <sup>2</sup> =0.332
Age	<b>-0.337<sup>c</sup></b>	<b>-0.222<sup>c</sup></b>	<b>-0.438<sup>c</sup></b>	<b>-0.389<sup>c</sup></b>
BMI	<b>0.315<sup>c</sup></b>	<b>0.274<sup>c</sup></b>	<b>0.185<sup>c</sup></b>	<b>0.266<sup>c</sup></b>
A/G FMR	<b>-0.135<sup>c</sup></b>	<b>-0.086<sup>c</sup></b>	<b>-0.083<sup>c</sup></b>	<b>-0.052<sup>b</sup></b>
Appendicular LM	<b>0.186<sup>c</sup></b>	<b>0.152<sup>c</sup></b>	<b>0.180<sup>c</sup></b>	<b>0.166<sup>c</sup></b>

Note. Results expressed as standard  $\beta$  coefficients. Multiple linear regression analyses including age, BMI, A/G FMR, appendicular lean mass, smoke and alcohol. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

<sup>a</sup> $P < 0.05$ ; <sup>b</sup> $P < 0.01$ ; <sup>c</sup> $P < 0.001$ .

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

● Males  
■ Females



## SUPPLEMENTARY INFORMATION

**Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study**Zeyu Xiao <sup>a, b, c</sup>, Hao Xu <sup>a, c, \*</sup>

<sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University, Guangzhou, PR China

<sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

<sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

\* Corresponding author: Hao Xu.

Table S1. Pearson's correlation between study variables in males &lt;50 years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.741***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.719***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.841***	.696***	.872***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S2. Pearson's correlation between study variables in males  $\geq 50$  years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.770***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.769***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.840***	.702***	.913***

*Note.* Results expressed as  $r$  coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .



Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.775***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.825***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.835***	.720***	.912***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(b) Report category boundaries when continuous variables were categorized	6-7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032268.R1
Article Type:	Original research
Date Submitted by the Author:	23-Sep-2019
Complete List of Authors:	Xiao, Zeyu; The first affiliated hospital of Jinan University, Radiology; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Tan, Zhiqiang; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Shang, Jingjie; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Cheng, Yong; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Tang, Yongjin; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Guo, Bin; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Gong, Jian; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Xu, Hao; The first affiliated hospital of Jinan University, Nuclear medicine; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University
<b>Primary Subject Heading</b>:	Nutrition and metabolism
Secondary Subject Heading:	Public health
Keywords:	body composition, aging, bone mineral density, fat distribution, appendicular lean mass

SCHOLARONE™  
Manuscripts

1  
2  
3  
4 **Sex- and age-specific characteristics of body composition and its**  
5  
6 **effect on bone mineral density in southern Chinese adults: a cross-**  
7  
8 **sectional study**  
9  
10

11  
12  
13 Zeyu Xiao <sup>a, b, c</sup>, Zhiqiang Tan <sup>a, c</sup>, Jingjie Shang <sup>a, c</sup>, Yong Cheng <sup>a, c</sup>, Yongjin Tang <sup>a, c</sup>,  
14  
15 Bin Guo <sup>a, c</sup>, Jian Gong <sup>a, c</sup>, Hao Xu <sup>a, c, \*</sup>  
16  
17

18  
19  
20  
21 <sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University,  
22  
23 Guangzhou, PR China  
24

25  
26 <sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University,  
27  
28 Guangzhou, Guangdong, China  
29

30  
31 <sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University,  
32  
33 Guangzhou, Guangdong, China  
34  
35  
36  
37

38 **Corresponding Author:**

39  
40 Hao Xu, e-mail: [txh@jnu.edu.cn](mailto:txh@jnu.edu.cn);

41  
42 Address: No.613, Huangpu Road West, Tianhe District, Guangzhou, Guangdong  
43  
44 Province, China, 510630.

45  
46 Tel: +86-2038688405.

47  
48 Fax: +86-2038688888.  
49  
50

51  
52 **Keywords:** body composition; aging; bone mineral density; fat distribution;  
53  
54 appendicular lean mass.  
55

56  
57  
58 **Word count:** 5048  
59  
60

## Abstract

**Objectives:** This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD).

**Design:** Cross-sectional study.

**Setting and Participants** A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

**Primary outcome measures:** Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between body composition, adipose distribution, and BMD of each skeletal site.

**Results:** Whole-body FM, percentage of whole-body fat mass, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, body mass index, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard  $\beta$  ranged from 0.207 to 0.405,  $P < 0.001$ ), although not the largest but still a positive predictor of BMD in females (standard  $\beta$  ranged from 0.074 to 0.186,  $P < 0.05$ ). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard  $\beta$  ranged from -0.249 to -0.052,  $P < 0.01$ ) but not in males.

**Conclusions:** In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

## Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.
- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

## Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean mass (LM), fat mass (FM) and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different



1  
2  
3  
4 methods or indexes, the findings regarding the relationship of central adipose with BMD are more  
5 controversial. Several studies indicate that central adipose accumulation is negatively related to  
6 BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD  
7 in postmenopausal women [14]. These heterogeneous findings may result from the rather complex  
8 mechanisms underlying the relationship between fat and bone, including mechanical loading as well  
9 as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism  
10 to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the  
11 relationship between BMD with ALM and central FM have not been well studied.

12  
13  
14  
15  
16  
17  
18  
19 To our knowledge, only a few other studies have documented the relationships of ALM and  
20 android/gynoid fat mass ratio (A/G FMR) with BMD at multiple sites in different ages, menopausal  
21 status, and in both genders. In the current study, we aim to investigate the relationship between  
22 BMD and body composition, especially the effect of regional body composition on BMD. We also  
23 want to examine whether these relationships differ by gender, age, and menopausal status in a large  
24 population-based sample of Chinese adults.

## 31 32 33 **Methods**

### 34 35 **Subjects**

36  
37 The present study included healthy Chinese men and women aged 20 to 95 years old. The  
38 participants were recruited from the body composition and osteoporosis study at the First Affiliated  
39 Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study  
40 were Chinese individuals who appeared to be in good health and functionally independent. Subjects  
41 were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication  
42 known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen  
43 drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism,  
44 hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants  
45 (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or  
46 non-natural menopause (natural menopause was designated if there was a complete natural cessation  
47 of menses for more than twelve months). And the current smoking and drinking situation has also  
48 been recorded. In the end, 1703 men and 4046 women were included in our study. All subjects  
49 provided written informed consent to participate in the study, which was approved by the Ethics  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Committee of the First Affiliated Hospital of Jinan University.

### **Anthropometry, BMD and body composition measurement**

A research physician obtained information on medical history, medication use, smoking, and alcohol history in a personal interview. Height and body weight were obtained based on standard methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg. BMI was calculated as body weight divided by height squared ( $\text{kg}/\text{m}^2$ ). Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086; GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android and Gynoid regions were automatically attained using the software provided by the manufacturer. Android region is defined as the portion of the abdomen included between the line joining the two superior iliac crests, extending cranially up to 20% of the distance between this line and the chin. Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter, directed caudally up to twice the height of the android region. The appendicular region is defined as the areas including both the left and right arms and legs. Daily quality assurance scans were performed by scanning the spine phantom according to the manufacturer's instructions; the same trained technologist conducted all DXA measurements throughout the study. The coefficient of variation was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD, and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was determined by duplicate scans with repositioning between each measurement in 30 volunteer subjects.

### **Statistical analyses**

Subjects were categorized into four groups according to gender, age, and menopausal status (786 men < 50 years, 917 men  $\geq$  50 years, 1534 premenopausal women, and 2512 postmenopausal women). The values of continuous variables were presented as the mean  $\pm$  standard deviation (SD). Unpaired-sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's correlation coefficients (*r*) were conducted to determine the linear relationships among various parameters. We performed linear regressions to assess the association strength between ALM, A/G FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used as dependent variables, and ALM and A/G FMR were treated as independent variables; age, BMI,

1  
2  
3  
4 and lifestyle factors (smoking and alcohol history) were also included. When we performed linear  
5 regression analyses, we chose the enter methods and expressed the results as standard  $\beta$  coefficients. All  
6 tests were two-sided, and  $P < 0.05$  was considered statistically significant. All statistical analyses  
7 were performed using the statistical package for social sciences (Version 19.0) (SPSS Inc., Chicago,  
8 IL, USA).  
9  
10  
11  
12

### 13 **Patient and Public Involvement**

14  
15 There was no patient or public involvement in this study.  
16  
17

## 18 **Results**

### 19 **Basal characteristics of subjects**

20  
21 Table 1 details the subject characteristics in each group. Males  $\geq 50$  years had higher BMI, whole-  
22 body FM, percentage of whole-body fat mass (fat%), trunk FM, and appendicular FM, but lower  
23 weight and lumbar spine BMD than males  $< 50$  years ( $P < 0.001$ ). Postmenopausal females had  
24 higher values for whole-body FM, whole-body LM, trunk FM, appendicular FM, and A/G FMR,  
25 and lower BMD at each site than premenopausal females ( $P < 0.05$ ).  
26  
27  
28  
29  
30  
31  
32

### 33 **Changes of BMD and body composition with age**

34  
35 To further explore the distribution characteristics of body composition and BMD regarding age, we  
36 divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table  
37 2 and Figure 1, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in  
38 both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip  
39 BMD were observed in the second decade and then decreased slightly with age in males. BMD at  
40 each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in  
41 females, and then decreased dramatically after menopause. Interestingly, appendicular LM started  
42 to decline after 50 years old in both males and females.  
43  
44  
45  
46  
47  
48  
49

### 50 **Associations of BMD with whole and regional body composition in different groups**

51  
52 In Pearson's correlation analyses, significant positive correlations were found between BMD at all  
53 sites with height, weight, BMI, whole-body LM, whole-body FM, fat%, Android FM, Gynoid FM,  
54 and ALM in all groups ( $r = 0.218-0.616$ ,  $P < 0.05$ ). A/G FMR showed positive correlations with  
55 whole-body, lumbar spine, femoral neck, and total hip BMDs in men  $< 50$  years and  $\geq 50$  years old  
56 ( $r = 0.089-0.318$ ,  $P < 0.001$ ). However, A/G FMR was negatively correlated with whole-body and  
57  
58  
59  
60

1  
2  
3  
4 femoral neck BMDs in postmenopausal females, though the correlation strengths were weak ( $r=-$   
5 0.075,  $P<0.001$  and  $r=-0.091$ ,  $P<0.001$ , respectively). A/G FMR was insignificantly correlated with  
6 BMD in premenopausal females (Shown in supplemental table 1-4).  
7  
8

9 To further explore the independent predictive value of A/G FMR and ALM for BMD at all  
10 sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that  
11 associated with BMD were also included in the multiple linear regression analyses (shown in Table  
12 3 and 4). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD.  
13 Considering the dynamic change of BMD between period of bone modeling (20-29 years) and that  
14 of bone remodeling (30-50 years), and the subjects aged 20-29 years were excluded in the regression  
15 analyses. The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal  
16 site and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck,  
17 and total hip BMDs in both premenopausal and postmenopausal women (standard  $\beta=-0.249\sim-0.052$ ),  
18 while men had no significant relationship between A/G FMR and each part of BMD after adjustment.  
19 ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs  
20 in both males and females, and the correlations were higher in males (standard  $\beta=0.207\sim0.405$ ) than  
21 that in females (standard  $\beta=0.074\sim0.186$ ), in both younger adults and older adults after adjustment.  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36

### 37 Discussion

38 The global epidemic of obesity has become a significant concern in our daily life as it not only has  
39 a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health  
40 [15]. As a part of body composition, bone density was mainly determined by body weight and BMI.  
41 Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females  
42 [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 90 years old  
43 to further explore the factors that may influence bone health. We divided the participants into  
44 different age groups to investigate the changes in body composition and BMD with age in males  
45 and females. We also performed multivariable regression analyses to confirm that whether A/G  
46 FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and  
47 alcohol consumption. The current report provided more detailed and impressive results which were  
48 different from previous studies performed in America [13] and Australia [1]. We found that ALM  
49 positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 as an indicator of central adipose accumulation was inversely associated with BMD in females but  
5 not in males. These results, based on a large population of Chinese adults, were convincing.  
6

7  
8 In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and  
9 then decreased gradually in both genders, whereas whole-body FM steadily increased from youth  
10 to older age in both genders. After analyzing the baseline characteristics, we found that the  
11 decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the  
12 increased whole-body FM in older men and women mainly arose from the increase of Trunk FM.  
13 In the meantime, we found that the A/G FMR increased with age in both males and females. Men  
14 had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD  
15 at all sites decreased slightly in older men, but more obviously in postmenopausal women. These  
16 results provided us a healthy bone mass for each age group in both men and women. The BMD at  
17 each region lower than the guidance ranges in the respective age group should alarm the physician  
18 for appropriate intervention.  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28

29 In our study, the results showed that both total LM and total FM are positively associated with  
30 BMD in both genders. The effect size of total LM and total FM to BMD was different according to  
31 gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in  
32 men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in  
33 postmenopausal women. Several potential theories may explain the observed findings. The  
34 influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces  
35 a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted  
36 for a large proportion of body weight in both males and females, would perform a gravitational  
37 loading on the bone. On the other hand, the contraction strength of lean muscle should also be  
38 considered a specific mechanism of action. A previous study reported that the augmentation and  
39 thickening of bone trabecula was an adaptation to increased mechanical stress. However, whole-body  
40 FM only accounted for a small proportion of body weight in both males and females, but it still  
41 performed a significant and positive correlation with BMD, especially in postmenopausal women,  
42 in whom a higher standard  $\beta$  value with BMD in all the skeletal sites was shown compared with whole-body LM.  
43 Several mechanisms could explain the association between fat tissue and BMD. The outcomes of  
44 fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight  
45 bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 mechanism may help to interpret this finding, as the postmenopausal women also had the highest  
5 whole-body FM, more than males and premenopausal women in our study. Several hormones,  
6 including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from  
7 adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the  
8 enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated  
9 estrogen level. These bone protective hormones led to a positive influence on bone formation via  
10 stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption.  
11 This finding further confirmed the results from previous studies that FM should have a positive  
12 relationship with bone mass [8, 17].  
13  
14  
15  
16  
17  
18  
19  
20

21        Though both whole-body LM and FM were found to be positively associated with BMD in  
22 both genders, how regional body compositions and differences in fat distribution influence bone  
23 metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with  
24 various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which  
25 may have close relationships with BMD, were considered in multiple linear regression analyses. In  
26 the current study, we found that ALM was positively related to BMD at all sites after adjustment  
27 for BMI and age in both genders. ALM is considered one of the most important indexes of the  
28 diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low  
29 ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and  
30 osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7]  
31 also found that ALM was most strongly associated with femoral neck BMD independent of  
32 nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may  
33 explain the observed association between ALM and BMD. The amount of ALM was smaller than  
34 trunk LM in this study, suggesting ALM may effect on bone via contraction strength instead of  
35 gravitational loading, especially in males younger than 50 years old, in whom the strongest  
36 relationships with BMD in all sites were demonstrated, compared with other groups. Systemic  
37 factors that simultaneously involve both ALM and bone metabolism may exist as the decline of  
38 ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can  
39 strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which  
40 leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to  
41 explore the potential mechanism further.  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 Depot-specific fat has been known to play a different role in terms of obesity and metabolism.  
5  
6 A previous study indicated that different fat depots might have distinct relationships with bone mass  
7  
8 [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD  
9  
10 in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative  
11  
12 [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with  
13  
14 BMD and regarded as an independent and protective factor on the presence of osteoporosis or  
15  
16 osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with  
17  
18 increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution  
19  
20 difference seems to produce a meaningful but contradicted effect on bone mass based on previous  
21  
22 studies. To further confirm this finding, we performed Pearson's correlation to assess the  
23  
24 relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The  
25  
26 results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males  
27  
28 and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies  
29  
30 reported abdominal fat and android fat measured by CT or DXA had a negative association with  
31  
32 BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for  
33  
34 bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males  
35  
36 and females. The results revealed that A/G FMR was positively correlated with each part of BMD  
37  
38 in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse  
39  
40 association with whole-body ( $r=-0.075$ ,  $P<0.001$ ) and femoral neck BMD ( $r=-0.091$ ,  $P<0.001$ ), and  
41  
42 had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported  
43  
44 that A/G FMR was inversely associated with the trabecular bone score after age adjustment ( $r=-$   
45  
46  $0.288$ ,  $P<0.05$ ), which was similar with our findings. Android fat mainly represents visceral fat in  
47  
48 the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher  
49  
50 A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a  
51  
52 higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to  
53  
54 be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat  
55  
56 storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association  
57  
58 among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu  
59  
60 et al. reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association  
with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and

1  
2  
3  
4 visceral fat had opposite effects on femoral bone structure and strength in healthy young females,  
5 and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a  
6 negative association with bone. These heterogeneous findings may be related to the use of diverse  
7 methods for measuring body composition and BMD, disparities in study design, or the different  
8 criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex  
9 mechanisms underlying the relationship between fat and bone. As a result, we subdivided the  
10 Chinese people into different age and gender groups and found that android fat increased with age,  
11 especially in females, whose android fat accounted for a more substantial proportion of body weight  
12 and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included  
13 A/G FMR instead of the total and regional body composition into the same multiple regression  
14 analysis when we explored the associations of regional fat depots with BMD, which provided a  
15 more reliable result.  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28

## 29 **Limitations**

30  
31 This study had several limitations. First, we did not obtain a blood sample from participants;  
32 thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on  
33 bone mass mainly referenced in previous reports based on our data and the statistical results. Second,  
34 we only collected cross-sectional data and cannot directly conclude the causality limited by its study  
35 design. Third, though we evaluated the relationships of body composition and fat distribution with  
36 BMD by adjusting age, BMI, smoking, and alcohol consumption, other confounders such as  
37 socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and  
38 metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a  
39 more substantial amount of visceral fat mass was found in Asians compared with the European  
40 people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when  
41 interpreting the findings.  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53

## 54 **Conclusions**

55  
56 In summary, in this large cohort of Chinese adults, ALM had a strong positive association with  
57 BMD in both genders and suggesting that low ALM is related to low BMD and may be considered  
58 an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was  
59  
60



1  
2  
3  
4 inversely associated with BMD in females but not in males.  
5  
6  
7  
8

### 9 **Contributors**

10  
11 Xiao, Tan, Shang, Cheng and Tang participated in collection, analysis, interpretation of data; and  
12  
13 Xiao, Guo and Gong wrote the paper. Xu, Principal Investigator, innovator for the project,  
14  
15 participated in the conception, design, and revision of the manuscript.  
16

### 17 **Conflict of interest**

18  
19 The authors have no conflicts of interest.  
20

### 21 **Funding**

22  
23 This work was supported by the National Natural Science Foundation of China (Grant No.  
24  
25 81871383), and the Medical Scientific Research Foundation of Guangdong Province, China  
26  
27 (Grant No. A2018132).  
28

### 29 **Ethics approval**

30  
31 The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.  
32

### 33 **Data sharing statement**

34  
35 The deidentified participant data will be available upon reasonable request from Prof. Xu  
36  
37 (txh@jnu.edu.cn).  
38

### 39 **Acknowledgements**

40  
41 The authors would like to express their gratitude to all participating subjects.  
42

### 43 **Abbreviations**

44  
45 BMD: bone mineral density; LM; lean mass; FM: fat mass; ALM: appendicular lean mass; DXA:  
46  
47 dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.  
48

### 49 **Figure legend**

50  
51 Fig.1 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM),  
52  
53 percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and  
54  
55 females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density;  
56  
57 LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density;  
58  
59 THBMD, total hip bone mineral density.  
60

## References

1. Zhu K, Hunter M, James A, et al. Associations between body mass index, lean and fat body mass and bone mineral density in middle-aged Australians: The Busselton Healthy Ageing Study. *Bone*. 2015; 74:146-52.
2. Chen SC, Chung WS, Wu PY, et al. Associations among Geriatric Nutrition Risk Index, bone mineral density, body composition and handgrip strength in patients receiving hemodialysis. *Nutrition*. 2019; 65:6-12.
3. Stroup BM, Hansen KE, Krueger D, et al. Sex differences in body composition and bone mineral density in phenylketonuria: A cross-sectional study. *Mol Genet Metab Rep*. 2018; 15:30-5.
4. Heiss CJ, Sanborn CF, Nichols DL, et al. Associations of body fat distribution, circulating sex hormones, and bone density in postmenopausal women. *J Clin Endocrinol Metab*. 1995; 80:1591-6.
5. Guo B, Wu Q, Gong J, et al. Gender Difference in Body Fat for Healthy Chinese Children and Adolescents. *Child Obes*. 2016; 12:144-54.
6. Guo B, Wu Q, Gong J, et al. Relationships between the lean mass index and bone mass and reference values of muscular status in healthy Chinese children and adolescents. *J Bone Miner Metab*. 2016; 34:703-13.
7. Blain H, Jaussent A, Thomas E, et al. Appendicular skeletal muscle mass is the strongest independent factor associated with femoral neck bone mineral density in adult and older men. *Exp Gerontol*. 2010; 45:679-84.
8. Bogl LH, Latvala A, Kaprio J, et al. An investigation into the relationship between soft tissue body composition and bone mineral density in a young adult twin sample. *J Bone Miner Res*. 2011; 26:79-87.
9. Cui LH, Shin MH, Kweon SS, et al. Relative contribution of body composition to bone mineral density at different sites in men and women of South Korea. *J Bone Miner Metab*. 2007; 25:165-71.
10. Walsh CJ, Phan CM, Misra M, et al. Women with anorexia nervosa: finite element and trabecular structure analysis by using flat-panel volume CT. *Radiology*. 2010; 257:167-74.
11. Kang SM, Yoon JW, Ahn HY, et al. Android fat depot is more closely associated with

- 1  
2  
3  
4 metabolic syndrome than abdominal visceral fat in elderly people. PLoS One. 2011; 6:e27694.
- 5  
6 12. Choi HS, Kim KJ, Kim KM, et al. Relationship between visceral adiposity and bone  
7  
8 mineral density in Korean adults. Calcif Tissue Int. 2010; 87:218-25.
- 9  
10 13. Katzmarzyk PT, Barreira TV, Harrington DM, et al. Relationship between abdominal fat  
11  
12 and bone mineral density in white and African American adults. Bone. 2012; 50:576-9.
- 13  
14 14. Warming L, Ravn P, Christiansen C. Visceral fat is more important than peripheral fat for  
15  
16 endometrial thickness and bone mass in healthy postmenopausal women. Am J Obstet Gynecol.  
17  
18 2003; 188:349-53.
- 19  
20 15. Shapses SA, Pop LC, Wang Y. Obesity is a concern for bone health with aging. Nutr Res.  
21  
22 2017; 39:1-13.
- 23  
24 16. De Laet C, Kanis JA, Oden A, et al. Body mass index as a predictor of fracture risk: a  
25  
26 meta-analysis. Osteoporos Int. 2005; 16:1330-8.
- 27  
28 17. Zhu K, Briffa K, Smith A, et al. Gender differences in the relationships between lean body  
29  
30 mass, fat mass and peak bone mass in young adults. Osteoporos Int. 2014; 25:1563-70.
- 31  
32 18. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the  
33  
34 elderly in New Mexico. Am J Epidemiol. 1998; 147:755-63.
- 35  
36 19. Melton LJ, 3rd, Khosla S, Crowson CS, et al. Epidemiology of sarcopenia. J Am Geriatr  
37  
38 Soc. 2000; 48:625-30.
- 39  
40 20. Verschueren S, Gielen E, O'Neill TW, et al. Sarcopenia and its relationship with bone  
41  
42 mineral density in middle-aged and elderly European men. Osteoporos Int. 2013; 24:87-98.
- 43  
44 21. Seeman E. Clinical review 137: Sexual dimorphism in skeletal size, density, and strength.  
45  
46 J Clin Endocrinol Metab. 2001; 86:4576-84.
- 47  
48 22. Kim JH, Choi HJ, Ku EJ, et al. Regional body fat depots differently affect bone  
49  
50 microarchitecture in postmenopausal Korean women. Osteoporos Int. 2016; 27:1161-8.
- 51  
52 23. Marques EA, Moreira P, Wanderley F, et al. Appendicular fat mass is positively associated  
53  
54 with femoral neck bone mineral density in older women. Menopause. 2012; 19:311-8.
- 55  
56 24. Kuwahata A, Kawamura Y, Yonehara Y, et al. Non-weight-bearing effect of trunk and  
57  
58 peripheral fat mass on bone mineral density in pre- and post-menopausal women. Maturitas.  
59  
60 2008; 60:244-7.
25. Yoo HJ, Park MS, Yang SJ, et al. The differential relationship between fat mass and bone

- 1  
2  
3  
4 mineral density by gender and menopausal status. *J Bone Miner Metab.* 2012; 30:47-53.
- 5  
6 26. Freitas P, Garcia Rosa ML, Gomes AM, et al. Central and peripheral fat body mass have  
7 a protective effect on osteopenia or osteoporosis in adults and elderly? *Osteoporos Int.* 2016;  
8 27:1659-63.
- 9  
10  
11 27. Sharma A, Flom PL, Rosen CJ, et al. Racial differences in bone loss and relation to  
12 menopause among HIV-infected and uninfected women. *Bone.* 2015; 77:24-30.
- 13  
14 28. Tchernof A, Desmeules A, Richard C, et al. Ovarian hormone status and abdominal  
15 visceral adipose tissue metabolism. *J Clin Endocrinol Metab.* 2004; 89:3425-30.
- 16  
17 29. Kim CJ, Oh KW, Rhee EJ, et al. Relationship between body composition and bone mineral  
18 density (BMD) in perimenopausal Korean women. *Clin Endocrinol (Oxf).* 2009; 71:18-26.
- 19  
20 30. Gilsanz V, Chalfant J, Mo AO, et al. Reciprocal relations of subcutaneous and visceral fat  
21 to bone structure and strength. *J Clin Endocrinol Metab.* 2009; 94:3387-93.
- 22  
23 31. Lesser IA, Gasevic D, Lear SA. The effect of body fat distribution on ethnic differences  
24 in cardiometabolic risk factors of Chinese and Europeans. *Appl Physiol Nutr Metab.* 2013;  
25 38:701-6.
- 26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Table 1** Baseline characteristics of subjects

	Male		Female	
	Age < 50 years	Age ≥ 50 years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0 <sup>c</sup>	37.4±8.7	63.9±9.1 <sup>c</sup>
Weight (kg)	63.9±12.4	63.8±10.8 <sup>c</sup>	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	22.4±3.9	22.9±3.3 <sup>c</sup>	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5 <sup>c</sup>	16.7±6.0	18.9±6.2 <sup>b</sup>
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0 <sup>a</sup>
Fat%	20.2±8.3	23.0±7.3 <sup>c</sup>	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4 <sup>c</sup>	8.7±3.6	10.6±3.7 <sup>b</sup>
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1 <sup>c</sup>	7.3±2.5	7.5±2.6 <sup>c</sup>
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15 <sup>c</sup>
Bone mineral density (g/cm <sup>2</sup> )				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106 <sup>c</sup>
Lumbar spine	1.114±0.162	1.099±0.200 <sup>c</sup>	1.124±0.155	0.950±0.186 <sup>c</sup>
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132 <sup>b</sup>
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144 <sup>b</sup>
Current Smoker (%)	17.9%	13.0%	2.4%	2.8%
Current alcohol user (%)	15.4%	12.8%	2.3%	1.5%

*Note.* Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with the same gender of the different age group (unpaired-sample *t*-tests or chi-squared test).

**Table 2** Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm <sup>2</sup> )	LSBMD (g/cm <sup>2</sup> )	FNBMD (g/cm <sup>2</sup> )	THBMD (g/cm <sup>2</sup> )
<b>Male</b>												
20-29	199	47.3±6.0 <sup>c</sup>	12.1±8.2 <sup>c</sup>	18.1±9.0 <sup>c</sup>	1.2±0.9 <sup>c</sup>	2.4±1.3 <sup>c</sup>	0.47±0.14 <sup>c</sup>	21.6±3.3 <sup>c</sup>	1.102±0.103	1.116±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9 <sup>c</sup>	12.8±7.3 <sup>c</sup>	19.4±8.2 <sup>c</sup>	1.4±0.9 <sup>c</sup>	2.4±1.3 <sup>a</sup>	0.55±0.16 <sup>c</sup>	21.0±3.3 <sup>c</sup>	1.090±0.113 <sup>c</sup>	1.110±0.149	0.909±0.140 <sup>b</sup>	0.922±0.154 <sup>c</sup>
40-49	333	48.3±6.0 <sup>c</sup>	15.4±7.2 <sup>c</sup>	22.1±7.6 <sup>c</sup>	1.7±0.9 <sup>c</sup>	2.6±1.0	0.63±0.17 <sup>c</sup>	21.5±3.2 <sup>c</sup>	1.119±0.108 <sup>b</sup>	1.111±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1 <sup>c</sup>	15.2±6.5	22.2±7.2 <sup>a</sup>	1.7±0.8 <sup>c</sup>	2.5±0.9	0.67±0.18 <sup>c</sup>	21.0±3.2 <sup>c</sup>	1.122±0.110	1.016±0.192	0.895±0.140	0.946±0.154 <sup>a</sup>
60-69	281	46.9±5.4 <sup>c</sup>	15.5±6.5	23.0±7.3 <sup>a</sup>	1.8±0.8 <sup>c</sup>	2.5±0.9	0.71±0.19 <sup>c</sup>	20.4±2.8 <sup>c</sup>	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2 <sup>c</sup>	15.0±6.5	23.8±7.5	1.7±0.9 <sup>b</sup>	2.4±0.9	0.70±0.19 <sup>c</sup>	18.4±2.7 <sup>c</sup>	1.086±0.101	1.010±0.215 <sup>c</sup>	0.783±0.135 <sup>c</sup>	0.863±0.147 <sup>a</sup>
<b>Female</b>												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.113±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.112±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.111±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.008±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	0.911±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	0.889±0.177	0.672±0.105	0.732±0.125

*Note.* Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with female of the same age group (unpaired-sample t-tests).

**Table 3** Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in males.

Males	WBBMD			LSBMD			FNBMD			THBMD		
	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.
<b>&lt;50 y</b>												
Age	<b>0.066</b>	1.991	0.047	-0.018	-0.459	0.647	-0.044	-1.161	0.247	0.029	0.821	0.412
Smoke	-0.057	-1.783	0.075	-0.043	-1.116	0.265	-0.047	-1.267	0.207	-0.050	-1.473	0.141
Alcohol	<b>0.063</b>	1.988	0.047	0.041	1.081	0.280	0.011	0.303	0.763	0.009	0.279	0.780
BMI	<b>0.266</b>	4.998	0.000	<b>0.170</b>	2.668	0.008	<b>0.139</b>	2.269	0.024	<b>0.222</b>	3.920	0.000
A/G FMR	0.044	1.028	0.304	-0.063	-1.223	0.222	-0.040	-0.811	0.417	0.014	0.315	0.753
Appendicular LM	<b>0.402</b>	9.240	0.000	<b>0.309</b>	5.923	0.000	<b>0.395</b>	7.872	0.000	<b>0.405</b>	8.757	0.000
<b><math>\geq 50</math> y</b>												
Age	-0.015	-0.486	0.627	<b>0.087</b>	2.673	0.008	<b>-0.220</b>	-7.086	0.000	<b>-0.124</b>	-3.989	0.000
Smoke	-0.023	-0.786	0.432	-0.027	-0.865	0.387	0.005	0.165	0.869	-0.006	-0.215	0.830
Alcohol	0.023	0.794	0.427	0.059	1.920	0.055	0.022	0.747	0.452	0.020	0.697	0.486
BMI	<b>0.260</b>	5.915	0.000	<b>0.268</b>	5.704	0.000	<b>0.190</b>	4.257	0.000	<b>0.261</b>	5.817	0.000
A/G FMR	0.008	0.241	0.809	0.027	0.759	0.448	-0.054	-1.585	0.111	-0.035	-1.032	0.302
Appendicular LM	<b>0.321</b>	7.814	0.000	<b>0.207</b>	4.719	0.000	<b>0.264</b>	6.328	0.000	<b>0.256</b>	6.127	0.000

Note. Results expressed as standard  $\beta$  coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

**Table 4** Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in females.

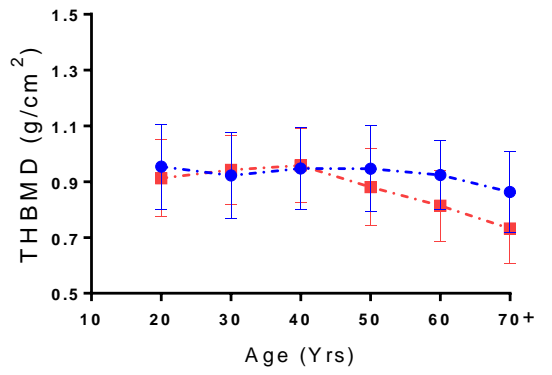
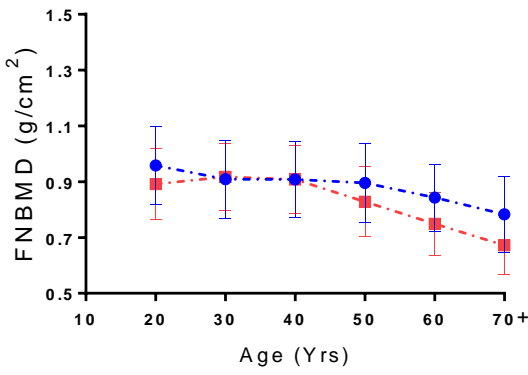
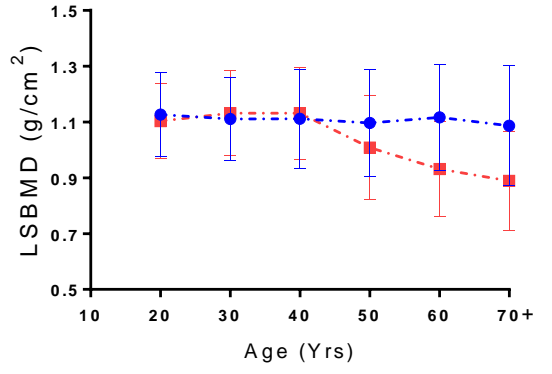
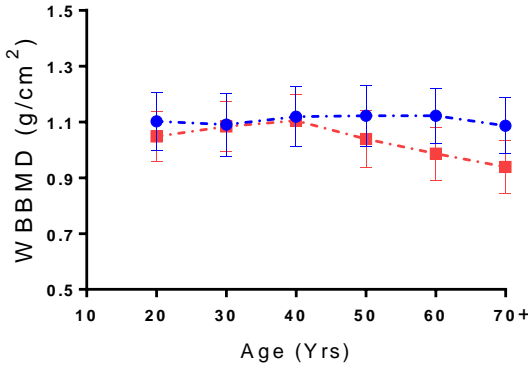
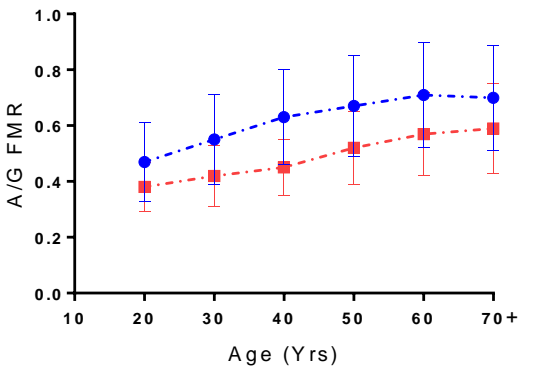
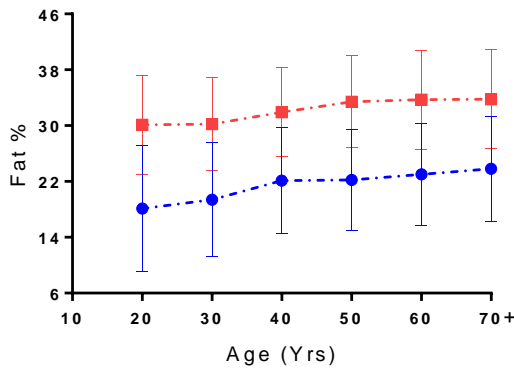
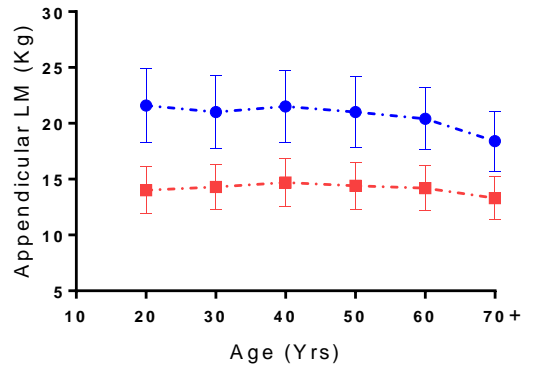
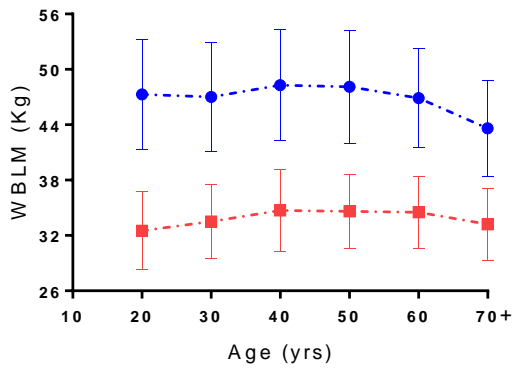
Females	WBBMD			LSBMD			FNBMD			THBMD		
	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.
<b>Premenopausal</b>												
Age	0.039	1.483	0.138	<b>-0.074</b>	-2.665	0.008	<b>-0.098</b>	-3.483	0.000	-0.008	-0.278	0.781
Smoke	0.024	0.958	0.338	0.022	0.794	0.427	0.033	1.196	0.233	0.030	1.133	0.258
Alcohol	-0.005	-0.197	0.844	0.008	0.289	0.773	0.013	0.467	0.644	0.012	0.451	0.652
BMI	<b>0.413</b>	11.055	0.000	<b>0.384</b>	9.659	0.000	<b>0.277</b>	6.901	0.000	<b>0.360</b>	9.177	0.000
A/G FMR	<b>-0.249</b>	-8.421	0.000	<b>-0.193</b>	-6.152	0.000	<b>-0.155</b>	-4.872	0.000	<b>-0.157</b>	-5.083	0.000
Appendicular LM	<b>0.179</b>	5.360	0.000	<b>0.074</b>	2.099	0.036	<b>0.159</b>	4.451	0.000	<b>0.138</b>	3.940	0.000
<b>Postmenopausal</b>												
Age	<b>-0.337</b>	-19.556	0.000	<b>-0.222</b>	-11.701	0.000	<b>-0.438</b>	-25.343	0.000	<b>-0.389</b>	-22.318	0.000
Smoke	-0.024	-1.482	0.139	0.007	.383	0.702	-0.019	-1.146	0.253	-0.024	-1.461	0.144
Alcohol	-0.015	-0.898	0.369	-0.029	-1.649	0.099	-0.008	-0.504	0.613	-0.020	-1.213	0.225
BMI	<b>0.315</b>	14.922	0.000	<b>0.274</b>	11.767	0.000	<b>0.185</b>	8.718	0.000	<b>0.266</b>	12.451	0.000
A/G FMR	<b>-0.135</b>	-7.585	0.000	<b>-0.086</b>	-4.402	0.000	<b>-0.083</b>	-4.644	0.000	<b>-0.052</b>	-2.867	0.004
Appendicular LM	<b>0.186</b>	9.076	0.000	<b>0.152</b>	6.744	0.000	<b>0.180</b>	8.787	0.000	<b>0.166</b>	7.998	0.000

*Note.* Results expressed as standard  $\beta$  coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

● Males  
■ Females



## SUPPLEMENTARY INFORMATION

**Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study**Zeyu Xiao <sup>a, b, c</sup>, Hao Xu <sup>a, c, \*</sup>

<sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University, Guangzhou, PR China

<sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

<sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

\* Corresponding author: Hao Xu.

Table S1. Pearson's correlation between study variables in males &lt;50 years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.741***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.719***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.841***	.696***	.872***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S2. Pearson's correlation between study variables in males  $\geq 50$  years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.770***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.769***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.840***	.702***	.913***

*Note.* Results expressed as  $r$  coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.775***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.825***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.835***	.720***	.912***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(b) Report category boundaries when continuous variables were categorized	6-7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).



# BMJ Open

## Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032268.R2
Article Type:	Original research
Date Submitted by the Author:	05-Nov-2019
Complete List of Authors:	Xiao, Zeyu; The first affiliated hospital of Jinan University, Radiology; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Tan, Zhiqiang; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Shang, Jingjie; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Cheng, Yong; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Tang, Yongjin; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Guo, Bin; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Gong, Jian; The first affiliated hospital of Jinan University, Nuclear medicine Guangzhou, CN; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University Xu, Hao; The first affiliated hospital of Jinan University, Nuclear medicine; Molecular Imaging Institute, the First Affiliated Hospital, Jinan University
<b>Primary Subject Heading</b>:	Nutrition and metabolism
Secondary Subject Heading:	Public health
Keywords:	body composition, aging, bone mineral density, fat distribution, appendicular lean mass

SCHOLARONE™  
Manuscripts

1  
2  
3  
4 **Sex- and age-specific characteristics of body composition and its**  
5  
6 **effect on bone mineral density in southern Chinese adults: a cross-**  
7  
8 **sectional study**  
9  
10

11  
12  
13 Zeyu Xiao <sup>a, b, c</sup>, Zhiqiang Tan <sup>a, c</sup>, Jingjie Shang <sup>a, c</sup>, Yong Cheng <sup>a, c</sup>, Yongjin Tang <sup>a, c</sup>,

14  
15  
16 Bin Guo <sup>a, c</sup>, Jian Gong <sup>a, c</sup>, Hao Xu <sup>a, c, \*</sup>  
17  
18

19  
20  
21 <sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University,

22  
23 Guangzhou, PR China  
24

25  
26 <sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University,

27  
28 Guangzhou, Guangdong, China  
29

30  
31 <sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University,

32  
33 Guangzhou, Guangdong, China  
34  
35  
36  
37

38 **Corresponding Author:**

39  
40 Hao Xu, e-mail: [txh@jnu.edu.cn](mailto:txh@jnu.edu.cn);

41  
42 Address: No.613, Huangpu Road West, Tianhe District, Guangzhou, Guangdong

43  
44 Province, China, 510630.

45  
46 Tel: +86-2038688405.

47  
48 Fax: +86-2038688888.  
49  
50

51 **Keywords:** body composition; aging; bone mineral density; fat distribution;

52  
53 appendicular lean mass.  
54  
55

56  
57 **Word count:** 5048  
58  
59  
60

## Abstract

**Objectives:** This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD).

**Design:** Cross-sectional study.

**Setting and Participants** A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

**Primary outcome measures:** Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between body composition, adipose distribution, and BMD of each skeletal site.

**Results:** Whole-body FM, percentage of whole-body fat mass, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, body mass index, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard  $\beta$  ranged from 0.207 to 0.405,  $P < 0.001$ ), although not the largest but still a positive predictor of BMD in females (standard  $\beta$  ranged from 0.074 to 0.186,  $P < 0.05$ ). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard  $\beta$  ranged from -0.249 to -0.052,  $P < 0.01$ ) but not in males.

**Conclusions:** In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

## Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.
- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

## Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean mass (LM), fat mass (FM) and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different

1  
2  
3  
4 methods or indexes, the findings regarding the relationship of central adipose with BMD are more  
5 controversial. Several studies indicate that central adipose accumulation is negatively related to  
6 BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD  
7 in postmenopausal women [14]. These heterogeneous findings may result from the rather complex  
8 mechanisms underlying the relationship between fat and bone, including mechanical loading as well  
9 as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism  
10 to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the  
11 relationship between BMD with ALM and central FM have not been well studied.

12  
13  
14  
15  
16  
17  
18  
19 To our knowledge, only a few other studies have documented the relationships of ALM and  
20 android/gynoid fat mass ratio (A/G FMR) with BMD at multiple sites in different ages, menopausal  
21 status, and in both genders. In the current study, we aim to investigate the relationship between  
22 BMD and body composition, especially the effect of regional body composition on BMD. We also  
23 want to examine whether these relationships differ by gender, age, and menopausal status in a large  
24 population-based sample of Chinese adults.

## 31 32 33 **Methods**

### 34 35 **Subjects**

36  
37 The present study included healthy Chinese men and women aged 20 to 95 years old. The  
38 participants were recruited from the body composition and osteoporosis study at the First Affiliated  
39 Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study  
40 were Chinese individuals who appeared to be in good health and functionally independent. Subjects  
41 were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication  
42 known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen  
43 drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism,  
44 hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants  
45 (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or  
46 non-natural menopause (natural menopause was designated if there was a complete natural cessation  
47 of menses for more than twelve months). The inclusion and exclusion criteria flowchart of study  
48 was shown in Figure 1. And the current smoking and drinking situation has also been recorded. In  
49 the end, 1703 men and 4046 women were included in our study. All subjects provided written  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 informed consent to participate in the study, which was approved by the Ethics Committee of the  
4 First Affiliated Hospital of Jinan University.  
5  
6

### 7 **Anthropometry, BMD and body composition measurement**

8  
9 A research physician obtained information on medical history, medication use, smoking, and  
10 alcohol history in a personal interview. Height and body weight were obtained based on standard  
11 methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing  
12 to the nearest 0.1 kg. BMI was calculated as body weight divided by height squared ( $\text{kg}/\text{m}^2$ ).  
13 Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086;  
14 GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and  
15 total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android  
16 and Gynoid regions were automatically attained using the software provided by the manufacturer.  
17 Android region is defined as the portion of the abdomen included between the line joining the two  
18 superior iliac crests, extending cranially up to 20% of the distance between this line and the chin.  
19 Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter,  
20 directed caudally up to twice the height of the android region. The appendicular region is defined  
21 as the areas including both the left and right arms and legs. Daily quality assurance scans were  
22 performed by scanning the spine phantom according to the manufacturer's instructions; the same  
23 trained technologist conducted all DXA measurements throughout the study. The coefficient of  
24 variation was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD,  
25 and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was  
26 determined by duplicate scans with repositioning between each measurement in 30 volunteer  
27 subjects.  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

### 46 **Statistical analyses**

47  
48 Subjects were categorized into four groups according to gender, age, and menopausal status (786  
49 men < 50 years, 917 men  $\geq$  50 years, 1534 premenopausal women, and 2512 postmenopausal women).  
50 The values of continuous variables were presented as the mean  $\pm$  standard deviation (SD). Unpaired-  
51 sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's  
52 correlation coefficients (*r*) were conducted to determine the linear relationships among various  
53 parameters. We performed linear regressions to assess the association strength between ALM, A/G  
54 FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 as dependent variables, and ALM and A/G FMR were treated as independent variables; age, BMI,  
5 and lifestyle factors (smoking and alcohol history) were also included. When we performed linear  
6 regression analyses, we chose the enter methods and expressed the results as standard  $\beta$  coefficients. All  
7 tests were two-sided, and  $P < 0.05$  was considered statistically significant. All statistical analyses  
8 were performed using the statistical package for social sciences (Version 19.0) (SPSS Inc., Chicago,  
9 IL, USA).

### 15 **Patient and Public Involvement**

16 There was no patient or public involvement in this study.

## 21 **Results**

### 23 **Basal characteristics of subjects**

24 Table 1 details the subject characteristics in each group. Males  $\geq 50$  years had higher BMI, whole-  
25 body FM, percentage of whole-body fat mass (fat%), trunk FM, and appendicular FM, but lower  
26 weight and lumbar spine BMD than males  $< 50$  years ( $P < 0.001$ ). Postmenopausal females had  
27 higher values for whole-body FM, whole-body LM, trunk FM, appendicular FM, and A/G FMR,  
28 and lower BMD at each site than premenopausal females ( $P < 0.05$ ).

### 34 **Changes of BMD and body composition with age**

35 To further explore the distribution characteristics of body composition and BMD regarding age, we  
36 divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table  
37 2 and Figure 2, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in  
38 both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip  
39 BMD were observed in the second decade and then decreased slightly with age in males. BMD at  
40 each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in  
41 females, and then decreased dramatically after menopause. Interestingly, appendicular LM started  
42 to decline after 50 years old in both males and females.

### 52 **Associations of BMD with whole and regional body composition in different groups**

53 In Pearson's correlation analyses, significant positive correlations were found between BMD at all  
54 sites with height, weight, BMI, whole-body LM, whole-body FM, fat%, Android FM, Gynoid FM,  
55 and ALM in all groups ( $r = 0.218-0.616$ ,  $P < 0.05$ ). A/G FMR showed positive correlations with  
56 whole-body, lumbar spine, femoral neck, and total hip BMDs in men  $< 50$  years and  $\geq 50$  years old  
57  
58  
59  
60

( $r=0.089\sim 0.318$ ,  $P < 0.001$ ). However, A/G FMR was negatively correlated with whole-body and femoral neck BMDs in postmenopausal females, though the correlation strengths were weak ( $r=-0.075$ ,  $P < 0.001$  and  $r=-0.091$ ,  $P < 0.001$ , respectively). A/G FMR was insignificantly correlated with BMD in premenopausal females (Shown in supplemental table 1-4).

To further explore the independent predictive value of A/G FMR and ALM for BMD at all sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that associated with BMD were also included in the multiple linear regression analyses (shown in Table 3 and 4). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD. Considering the dynamic change of BMD between period of bone modeling (20-29 years) and that of bone remodeling (30-50 years), and the subjects aged 20-29 years were excluded in the regression analyses. The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal site and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck, and total hip BMDs in both premenopausal (standard  $\beta$  from -0.249 to -0.155,  $P < 0.001$ ) and postmenopausal women (standard  $\beta$  from -0.135 to -0.052,  $P < 0.01$ ), while men had no significant relationship between A/G FMR and each part of BMD after adjustment. ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs in both males and females, and the correlations were higher in males than that in females (standard  $\beta$  from 0.309 to 0.405 of men with  $< 50$ y vs. standard  $\beta$  from 0.074 to 0.179 of premenopausal women,  $P < 0.001$ ; standard  $\beta$  from 0.207 to 0.321 of males with  $\geq 50$ y vs. standard  $\beta$  from 0.152 to 0.186 of postmenopausal women,  $P < 0.001$ ).

## Discussion

The global epidemic of obesity has become a significant concern in our daily life as it not only has a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health [15]. As a part of body composition, bone density was mainly determined by body weight and BMI. Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 95 years old to further explore the factors that may influence bone health. We divided the participants into different age groups to investigate the changes in body composition and BMD with age in males and females. We also performed multivariable regression analyses to confirm that whether A/G



1  
2  
3  
4 FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and  
5 alcohol consumption. The current report provided more detailed and impressive results which were  
6 different from previous studies performed in America [13] and Australia [1]. We found that ALM  
7 positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR  
8 as an indicator of central adipose accumulation was inversely associated with BMD in females but  
9 not in males. These results, based on a large population of Chinese adults, were convincing.

10  
11  
12  
13  
14  
15 In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and  
16 then decreased gradually in both genders, whereas whole-body FM steadily increased from youth  
17 to older age in both genders. After analyzing the baseline characteristics, we found that the  
18 decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the  
19 increased whole-body FM in older men and women mainly arose from the increase of Trunk FM.  
20 In the meantime, we found that the A/G FMR increased with age in both males and females. Men  
21 had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD  
22 at all sites decreased slightly in older men, but more obviously in postmenopausal women. These  
23 results provided us a healthy bone mass for each age group in both men and women. The BMD at  
24 each region lower than the guidance ranges in the respective age group should alarm the physician  
25 for appropriate intervention.

26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37 In our study, the results showed that both total LM and total FM are positively associated with  
38 BMD in both genders. The effect size of total LM and total FM to BMD was different according to  
39 gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in  
40 men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in  
41 postmenopausal women. Several potential theories may explain the observed findings. The  
42 influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces  
43 a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted  
44 for a large proportion of body weight in both males and females, would perform a gravitational  
45 loading on the bone. On the other hand, the contraction strength of lean muscle should also be  
46 considered a specific mechanism of action. A previous study reported that the augmentation and  
47 thickening of bone trabecula was an adaption to increased mechanical stress. However, whole-body  
48 FM only accounted for a small proportion of body weight in both males and females, but it still  
49 performed a significant and positive correlation with BMD, especially in postmenopausal women,  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 in whom a higher standard  $\beta$  value with BMD in all the skeletal sites was shown compared with whole-body LM.  
5  
6 Several mechanisms could explain the association between fat tissue and BMD. The outcomes of  
7  
8 fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight  
9  
10 bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related  
11  
12 mechanism may help to interpret this finding, as the postmenopausal women also had the highest  
13  
14 whole-body FM, more than males and premenopausal women in our study. Several hormones,  
15  
16 including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from  
17  
18 adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the  
19  
20 enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated  
21  
22 estrogen level. These bone protective hormones led to a positive influence on bone formation via  
23  
24 stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption.  
25  
26 This finding further confirmed the results from previous studies that FM should have a positive  
27  
28 relationship with bone mass [8, 17].

29  
30 Though both whole-body LM and FM were found to be positively associated with BMD in  
31  
32 both genders, how regional body compositions and differences in fat distribution influence bone  
33  
34 metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with  
35  
36 various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which  
37  
38 may have close relationships with BMD, were considered in multiple linear regression analyses. In  
39  
40 the current study, we found that ALM was positively related to BMD at all sites after adjustment  
41  
42 for BMI and age in both genders. ALM is considered one of the most important indexes of the  
43  
44 diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low  
45  
46 ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and  
47  
48 osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7]  
49  
50 also found that ALM was most strongly associated with femoral neck BMD independent of  
51  
52 nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may  
53  
54 explain the observed association between ALM and BMD. The amount of ALM was smaller than  
55  
56 trunk LM in this study, suggesting ALM may effect on bone via contraction strength instead of  
57  
58 gravitational loading, especially in males younger than 50 years old, in whom the strongest  
59  
60 relationships with BMD in all sites were demonstrated, compared with other groups. Systemic  
factors that simultaneously involve both ALM and bone metabolism may exist as the decline of

1  
2  
3  
4 ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can  
5 strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which  
6 leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to  
7 explore the potential mechanism further.  
8  
9

10  
11 Depot-specific fat has been known to play a different role in terms of obesity and metabolism.  
12 A previous study indicated that different fat depots might have distinct relationships with bone mass  
13 [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD  
14 [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD  
15 [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD  
16 [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD  
17 in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative  
18 [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with  
19 BMD and regarded as an independent and protective factor on the presence of osteoporosis or  
20 osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with  
21 increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution  
22 difference seems to produce a meaningful but contradicted effect on bone mass based on previous  
23 studies. To further confirm this finding, we performed Pearson's correlation to assess the  
24 relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The  
25 results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males  
26 and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies  
27 reported abdominal fat and android fat measured by CT or DXA had a negative association with  
28 BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for  
29 bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males  
30 and females. The results revealed that A/G FMR was positively correlated with each part of BMD  
31 in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse  
32 association with whole-body ( $r=-0.075$ ,  $P<0.001$ ) and femoral neck BMD ( $r=-0.091$ ,  $P<0.001$ ), and  
33 had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported  
34 that A/G FMR was inversely associated with the trabecular bone score after age adjustment ( $r=-$   
35  $0.288$ ,  $P<0.05$ ), which was similar with our findings. Android fat mainly represents visceral fat in  
36 the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher  
37 A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a  
38 higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to  
39 be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association  
5  
6 among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu  
7  
8 et al. reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association  
9  
10 with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and  
11  
12 visceral fat had opposite effects on femoral bone structure and strength in healthy young females,  
13  
14 and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a  
15  
16 negative association with bone. These heterogeneous findings may be related to the use of diverse  
17  
18 methods for measuring body composition and BMD, disparities in study design, or the different  
19  
20 criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex  
21  
22 mechanisms underlying the relationship between fat and bone. As a result, we subdivided the  
23  
24 Chinese people into different age and gender groups and found that android fat increased with age,  
25  
26 especially in females, whose android fat accounted for a more substantial proportion of body weight  
27  
28 and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included  
29  
30 A/G FMR instead of the total and regional body composition into the same multiple regression  
31  
32 analysis when we explored the associations of regional fat depots with BMD, which provided a  
33  
34 more reliable result.

### 35 36 37 **Limitations**

38  
39 This study had several limitations. First, we did not obtain a blood sample from participants;  
40  
41 thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on  
42  
43 bone mass mainly referenced in previous reports based on our data and the statistical results. Second,  
44  
45 we only collected cross-sectional data and cannot directly conclude the causality limited by its study  
46  
47 design. Third, though we evaluated the relationships of body composition and fat distribution with  
48  
49 BMD by adjusting age, BMI, smoking, and alcohol consumption, other confounders such as  
50  
51 socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and  
52  
53 metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a  
54  
55 more substantial amount of visceral fat mass was found in Asians compared with the European  
56  
57 people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when  
58  
59 interpreting the findings.  
60

## Conclusions

In summary, in this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders and suggesting that low ALM is related to low BMD and may be considered an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

## Contributors

Xiao, Tan, Shang, Cheng and Tang participated in collection, analysis, interpretation of data; and Xiao, Guo and Gong wrote the paper. Xu, Principal Investigator, innovator for the project, participated in the conception, design, and revision of the manuscript.

## Conflict of interest

The authors have no conflicts of interest.

## Funding

This work was supported by the National Natural Science Foundation of China (Grant No. 81871383), and the Medical Scientific Research Foundation of Guangdong Province, China (Grant No. A2018132).

## Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

## Data sharing statement

The deidentified participant data will be available upon reasonable request from Prof. Xu (txh@jnu.edu.cn).

## Acknowledgements

The authors would like to express their gratitude to all participating subjects.

## Abbreviations

BMD: bone mineral density; LM: lean mass; FM: fat mass; ALM: appendicular lean mass; DXA: dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.

## Figure legend

Fig. 1 The study inclusion/exclusion criteria flowchart. DXA, dual-energy X-ray absorptiometry.

Fig.2 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM),

percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

## References

1. Zhu K, Hunter M, James A, et al. Associations between body mass index, lean and fat body mass and bone mineral density in middle-aged Australians: The Busselton Healthy Ageing Study. *Bone*. 2015; 74:146-52.
2. Chen SC, Chung WS, Wu PY, et al. Associations among Geriatric Nutrition Risk Index, bone mineral density, body composition and handgrip strength in patients receiving hemodialysis. *Nutrition*. 2019; 65:6-12.
3. Stroup BM, Hansen KE, Krueger D, et al. Sex differences in body composition and bone mineral density in phenylketonuria: A cross-sectional study. *Mol Genet Metab Rep*. 2018; 15:30-5.
4. Heiss CJ, Sanborn CF, Nichols DL, et al. Associations of body fat distribution, circulating sex hormones, and bone density in postmenopausal women. *J Clin Endocrinol Metab*. 1995; 80:1591-6.
5. Guo B, Wu Q, Gong J, et al. Gender Difference in Body Fat for Healthy Chinese Children and Adolescents. *Child Obes*. 2016; 12:144-54.
6. Guo B, Wu Q, Gong J, et al. Relationships between the lean mass index and bone mass and reference values of muscular status in healthy Chinese children and adolescents. *J Bone Miner Metab*. 2016; 34:703-13.
7. Blain H, Jaussent A, Thomas E, et al. Appendicular skeletal muscle mass is the strongest independent factor associated with femoral neck bone mineral density in adult and older men. *Exp Gerontol*. 2010; 45:679-84.
8. Bogl LH, Latvala A, Kaprio J, et al. An investigation into the relationship between soft tissue body composition and bone mineral density in a young adult twin sample. *J Bone Miner Res*. 2011; 26:79-87.
9. Cui LH, Shin MH, Kweon SS, et al. Relative contribution of body composition to bone

1  
2  
3  
4 mineral density at different sites in men and women of South Korea. *J Bone Miner Metab.*  
5 2007; 25:165-71.

6  
7 10. Walsh CJ, Phan CM, Misra M, et al. Women with anorexia nervosa: finite element and  
8 trabecular structure analysis by using flat-panel volume CT. *Radiology.* 2010; 257:167-74.

9  
10 11. Kang SM, Yoon JW, Ahn HY, et al. Android fat depot is more closely associated with  
11 metabolic syndrome than abdominal visceral fat in elderly people. *PLoS One.* 2011; 6:e27694.

12  
13 12. Choi HS, Kim KJ, Kim KM, et al. Relationship between visceral adiposity and bone  
14 mineral density in Korean adults. *Calcif Tissue Int.* 2010; 87:218-25.

15  
16 13. Katzmarzyk PT, Barreira TV, Harrington DM, et al. Relationship between abdominal fat  
17 and bone mineral density in white and African American adults. *Bone.* 2012; 50:576-9.

18  
19 14. Warming L, Ravn P, Christiansen C. Visceral fat is more important than peripheral fat for  
20 endometrial thickness and bone mass in healthy postmenopausal women. *Am J Obstet Gynecol.*  
21 2003; 188:349-53.

22  
23 15. Shapses SA, Pop LC, Wang Y. Obesity is a concern for bone health with aging. *Nutr Res.*  
24 2017; 39:1-13.

25  
26 16. De Laet C, Kanis JA, Oden A, et al. Body mass index as a predictor of fracture risk: a  
27 meta-analysis. *Osteoporos Int.* 2005; 16:1330-8.

28  
29 17. Zhu K, Briffa K, Smith A, et al. Gender differences in the relationships between lean body  
30 mass, fat mass and peak bone mass in young adults. *Osteoporos Int.* 2014; 25:1563-70.

31  
32 18. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the  
33 elderly in New Mexico. *Am J Epidemiol.* 1998; 147:755-63.

34  
35 19. Melton LJ, 3rd, Khosla S, Crowson CS, et al. Epidemiology of sarcopenia. *J Am Geriatr*  
36 *Soc.* 2000; 48:625-30.

37  
38 20. Verschueren S, Gielen E, O'Neill TW, et al. Sarcopenia and its relationship with bone  
39 mineral density in middle-aged and elderly European men. *Osteoporos Int.* 2013; 24:87-98.

40  
41 21. Seeman E. Clinical review 137: Sexual dimorphism in skeletal size, density, and strength.  
42 *J Clin Endocrinol Metab.* 2001; 86:4576-84.

43  
44 22. Kim JH, Choi HJ, Ku EJ, et al. Regional body fat depots differently affect bone  
45 microarchitecture in postmenopausal Korean women. *Osteoporos Int.* 2016; 27:1161-8.

46  
47 23. Marques EA, Moreira P, Wanderley F, et al. Appendicular fat mass is positively associated  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 with femoral neck bone mineral density in older women. *Menopause*. 2012; 19:311-8.
- 5  
6 24. Kuwahata A, Kawamura Y, Yonehara Y, et al. Non-weight-bearing effect of trunk and  
7  
8 peripheral fat mass on bone mineral density in pre- and post-menopausal women. *Maturitas*.  
9  
10 2008; 60:244-7.
- 11  
12 25. Yoo HJ, Park MS, Yang SJ, et al. The differential relationship between fat mass and bone  
13  
14 mineral density by gender and menopausal status. *J Bone Miner Metab*. 2012; 30:47-53.
- 15  
16 26. Freitas P, Garcia Rosa ML, Gomes AM, et al. Central and peripheral fat body mass have  
17  
18 a protective effect on osteopenia or osteoporosis in adults and elderly? *Osteoporos Int*. 2016;  
19  
20 27:1659-63.
- 21  
22 27. Sharma A, Flom PL, Rosen CJ, et al. Racial differences in bone loss and relation to  
23  
24 menopause among HIV-infected and uninfected women. *Bone*. 2015; 77:24-30.
- 25  
26 28. Tchernof A, Desmeules A, Richard C, et al. Ovarian hormone status and abdominal  
27  
28 visceral adipose tissue metabolism. *J Clin Endocrinol Metab*. 2004; 89:3425-30.
- 29  
30 29. Kim CJ, Oh KW, Rhee EJ, et al. Relationship between body composition and bone mineral  
31  
32 density (BMD) in perimenopausal Korean women. *Clin Endocrinol (Oxf)*. 2009; 71:18-26.
- 33  
34 30. Gilsanz V, Chalfant J, Mo AO, et al. Reciprocal relations of subcutaneous and visceral fat  
35  
36 to bone structure and strength. *J Clin Endocrinol Metab*. 2009; 94:3387-93.
- 37  
38 31. Lesser IA, Gasevic D, Lear SA. The effect of body fat distribution on ethnic differences  
39  
40 in cardiometabolic risk factors of Chinese and Europeans. *Appl Physiol Nutr Metab*. 2013;  
41  
42 38:701-6.  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



**Table 1** Baseline characteristics of subjects

	Male		Female	
	Age < 50 years	Age ≥ 50 years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0 <sup>c</sup>	37.4±8.7	63.9±9.1 <sup>c</sup>
Weight (kg)	63.9±12.4	63.8±10.8 <sup>c</sup>	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	22.4±3.9	22.9±3.3 <sup>c</sup>	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5 <sup>c</sup>	16.7±6.0	18.9±6.2 <sup>b</sup>
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0 <sup>a</sup>
Fat%	20.2±8.3	23.0±7.3 <sup>c</sup>	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4 <sup>c</sup>	8.7±3.6	10.6±3.7 <sup>b</sup>
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1 <sup>c</sup>	7.3±2.5	7.5±2.6 <sup>c</sup>
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15 <sup>c</sup>
Bone mineral density (g/cm <sup>2</sup> )				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106 <sup>c</sup>
Lumbar spine	1.114±0.162	1.099±0.200 <sup>c</sup>	1.124±0.155	0.950±0.186 <sup>c</sup>
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132 <sup>b</sup>
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144 <sup>b</sup>
Current Smoker (%)	n=141 (17.9%)	n=119 (13.0%)	n=37 (2.4%)	n=70 (2.8%)
Current alcohol user (%)	n=121 (15.4%)	n=117 (12.8%)	n=35 (2.3%)	n=38 (1.5%)

*Note.* Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with the same gender of the different age group (unpaired-sample *t*-tests or chi-squared test).

**Table 2** Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm <sup>2</sup> )	LSBMD (g/cm <sup>2</sup> )	FNBMD (g/cm <sup>2</sup> )	THBMD (g/cm <sup>2</sup> )
<b>Male</b>												
20-29	199	47.3±6.0 <sup>c</sup>	12.1±8.2 <sup>c</sup>	18.1±9.0 <sup>c</sup>	1.2±0.9 <sup>c</sup>	2.4±1.3 <sup>c</sup>	0.47±0.14 <sup>c</sup>	21.6±3.3 <sup>c</sup>	1.102±0.103	1.116±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9 <sup>c</sup>	12.8±7.3 <sup>c</sup>	19.4±8.2 <sup>c</sup>	1.4±0.9 <sup>c</sup>	2.4±1.3 <sup>a</sup>	0.55±0.16 <sup>c</sup>	21.0±3.3 <sup>c</sup>	1.090±0.113 <sup>c</sup>	1.110±0.149	0.909±0.140 <sup>b</sup>	0.922±0.154 <sup>c</sup>
40-49	333	48.3±6.0 <sup>c</sup>	15.4±7.2 <sup>c</sup>	22.1±7.6 <sup>c</sup>	1.7±0.9 <sup>c</sup>	2.6±1.0	0.63±0.17 <sup>c</sup>	21.5±3.2 <sup>c</sup>	1.119±0.108 <sup>b</sup>	1.111±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1 <sup>c</sup>	15.2±6.5	22.2±7.2 <sup>a</sup>	1.7±0.8 <sup>c</sup>	2.5±0.9	0.67±0.18 <sup>c</sup>	21.0±3.2 <sup>c</sup>	1.122±0.110	1.016±0.192	0.895±0.140	0.946±0.154 <sup>a</sup>
60-69	281	46.9±5.4 <sup>c</sup>	15.5±6.5	23.0±7.3 <sup>a</sup>	1.8±0.8 <sup>c</sup>	2.5±0.9	0.71±0.19 <sup>c</sup>	20.4±2.8 <sup>c</sup>	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2 <sup>c</sup>	15.0±6.5	23.8±7.5	1.7±0.9 <sup>b</sup>	2.4±0.9	0.70±0.19 <sup>c</sup>	18.4±2.7 <sup>c</sup>	1.086±0.101	1.010±0.215 <sup>c</sup>	0.783±0.135 <sup>c</sup>	0.863±0.147 <sup>a</sup>
<b>Female</b>												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.113±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.112±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.111±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.008±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	0.911±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	0.889±0.177	0.672±0.105	0.732±0.125

*Note.* Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. <sup>a</sup>*P* < 0.05; <sup>b</sup>*P* < 0.01; <sup>c</sup>*P* < 0.001. Compared with female of the same age group (unpaired-sample t-tests).

**Table 3** Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in males.

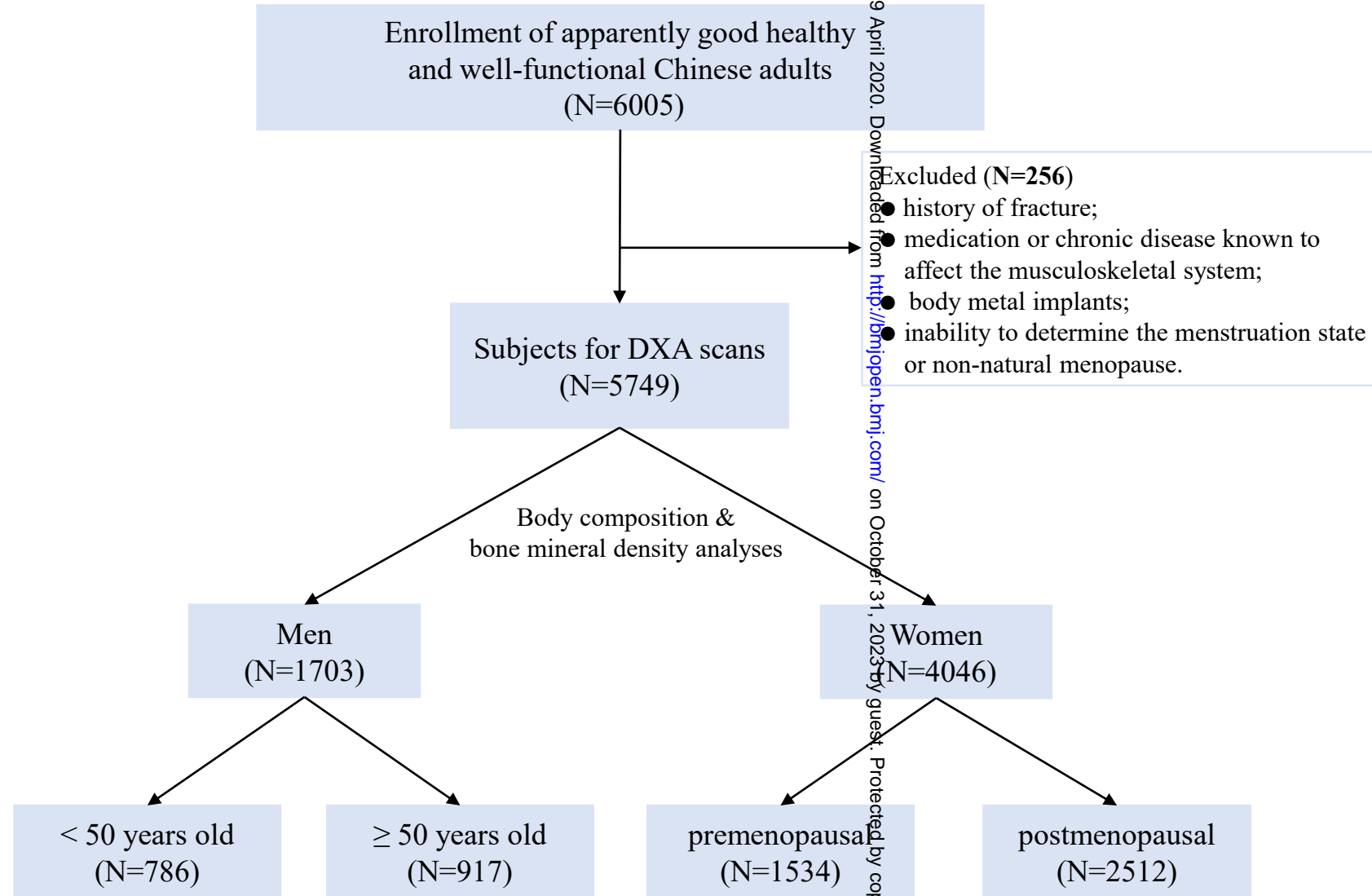
Males	WBBMD			LSBMD			FNBMD			THBMD		
	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.
<b>&lt;50 y</b>												
Age	<b>0.066</b>	1.991	0.047	-0.018	-0.459	0.647	-0.044	-1.161	0.246	0.029	0.821	0.412
Smoke	-0.057	-1.783	0.075	-0.043	-1.116	0.265	-0.047	-1.267	0.206	-0.050	-1.473	0.141
Alcohol	<b>0.063</b>	1.988	0.047	0.041	1.081	0.280	0.011	0.303	0.762	0.009	0.279	0.780
BMI	<b>0.266</b>	4.998	<0.001	<b>0.170</b>	2.668	0.008	<b>0.139</b>	2.269	0.024	<b>0.222</b>	3.920	<0.001
A/G FMR	0.044	1.028	0.304	-0.063	-1.223	0.222	-0.040	-0.811	0.418	0.014	0.315	0.753
Appendicular LM	<b>0.402</b>	9.240	<0.001	<b>0.309</b>	5.923	<0.001	<b>0.395</b>	7.872	<0.001	<b>0.405</b>	8.757	<0.001
<b>≥50 y</b>												
Age	-0.015	-0.486	0.627	<b>0.087</b>	2.673	0.008	<b>-0.220</b>	-7.086	<0.001	<b>-0.124</b>	-3.989	<0.001
Smoke	-0.023	-0.786	0.432	-0.027	-0.865	0.387	0.005	0.165	0.869	-0.006	-0.215	0.830
Alcohol	0.023	0.794	0.427	0.059	1.920	0.055	0.022	0.747	0.455	0.020	0.697	0.486
BMI	<b>0.260</b>	5.915	<0.001	<b>0.268</b>	5.704	<0.001	<b>0.190</b>	4.257	<0.001	<b>0.261</b>	5.817	<0.001
A/G FMR	0.008	0.241	0.809	0.027	0.759	0.448	-0.054	-1.585	0.113	-0.035	-1.032	0.302
Appendicular LM	<b>0.321</b>	7.814	<0.001	<b>0.207</b>	4.719	<0.001	<b>0.264</b>	6.328	<0.001	<b>0.256</b>	6.127	<0.001

Note. Results expressed as standard  $\beta$  coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

**Table 4** Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in females.

Females	WBBMD			LSBMD			FNBMD			THBMD		
	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.	Standard $\beta$	t	Sig.
<b>Premenopausal</b>												
Age	0.039	1.483	0.138	<b>-0.074</b>	-2.665	0.008	<b>-0.098</b>	-3.483	0.001	-0.008	-0.278	0.781
Smoke	0.024	0.958	0.338	0.022	0.794	0.427	0.033	1.196	0.232	0.030	1.133	0.258
Alcohol	-0.005	-0.197	0.844	0.008	0.289	0.773	0.013	0.467	0.640	0.012	0.451	0.652
BMI	<b>0.413</b>	11.055	<0.001	<b>0.384</b>	9.659	<0.001	<b>0.277</b>	6.901	<0.001	<b>0.360</b>	9.177	<0.001
A/G FMR	<b>-0.249</b>	-8.421	<0.001	<b>-0.193</b>	-6.152	<0.001	<b>-0.155</b>	-4.872	<0.001	<b>-0.157</b>	-5.083	<0.001
Appendicular LM	<b>0.179</b>	5.360	<0.001	<b>0.074</b>	2.099	0.036	<b>0.159</b>	4.451	<0.001	<b>0.138</b>	3.940	<0.001
<b>Postmenopausal</b>												
Age	<b>-0.337</b>	-19.556	<0.001	<b>-0.222</b>	-11.701	<0.001	<b>-0.438</b>	-25.343	<0.001	<b>-0.389</b>	-22.318	<0.001
Smoke	-0.024	-1.482	0.139	0.007	.383	0.702	-0.019	-1.146	0.252	-0.024	-1.461	0.144
Alcohol	-0.015	-0.898	0.369	-0.029	-1.649	0.099	-0.008	-0.504	0.614	-0.020	-1.213	0.225
BMI	<b>0.315</b>	14.922	<0.001	<b>0.274</b>	11.767	<0.001	<b>0.185</b>	8.718	<0.001	<b>0.266</b>	12.451	<0.001
A/G FMR	<b>-0.135</b>	-7.585	<0.001	<b>-0.086</b>	-4.402	<0.001	<b>-0.083</b>	-4.644	<0.001	<b>-0.052</b>	-2.867	0.004
Appendicular LM	<b>0.186</b>	9.076	<0.001	<b>0.152</b>	6.744	<0.001	<b>0.180</b>	8.787	<0.001	<b>0.166</b>	7.998	<0.001

*Note.* Results expressed as standard  $\beta$  coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

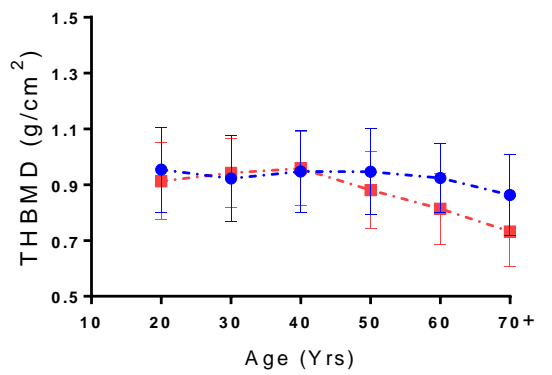
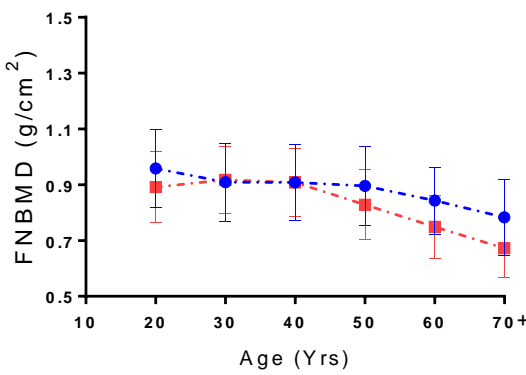
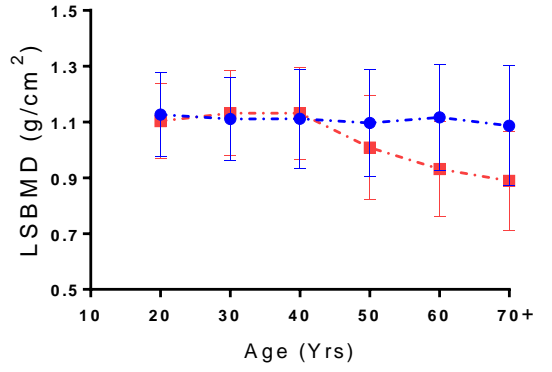
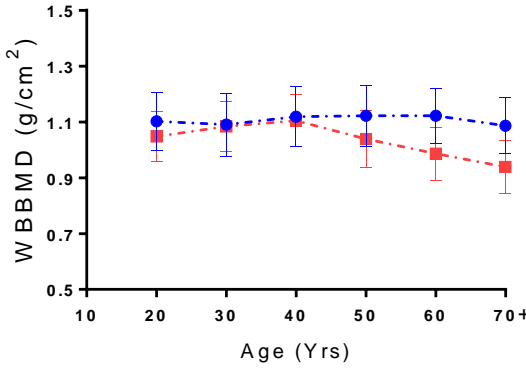
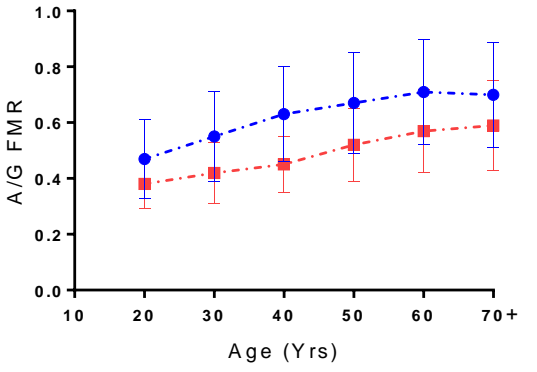
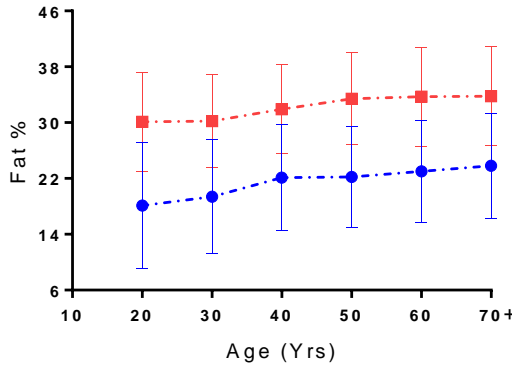
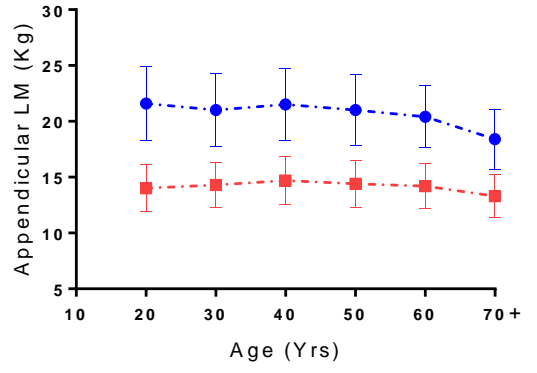
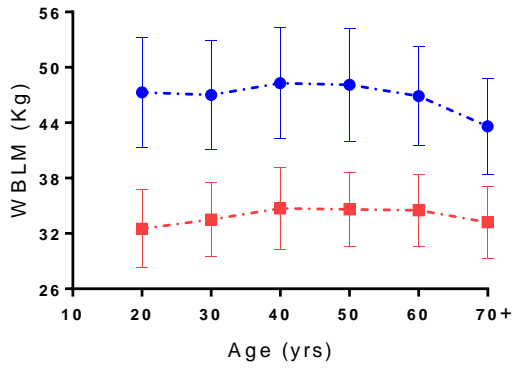


19-032268 on 19 April 2020. Downloaded from <http://bmjopen.bmj.com/> on October 31, 2023 by guest. Protected by copyright.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

● Males  
■ Females



## SUPPLEMENTARY INFORMATION

**Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study**

Zeyu Xiao <sup>a, b, c</sup>, Zhiqiang Tan <sup>a, c</sup>, Jingjie Shang <sup>a, c</sup>, Yong Cheng <sup>a, c</sup>, Yongjin Tang <sup>a, c</sup>,  
Bin Guo <sup>a, c</sup>, Jian Gong <sup>a, c</sup>, Hao Xu <sup>a, c, \*</sup>

<sup>a</sup> Molecular Imaging Institute, the First Affiliated Hospital, Jinan University, Guangzhou, PR China

<sup>b</sup> Department of Radiology, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

<sup>c</sup> Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

\* Corresponding author: Hao Xu.

Table S1. Pearson's correlation between study variables in males &lt;50 years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.741***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.719***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.841***	.696***	.872***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .



Table S2. Pearson's correlation between study variables in males  $\geq 50$  years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.770***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.769***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.840***	.702***	.913***

*Note.* Results expressed as  $r$  coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.775***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.825***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.835***	.720***	.912***

*Note.* Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

\* $P < 0.05$ ; \*\* $P < 0.05$ ; \*\*\* $P < 0.001$ .

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(b) Report category boundaries when continuous variables were categorized	6-7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).