

VERTEBRAL ABNORMALITIES AND BONE QUALITY IN OLDER ADULTS:  
EFFECTS OF WEIGHT LOSS

By

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## ABSTRACT OF THE THESIS

### Vertebral Abnormalities and Bone Quality in Older Adults: Effects of Weight Loss

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Obesity is a risk factor for osteoarthritis and spinal stenosis. Weight loss can cause declines in bone mineral density (BMD), this is not consistently observed at the lumbar spine (LS). It is hypothesized that this inconsistency may be due vertebral structural abnormalities, and so, excluding these defects along with examining the LS trabecular bone score (TBS) may be a more sensitive indicator of bone changes due to weight loss and aging. Retrospective analysis of BMD and TBS in 131 older overweight/obese women and men (body mass index, BMI,  $32.72 \pm 4.6 \text{ kg/m}^2$  and  $60 \pm 6$  years) who participated in previous weight loss studies. To control for abnormalities in the lumbar spine image, we assessed dual energy x-ray absorptiometry LS images for vertebral body exclusion (VE) criteria. At study completion participants were divided into those who had a weight loss of less than or greater than 5%. Mean LS-BMD value was lower after correction for abnormalities ( $p < 0.05$ ). In only the corrected LS-BMD there was a decrease that trended towards being greater due to weight loss. TBS was partially degraded in ~50% of these older individuals. Repeated measures ANOVA (group by time) indicated no significant TBS interaction with weight loss and time. The vertebral abnormalities differentially effected LS BMD during weight loss and aging and because of this, all LS BMD images should be analyzed for vertebral abnormalities.

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## 1. Introduction

Obesity is an epidemic in the United States, according to the Centers for Disease Control (CDC), over 71.6% of adult Americans are either overweight (BMI  $>25$  kg/m<sup>2</sup>) or obese (BMI  $>30$  kg/m<sup>2</sup>), with 39.8% of them being obese [1]. Obesity is a risk factor for many chronic diseases, so, with the rising obesity rates, there has also been an increase in chronic diseases, such as type II diabetes, cardiovascular diseases, hypertension, dyslipidemia, and dementia. Osteoporosis is a bone disease, which develops when individuals have low bone mass which increases their risk for fracture [2]. According to the CDC, 24.5% of women over the age of 65 have osteoporosis, osteoporosis is defined by the CDC as a bone mineral density value that is 2.5 standard deviations (SD) or more below the mean BMD of the reference group which is comprised of young white females [1]. BMD measured by dual x-ray absorptiometry (DXA) is most often used to diagnose osteoporosis and examine fracture risk. T-scores help diagnose osteoporosis; a t-score is the result of the comparison of your BMD to a healthy adult with peak bone density. Post-menopausal women experience an increased risk for low BMD partially due to the decrease in estrogen, but there are lifestyle components such as deficiencies in vitamin D and calcium and lack of resistance exercise [2,3]. Osteoporosis has been wrongly assumed to be a disease found predominantly in women, but fracture risk has been shown to increase in men over 50 years old [4]. Bone turnover is the combination of both bone formation and bone resorption. In growing children, the rate of formation is greater than resorption, resulting in a net positive bone formation [5]. However, with aging, the rate of resorption becomes greater than formation, resulting in



bone loss [5]. This net negative loss of bone can be partially attributed to the decline in both estrogen and testosterone [5].

### Obesity : Metabolic Profile & Risk of Fracture

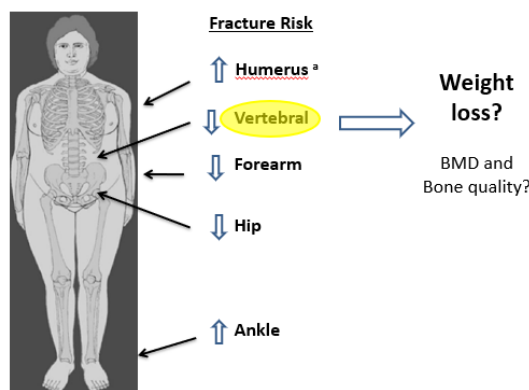
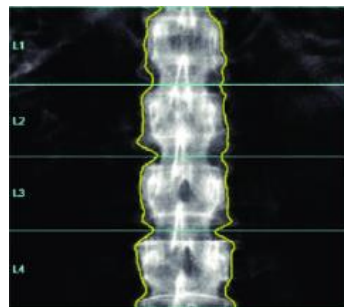


Figure 1 shows the direction of fracture risk due to obesity at each site. It is similar in women and men, except humerus that is higher and lower with increasing BMI in women and men, respectively [6].

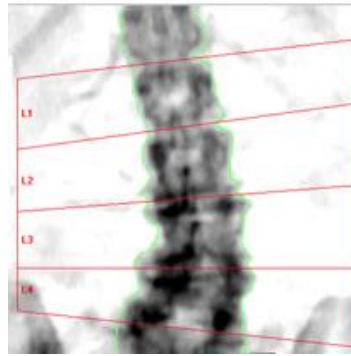
The use of BMD to ascertain fracture risk works well in those who are normal weight. However, BMD has been shown to be positively associated with BMI which indicates that as BMI increases, so does BMD, which means that those who are in the obese category have elevated BMD [6]. It was believed that this elevation is due to the weight bearing effect of obesity and it theorizes that obesity increases BMD due to the mechanical loading of the excess weight on the bone [6]. From this theory it was concluded that being overweight is beneficial since it can be preventative for the development of low bone mass which has an overall net result of reducing fracture risk; but, this theory is proving to be contingent on the site measured [6, 7, 8, 9]. For example, abdominal obesity that is associated with the metabolic syndrome has been associated with a higher risk for hip fracture but not a fracture at the lumbar spine, this notion is illustrated in Figure 1 [10]. Bone sites that are surrounded by excess fat can result in

measurement errors [6]. The lumbar spine is a particularly problematic site to measure in the obese due to the excess abdominal fat surrounding the area [6]. Obesity increases the risk for spinal osteoarthritis and osteophytes or bone deposits which cause inaccurate DXA BMD measurements [6]. These osteophytes are just one example of the abnormalities that can confound the lumbar spine image [6]. Additional causes of these abnormalities are scoliosis, aortic calcification and collapsed vertebrae due to low BMD [11]. Figures 2a and 2b represent LS images. Figure 2a is a normal spine, Figure 2b is a lumbar spine image confounded with osteophytes and aortic calcification. It is thought that these vertebral abnormalities artificially elevate lumbar spine BMD (LS-BMD) which gives an abnormally elevated BMD result, that makes it seem like the bone is healthier than it really is [11]. Because of this, the International Society of Clinical Densitometry (ISCD) recommends excluding abnormal vertebrae to give a more accurate depiction of the health of the spine and therefore a more accurate fracture risk assessment at the lumbar spine can be completed [11].



Vertebrae	T-score	BMD
L1	0.8	0.922
L2	1.1	1.105
L3	1.0	1.005
L4	0.9	0.989

Figure 2a depicts a normal lumbar spine [11].



Vertebrae	T-score	BMD
L1	-1.7	0.922
L2	0.0	1.2
L3	1.8	1.414
L4	2.4	1.488

Figure 2b depicts a lumbar spine image that is confounded by osteophytes and aortic calcification on vertebrae L2-L4.[11].

To decrease the risk for the comorbidities in patients who are overweight or obese, a weight reduction of least 5% is recommended [12, 13,14]. This amount of weight loss has been shown to reduce the severity of the comorbidities, including reducing blood sugar and blood pressure [12,14]. However, recommending weight loss to prevent comorbidities due to obesity may come with side effects such as, evidence indicating that it negatively impacts bone health [15]. Bone mineral density decreases by 1 to 2.5% with moderate weight loss of 6% to 9% and may vary by composition of the diet or the amount of exercise [2,3,16,17,18,19]. It has been shown that weight loss or weight cycling increases fracture risk in those who are normal weight or obese [2, 3,16,17,18, 19]. In addition, not all bone sites respond in a similar manner to weight loss or treatments. For example, the decline in LS BMD during weight loss is not consistently observed like it is with other bone sites, such as the hip [3]. This either indicates that the spine is not affected by weight reduction or that it is not being examined properly to determine the effect of weight loss on the vertebral bone. Correcting the LS BMD for vertebral abnormalities is one method to examine the effect of weight loss, which is one of the aims of this thesis. In addition, bone quality is another way to examine bone and

its ultimate risk of fracturing, and this may be especially important at the lumbar spine in obese patients and with weight loss.

The lumbar spine bone quality can be assessed by examining the trabecular bone score (TBS). Trabecular bone score, like BMD, can be acquired from DXA. However, TBS examines bone microarchitecture and reflects bone quality, through examination of bone texture, which BMD does not do [20]. A higher TBS indicates a strong bone which is less likely to fracture [20]. A low TBS is associated with increased risk of fracture [21]. TBS is age dependent and follows similar trend to BMD with aging [20]. It has been reported that there is little change in TBS between the ages of 30 and 45, but, after 45, the decline in TBS is apparent [20]. TBS can be categorized based on degree of degradation. Partially degraded TBS is a score between, 1.20-1.35 and degraded is a score of  $\leq 1.20$  [34]. Many studies including, the Vitamin D and Omega 3 trial (VITAL) concluded that females have lower TBS than men, and those with a BMI  $>25 \text{ m/kg}^2$  have a lower TBS than those with a normal BMI [20,22]. TBS has also been shown to be lower in those with type 2 diabetes [23, 24, 25]. TBS has been criticized for not being reliable when the subjects' BMI is over  $37 \text{ kg/m}^2$  [26]. It is thought the accuracy of the score is attenuated by a high percentage of visceral adiposity associated with a high BMI [27, 28]. Even with this criticism, it is thought that analyzing TBS along with BMD together will more accurately depict the changes that occur at the LS BMD over one year of weight loss.

This thesis addresses the following are the aims:

1. To determine how correction for vertebral abnormalities affects lumbar spine (LS) bone mineral density (BMD) in older overweight and obese individuals.

2. To determine whether one year of weight loss differentially influences corrected and uncorrected LS BMD.
3. To examine trabecular bone score before and after one year of weight loss in older overweight and obese individuals.

*It is hypothesized that the BMD of the lumbar spine with vertebral abnormalities will be artificially elevated. Corrected BMD will decrease with aging or weight loss in this one-year study. In addition, it is hypothesized that weight loss will reduce bone quality, as indicated by a decrease in TBS.*

## **2. Materials and Methods**

### *2.1. Participants and Study Design*

This study is a retrospective analysis of two randomized controlled trials (RCT), with similar aims. The first trial is Osteoporosis, weight loss and endocrine (OWLE) where recruitment of participants and location was at the Department of Nutritional Sciences at Rutgers University, New Brunswick, NJ. The second trial was the Cooperative Lifestyle Intervention Program-II (CLIP-II) where participant recruitment and location were at The Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC with an intervention that took place at the YMCAs in NC. CLIP-II included 3 interventions: diet-induced weight loss (WL), WL+ aerobic exercise training or WL + resistance exercise training. In this study, we only included the diet-induced weight loss (WL) participants to match the OWLE weight loss protocol. The rationale for combining these two datasets is that it increased the number of persons to achieve adequate power to determine if there was a statistically

significant difference between the weight loss groups. In addition to similar weight loss interventions in the OWLE and CLIP-II, subjects had similar age and BMI inclusion criteria. In the OWLE dataset at Rutgers University, the BMI and age ranges were 25–43 kg/m<sup>2</sup> and 50–72 years, respectively. In the CLIP-II dataset at Wake Forest University, the BMI and age ranges were 28–42 kg/m<sup>2</sup> and 60–79 years, respectively [29]. Baseline characteristics of both studies compared in Appendix Table 1. All participants signed an informed consent. The Institutional Review Board at each university approved amendments and Data Use Agreements were approved for the respective studies.

Subjects in both weight loss studies received behavioral and dietary-based counseling to achieve moderate weight loss. This was completed by a registered dietitian who counseled the subjects weekly early in the intervention and then 2–3 times/month afterwards, in accordance with the respective protocols. Subjects were asked to maintain their same physical activity level during the intervention from prior to beginning the study. Subjects were also counseled to receive the recommended daily allowance of both vitamin D and calcium.

The participants were retrospectively divided into two groups, those who lost less than 5% or greater than 5% of their body weight this was done because at least 5% of weight loss is expected to influence bone [16,18,19, 19 ]. Using the combined datasets, there were 71 subjects in the <5% weight loss and 60 subjects in the >5% weight loss group.

## *2.2 Inclusion and Exclusion Criteria*

Overweight or obese, BMI >25 kg/m<sup>2</sup> community-dwelling men and postmenopausal women (50-79 years of age) were included.

Patients were excluded if they had a history of diabetes, myocardial infarction in the last 3 months, active cancer, severe heart disease, and osteoporosis (T score < -2.5 at the hip or spine), or if they had been taking any medication known to influence bone metabolism. Only those participants who were randomized to an intervention were included in the analysis.

## *2.3. Measurements*

### *2.3.1 Baseline demographics Bone outcomes*

Baseline demographics such as age, sex, race, and medical history were collected on the first day of recruitment. Subjects were given ID numbers to remain anonymous.

Bone mineral density was measured at baseline, 6 months and 12 months by (DXA, GE Lunar) at the lumbar spine (L1-L4), femoral neck, trochanter, and total hip. TBS (TBS iNsight™, Medimaps) was acquired for the L1-L4. After the scans, the TBS scores were analyzed and divided into 3 groups, either normal (>1.35), partially degraded (1.2-1.35) and degraded (<1.2). To assess an abnormality in the lumbar spine, the ISCD's vertebral body exclusion criteria was followed:

A vertebral abnormality assessment was previously conducted, the current analysis was compared to this. If there was any difference between the previous assessment and the current analysis a third person was used to adjudicate. A vertebral body was excluded if there was one or more of the following: 1) Presence of a focal structure defect 2) Discrepancy in T-score between adjacent vertebrae 3) Lack of increasing bone mineral content (BMC) from L1 to L4. As per ISCD criteria, if two adjacent vertebrae and 1 non-contiguous vertebrae were left (ie L1-L2 and L4), the mean T-score of the two adjacent vertebrae was used. If only two non-adjacent vertebrae remain (ie L1 and L3), the lower T-score of the two was chosen [11]. The rationale for using the lower T-score is so a person who has an increased fracture risk is not missed.

### *2.3.2 Statistical Analysis*

Descriptive statistics of all baseline characteristics were calculated. For missing data, last value carried forward was used. Paired sample T-test was used to find differences between corrected and uncorrected LS-BMD. Paired sample T-test was performed to compare change from baseline in the two LS-BMD values. Two-way ANOVA with repeated measures (group x time) was performed to determine differences between weight loss groups. One-way ANOVA was used to determine differences between sex and race and Student's T-test was used to find changes from baseline within each sex. No variables were significantly correlated. Site was used as a co-variate to control for differences due to location.

A power analysis was conducted on TBS using a subset of the data (OWLE) to determine the number of subjects to achieve a significant difference



between the two weight loss groups. It was determined that 60 persons per group would be needed to achieve a significant change in TBS with weight loss with  $\alpha$  set at 0.05, with the value of  $\beta$  set at 0.90. In addition, a power analysis using LS-BMD, indicated that there would need to be at least 0.019 g/cm<sup>2</sup> difference in BMD to observe a significant difference between groups ( $\alpha$  set at 0.05, and  $\beta$  set at 0.80). A  $p$  value of <0.05 was considered statistically significant. Data are represented as mean  $\pm$  SD, unless otherwise indicated. All statistical analyses were performed using SPSS statistical software (IBM, version 24.0).

### **3. Results**

#### *3.1. Baseline characteristics.*

Table 1 provides the baseline characteristics for all 131 subjects in this study. Average age was  $60 \pm 6$ , about 70% of the population were women. Average BMI was  $32.7 \pm 4.6$  kg/m<sup>2</sup>. Average TBS was  $1.347 \pm 0.09$  and about 50% of the population had either degraded or partially degraded TBS, which indicates degraded bone quality. Table 2 provides the baseline characteristics of each weight loss group, there were no statistically significant differences between the two groups at baseline.

**Table 1: Baseline Characteristics of Subjects**

Variables	Mean ( $\pm$ SD)
N	131
Age	60.6 $\pm$ 6
Sex (% female)	70%
Race	
White	81%
African American	16%
Other	3%
Weight (kg)	91.70 $\pm$ 17.84
BMI (kg/m <sup>2</sup> )	32.7 $\pm$ 4.6
<b>Bone Outcomes</b>	
Lumbar Spine	1.21 $\pm$ 0.18
Corrected Lumbar Spine	1.17 $\pm$ 0.16
Femoral Neck	0.936 $\pm$ 0.11
Trochanter	0.812 $\pm$ 0.12
Total Hip	0.998 $\pm$ 0.12
TBS	1.347 $\pm$ 0.09
% TBS normal	49.6%
% TBS partially degraded	47.3%
% TBS degraded	3.0%

Values are mean  $\pm$  SD

TBS: trabecular bone score

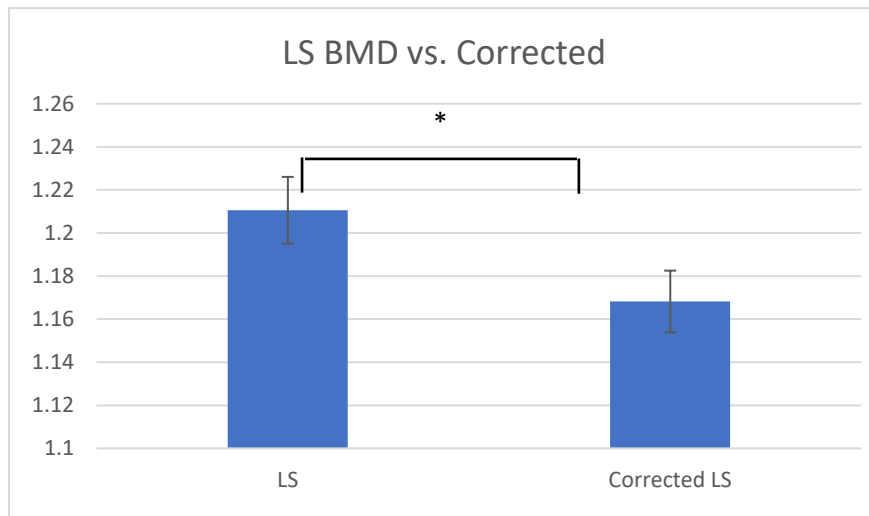
**Table 2: Baseline Characteristics of Subjects within in WL groups**

	<5% WL (71)	>5% WL (60)
TBS	1.348 $\pm$ 0.087	1.346 $\pm$ 0.088
<b>BMD Sites</b>		
LS	1.212 $\pm$ 0.18	1.210 $\pm$ 0.17
Corrected LS	1.180 $\pm$ 0.19	1.158 $\pm$ 0.13
Femoral Neck	0.942 $\pm$ 0.13	0.930 $\pm$ 0.09
Trochanter	0.817 $\pm$ 0.12	0.808 $\pm$ 0.12
Total Hip	1.007 $\pm$ 0.13	0.987 $\pm$ 0.11
<p>Values are mean <math>\pm</math> SD. There were no statistically significant differences between the two groups at baseline. Corrected LS is the mean value after vertebrae exclusion for those found to be abnormal</p>		

### 3.2. Assessment of influence of abnormalities on LS at baseline and over time

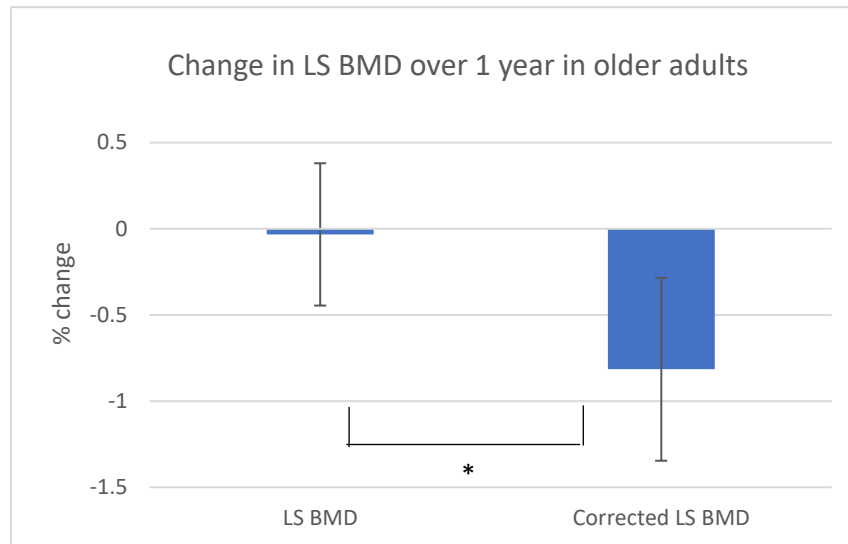
Vertebral exclusion was conducted on baseline images of the LS for all 131 participants to correct for the abnormalities. As indicated in Figure 3, vertebral abnormalities significantly artificially raised LS BMD. LS BMD was 1.210  $\pm$  0.18 and

when the corrections were completed the BMD significantly decreased to  $1.168 \pm 0.02$  ( $p=0.000$ ). There were no significant differences in TBS in those that had an abnormality at baseline compared to those who did not (Appendix Figure A1). In addition, our results indicate that the prevalence of a vertebral abnormality is higher in the Caucasian population when compared to the African American population (Appendix Figure A2).



**Figure 3.** Corrected LSBMD is significantly lower than uncorrected LS BMD ( $n=131$ ).  
 $*p < 0.05$ . BMD, bone mineral density. LS, lumbar spine

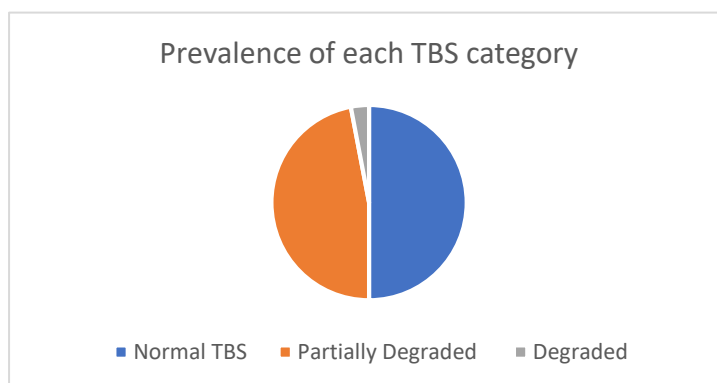
The presence of the vertebral abnormalities differentially influenced LS BMD over the one year. As indicated in Figure 4, the change from baseline in the uncorrected BMD was  $-0.03 \pm 4.73\%$ , but when the abnormalities were corrected for, the change from baseline decreased to  $-0.815 \pm 6.07\%$  ( $p<0.05$ ).



**Figure 4.** Corrected LS BMD decreases more than uncorrected LS BMD (n=131)  
 \* $p < 0.05$ . BMD, bone mineral density. LS, lumbar spine

### 3.3. Assessment of Bone Quality at Baseline (n=131)

Obesity compromises spinal bone quality, as measured by TBS and is shown in Figure 5, over 50% of the participants had partially or fully degraded bone microarchitecture at baseline. Normal microarchitecture is reflected by a TBS  $>1.35$ ; partially degraded microarchitecture is reflected by a TBS between 1.2 and 1.35; degraded microarchitecture is reflected by TBS a  $<1.2$  [34]. In addition, TBS was shown to be positively correlated with both LS BMD corrected ( $r=.534$ ,  $p=0.000$ ) and uncorrected at baseline ( $r=.568$ ,  $p=0.000$ ) (Figure Appendix Figure A4a and 4b). TBS was not significantly correlated with visceral adipose tissue ( $r=.158$ ,  $p=.145$ ) (shown in Appendix Table A3a)



**Figure 5.** Almost half of the overweight/obese individuals had degraded or Partially Degraded TBS at baseline. TBS, trabecular bone score

### 3.4. Assessment of the effect of Weight loss on Bone Outcomes

The <5% weight loss group lost  $2.64 \pm 2.86\%$  of their weight, while the >5% WL group lost about  $8.73 \pm 4.40\%$  of their weight. A repeated measures analysis, in Table 3, indicates that the BMD at the hip significantly decreased over time and only the trochanter and total hip BMD showed a significant interaction between time and WL group. There was no significant interaction for TBS, LS BMD or corrected LS BMD. Figure 6 depicts the change in LS BMD due to weight loss. It shows that only corrected LS-BMD trended towards a greater reduction in the >5% weight-loss group but this is not the case for any uncorrected BMD values

**Figure 6.** Change to 1 year for those who lost > 5% of their weight. There was a trend to decrease in BMD in the >5% weight loss after correction for vertebral abnormalities. BMD, bone mineral density; LS, lumbar spine

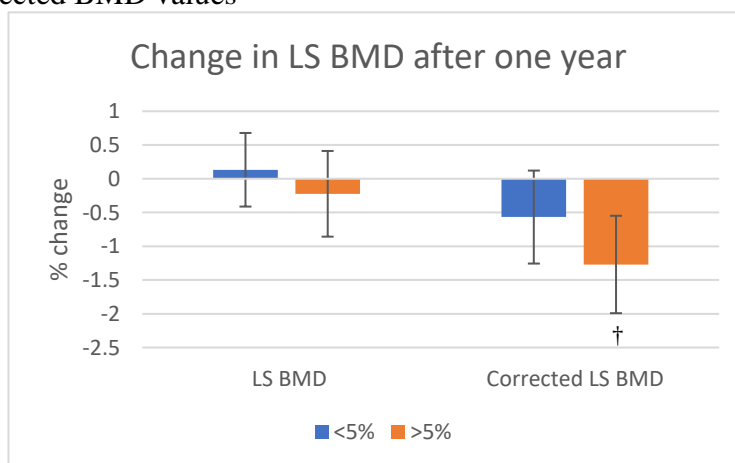
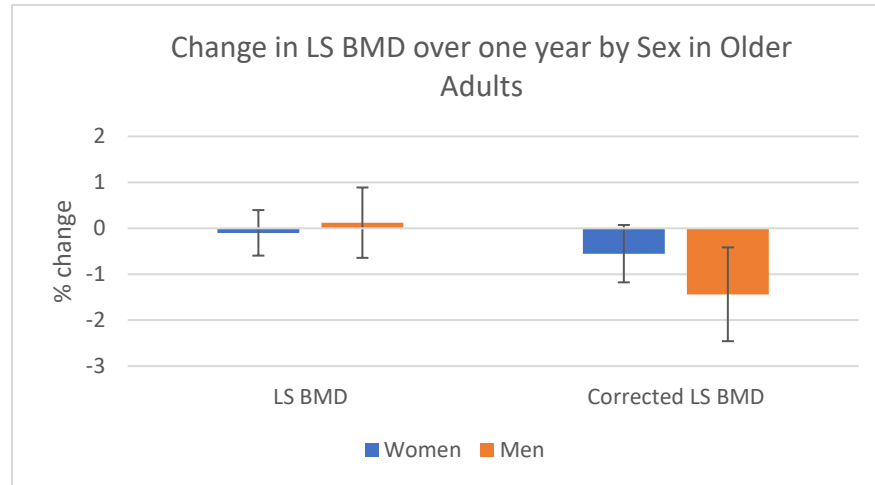


Table 3: Effect of weight loss on bone parameters

<5% (n=71)				>5% (n=60)			p		
	Baseline	6m	12m	Baseline	6m	12m	Group	Time	Group xTime
<b>LS TBS</b>	1.348 ± 0.087	1.345 ± 0.090	1.350 ± 0.089	1.346 ± 0.088	1.357 ± 0.080	1.346 ± 0.082	.541	.868	.167
LS BMD	1.212 ± 0.183	1.220 ± 0.181	1.212 ± 0.175	1.210 ± 0.171	1.213 ± 0.175	1.204 ± 0.169	.608	.801	.844
Corrected LS BMD	1.180 ± 0.187	1.180 ± 0.174	1.167 ± 0.177	1.158 ± 0.134	1.163 ± 0.147	1.142 ± 0.137	.308	.682	.921
Femoral Neck BMD	0.942 ± 0.129	0.940 ± 0.124	0.936 ± 0.111	0.930 ± 0.093	0.930 ± 0.096	0.922 ± 0.099	.583	.211	.643
Trochanter BMD	0.817 ± 0.118	0.812 ± 0.121	0.812 ± 0.123	0.808 ± 0.122	0.791 ± 0.127	0.786 ± 0.129	.540	.307	.031
Total Hip BMD	1.007 ± 0.128	1.002 ± 0.129	0.999 ± 0.129	0.987 ± 0.109	0.975 ± 0.113	0.968 ± 0.115	.252	.000	.044

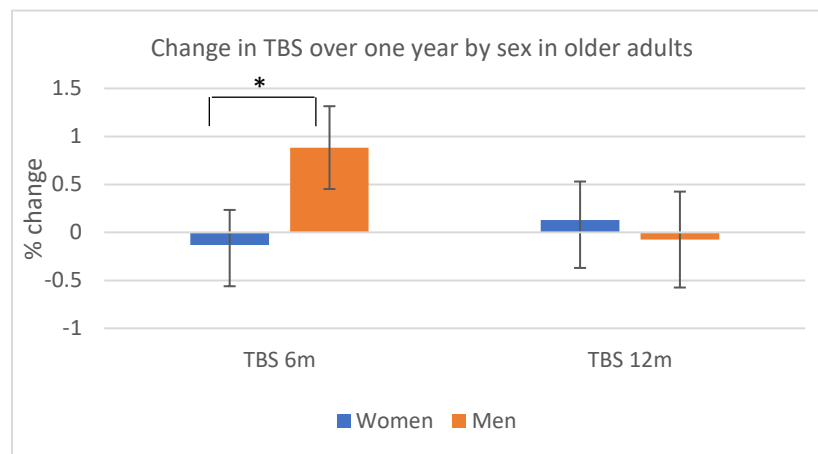
**Table 3** All values are mean ± SD. A repeated measures (GroupxTime) was performed. Group being amount of weight loss (WL), <5% or >5% change from baseline  
BMD, bone mineral density. LS, lumbar spine. TBS, trabecular bone score

### 3.5. Assessment of Effect of Sex on Bone Outcomes



**Figures 7a** There was no significant difference from baseline in LS BMD for either corrected or uncorrected values in women (92) and men (39)  
BMD, bone mineral density. LS, lumbar spine

Figures 7a and 7b reveal the effect of time and sex on spine health. Both men and women decrease from baseline at the LS BMD, although not significantly. Figure 7b, reveals the differentiating effect of sex on TBS at both 6 and 12 months. There is no significant change at 12 months in either men or women's TBS. However, at 6 month there is a significant increase in men.



**Figure 7b:** Comparison of women (n=92) and men (n=39) TBS. Differs from baseline \*p<0.05.  
LS, lumbar spine. TBS, trabecular bone score

#### 4. Discussion

The primary aim of this study was to determine how the correction for vertebral abnormalities affects LS BMD over one year. The second aim was to determine whether one year of weight loss differentially influences corrected and uncorrected LS BMD. The third aim was to examine TBS before and after one year of weight loss.

To our knowledge this is the first study the examines the effect of vertebral abnormalities on TBS and LS-BMD over a one-year weight loss trial. To begin, almost half of the population had the presence of a vertebral abnormality at baseline. There has been a recent body of literature refuting the protective effect of obesity on bone health [8,9]. Our results refute this notion as well, since these abnormalities, that can be caused by obesity, were shown to negatively affected BMD. As expected, LS BMD was lower in the corrected BMD when compared to the uncorrected [11]. There was also a significant difference in the change from baseline between the corrected and the uncorrected LS BMD over the one year. The corrected LS-BMD had a greater decrease from baseline than the uncorrected. In addition, these vertebral abnormalities differentially affected the change from baseline due to weight loss since there was a decrease in the >5% WL group in the corrected LS BMD but not the uncorrected, although this difference was not statistically significant. This indicates that these vertebral abnormalities may mask changes in LS BMD throughout aging and weight loss. The effect or lack thereof of a vertebral abnormality on TBS could be because the TBS analysis was done on the whole spine image meaning it did not exclude the vertebrae that had an abnormality. However, since LS-BMD was significantly increased due to these abnormalities and there was a significant difference between the change from baseline in LS BMD measurements, the protocol for assessing fracture risk in this population should incorporate a vertebral abnormality analysis and a subsequent correction,



as needed. Without this analysis the fracture risk assessments may not be accurate and therefore the fracture risk could be miscalculated.

Aging causes declines in BMD, this decline with aging is most likely due to changes in hormones which can cause imbalances in bone turnover, but lifestyle components also have a role [18]. Similar declines were seen in this study at the hip, but this decline was not seen with TBS. Declines in BMD should be monitored carefully since it can increase the risk for osteoporosis, osteopenia and fracture [6]. To combat the effects of aging on BMD, studies have shown that resistance training exercise can dwindle the decrease in BMD over time [3,6]. This type of exercise has been shown to be osteogenic and prevent low bone mass [3,30,31]. Resistance training is defined as weight bearing exercises, such as weightlifting. Therefore, due to its osteogenic effect, resistance training should be recommended to build strong bones and combat the effect of aging on bones [30]. But, more specific to this population of overweight and obese older adults who are asked to lose weight to prevent comorbidities, the osteogenic effect of resistance training could also be helpful to dwindle the bone loss that is so commonly observed with weight loss and was observed in this study at the hip and the trochanter.

Although it was hypothesized that TBS would respond similarly to BMD with weight loss, and thus also show a decrease, we found that TBS was not affected by weight loss. Over the 12-month study TBS did not significantly change from baseline in either WL group. Previous studies have observed an increase in TBS during weight loss, observed at 6-months, but this increase is not seen at 12-months. [3,32]. It is possible that this increase shown in the previous studies was due to the high proportion of visceral adiposity due to a high BMI which has been shown to attenuate the accuracy of the score. So, when the TBS score was modified this past year to correct for visceral adipose tissue, it was believed that the score would better reflect the

influence of weight loss on TBS and might also decline similar to BMD. However, there was no change in TBS in this population, and it is concluded that overall, weight loss has no effect on vertebral bone quality.

Moreover, when we examined the effect of sex on TBS, we found a significant increase in TBS at 6 months for men, but not women. The MrOS study which is a study of Osteoporotic Fractures in Men found that those who had >10% weight loss, also exhibited an increase in TBS [33]. But knowing that the accuracy of TBS is attenuated by high BMI and high proportion of visceral adiposity it can be concluded that this may influenced the MrOS findings[28, 27]. To help understand why the rise in TBS at 6 months occurred only in the men in the current study, a subset of persons (OWLE dataset) had visceral adipose tissue estimated with the DXA software. In this subset, men had a significantly higher percent of their total fat be from visceral adipose tissue, about 6%, when compared to about 3% in women. Since this increase at 6-month is only seen in the men, and not the women, it is possible that the higher proportion of visceral adiposity might have attenuated the accuracy of the TBS measurement and may account for the rise with weight loss in overweight and obese men, but not women.

TBS is hard to compare to different studies due to the use of different algorithms and certain modifications. For example, the modification to correct for high BMI used in this study only became available this year. So, studies published earlier did not have this available to them. For instance, in this study, mean TBS was higher in men when compared to women, 1.373 and 1.336, respectively. This is similar or slightly higher than the TBS values reported in the Vitamin D and Omega 3 Trial (VITAL); 1.331 and 1.278 in men and women, respectively [22]. However, a study that published reference ranges of TBS for each age range found TBS to be lower in men than women in the 60-69 years range which is where the average age of the current

study is (60 years old) [34]. This difference may be due to the use of an older algorithm, unlike the modified and newer one that we used [34]. The average BMI in the VITAL study was lower than in the current investigation because VITAL excluded those who had a BMI > 37 kg/m<sup>2</sup> as per the recommendation with the TBS algorithm used in that study [22]. In contrast, we included a wider range of BMI values since we used a new TBS algorithm that corrected for tissue thickness. Typically, leaner persons (BMI < 25 kg/m<sup>2</sup>) have a higher TBS score than overweight or obese persons (BMI > 25 kg/m<sup>2</sup>) [22]. This indicates obesity does reduce bone quality. The current study's findings also found this result, since almost 50% of the population had degraded TBS at baseline and in addition the mean TBS was in the partially degraded bone category with mean BMI of 32 kg/m<sup>2</sup> (range 25-43 kg/m<sup>2</sup>). Overall, TBS is a useful tool, but like BMD, its accuracy may be attenuated by high BMI. Thus, in the current study, examining an overweight and obese population and changes in the soft tissue surrounding bone that occurs with weight loss can complicate the ability to measure BMD or TBS with as much precision as in lean persons.

## **5. Strengths and Limitations**

A limitation of this project is that the outcome was a secondary analysis for previous trials that were designed to examine BMD. However, because both studies were addressing bone outcomes in older overweight and obese persons, there were similar inclusion and exclusion criteria. In addition, originally the TBS calculation was not corrected, and because the software is still relatively new to the field, it is unclear if further corrections will be necessary. In addition, the TBS was determined on all four vertebrae (as is typical for assessment of the lumbar spine), but a future modification to the TBS software could be to individualize the assessment to

determine whether vertebral abnormalities and exclusion assessed using BMD should also be applied to TBS analysis.

## **6. Conclusion**

In conclusion, vertebral abnormalities significantly elevated LS BMD, and masked the change from baseline in BMD. Because of this elevation, these abnormalities should be examined more closely when analyzing LS images and assessing fracture risk in the overweight and obese. TBS was partially degraded in this population, indicating that obesity does reduce bone quality, but it seems that TBS is relatively unaffected by weight loss and therefore we can conclude that weight loss does not seem to impact bone quality. Further research should be conducted on the effect of these vertebral abnormalities on TBS.

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	OWLE	CLIP-II
N	88	43
Age	57.8 ± 4.4	66.2 ± 4.6
% Female	68%	74%
<b>Race</b>		
White	90%	63%
African American	8%	32%
Other	2%	5%
TBS	1.361 ± 0.910	1.318 ± 0.071 *
L1-L4	1.191 ± 0.18	1.25 ± 0.17
Corrected L1-L4	1.151 ± 0.17	1.202 ± 0.15
Femoral Neck	0.939 ± 0.12	.931 ± 0.10
Trochanter	.817 ± 0.12	.802 ± 0.11
Total Hip	0.999 ± 0.13	.994 ± 0.10

Table A1: Baseline Characteristics of OWLE and CLIP-II Studies. Values are mean ± SD.  
TBS: trabecular bone score.

**Objective:** To examine the amount of visceral adipose tissue (VAT) in men and women during weight loss.

**Hypothesis:** Men will have a significantly higher VAT than women.

**Methods:** One way-ANOVA was performed to ascertain the difference between men and women.

**Results:** At baseline, men had a higher amount of VAT than women ( $p=0.000$ ). In addition, men had a higher proportion of VAT to Fat when compared to women. Of the men's total fat, about  $6.16 \pm 0.02\%$  of it was VAT, of the women's total fat, about  $2.66 \pm 0.01\%$  was VAT.

**Conclusion:** The higher proportion of VAT to fat in men could potentially attenuate the accuracy of the TBS value.

	Women (n=60)			Men (n=28)		
	Baseline	Final	Change (%)	Baseline	Final	Change (%)
Fat Free soft tissue (g)	43744 $\pm$ 5416	42713 $\pm$ 5142	-2.23 $\pm$ 4.42	59386 $\pm$ 9966 *	59893 $\pm$ 10265	1.92 $\pm$ 9.96
Total Fat (g)	38581 $\pm$ 9120	35440 $\pm$ 9430	-8.59 $\pm$ 9.58	35203 $\pm$ 9823	32884 $\pm$ 10242	-6.27 $\pm$ 13.27
VAT (g)	1033 $\pm$ 547	876 $\pm$ 507	-13.09 $\pm$ 32.20	2229 $\pm$ 925	1939 $\pm$ 802	-11.45 $\pm$ 33.44
VAT/Total Fat	2.66 $\pm$ 0.01%	2.46 $\pm$ 0.01 %	-1.00 $\pm$ 0.30 %	6.16 $\pm$ 0.02 %	5.72 $\pm$ 0.02 %	-4.06 $\pm$ 0.40 %

Table A2: Baseline characteristics of body composition in OWLE dataset.

Values are mean  $\pm$  SD

**Objective:** To ascertain if the presence of a vertebral abnormality also artificially elevated TBS.

**Hypothesis:** A vertebral abnormality will elevate TBS.

**Methods:** One-ANOVA compared the difference between those who had an abnormality at baseline to those who did not.

**Results:** A vertebral abnormality did not significantly increase TBS.

**Conclusion:** Although a vertebral abnormality did not alter TBS, it is suggested this may be because the TBS value reflects the whole lumbar spine (L1-L4) and did not exclude the vertebrae that had the abnormality. A future study should determine TBS for site-specific vertebrae to whether or not the abnormality affects TBS.

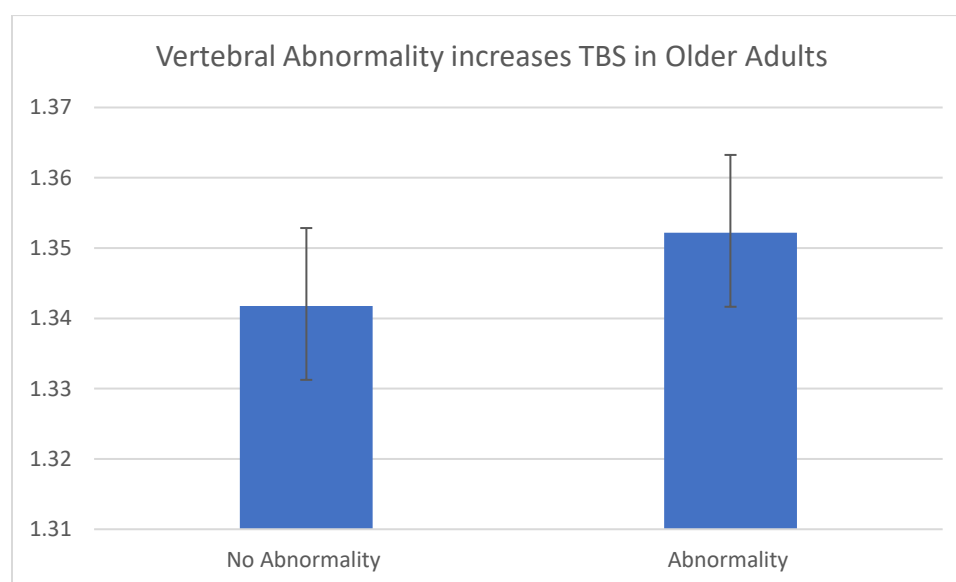


Figure A1: Vertebral Abnormality increases TBS, although not significantly.



**Objective:** To ascertain the prevalence of a vertebral abnormality in both Caucasian and African Americans and to determine if this differentially effects change in LS BMD.

**Hypothesis:** Abnormalities will be more prominent in the Caucasian population since they have a higher risk for fracture and low bone mass.

**Results:** 56.6% of Caucasians had an abnormality at baseline. 28.6% of African Americans had an abnormality at baseline. African Americans had a greater decrease in corrected LS-BMD when compared to Caucasians.

**Conclusion:** The Caucasian population have a higher risk for abnormalities at the lumbar spine than African Americans. However, there was a greater decrease in LS-BMD with correction of vertebral abnormalities in the African Americans, possibly indicating that the severity of the abnormalities may be greater in African Americans than Caucasians.

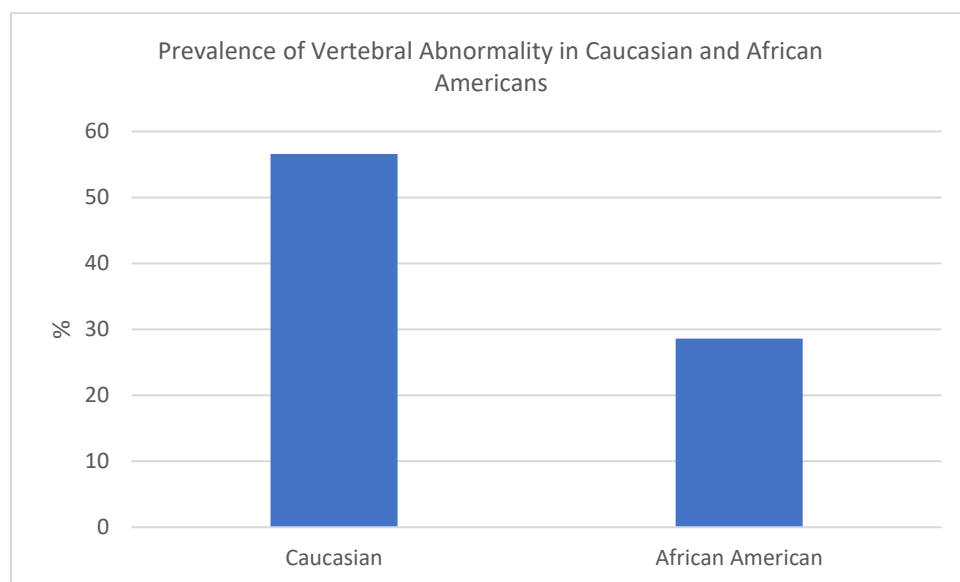


Figure A2a: Prevalence of a vertebral abnormality by race

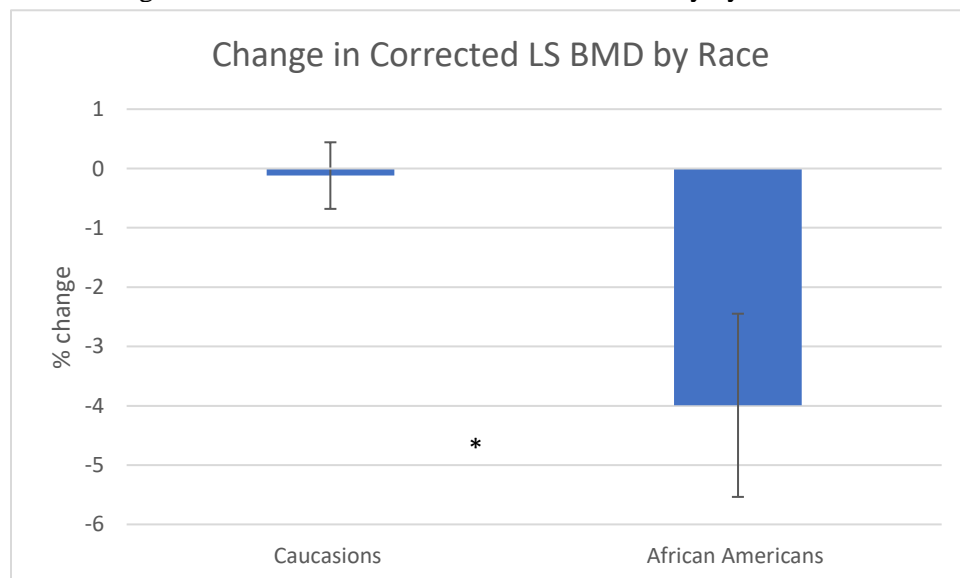


Figure A2b: Prevalence of a vertebral abnormality by race. \* Differs from Caucasians,  $p < 0.00$

**Objective:** To ascertain the prevalence of abnormalities in each BMI category.

**Hypothesis:** Those in the normal BMI category will have the most abnormalities due to their increased risk for bone fractures.

**Results:** About 50% of those with a normal BMI had an abnormality, about 20% in the overweight category had an abnormality and 40% of those with an obese BMI had an abnormality.

**Conclusion:** Low BMD associated with a normal BMI increases the risk for abnormality, but the degraded quality of bone seen in the obese category also increases the risk for an abnormality.

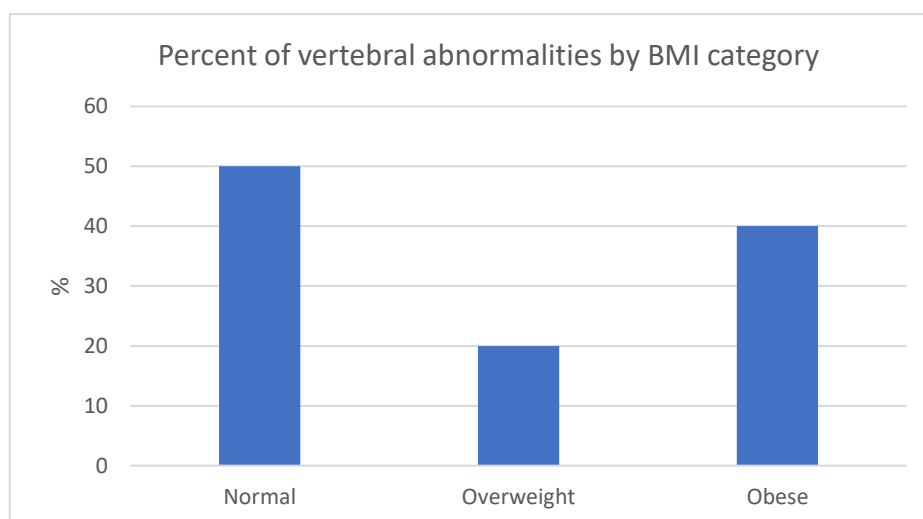


Figure A3: Prevalence of a vertebral abnormality by BMI category.

**Objective:** To ascertain the correlation between TBS and LS BMD.

**Hypothesis:** TBS will be positively correlated to both corrected and LS uncorrected LS BMD.

**Methods:** Pearson Correlation between TBS and LS BMD.

**Results:** TBS is positively correlated with corrected LS BMD ( $r=.568$ ,  $p=.000$ ) and uncorrected LS BMD ( $r=.534$ ,  $p=.000$ ).

**Conclusion:** TBS is positively correlated to both uncorrected and corrected LS BMD.

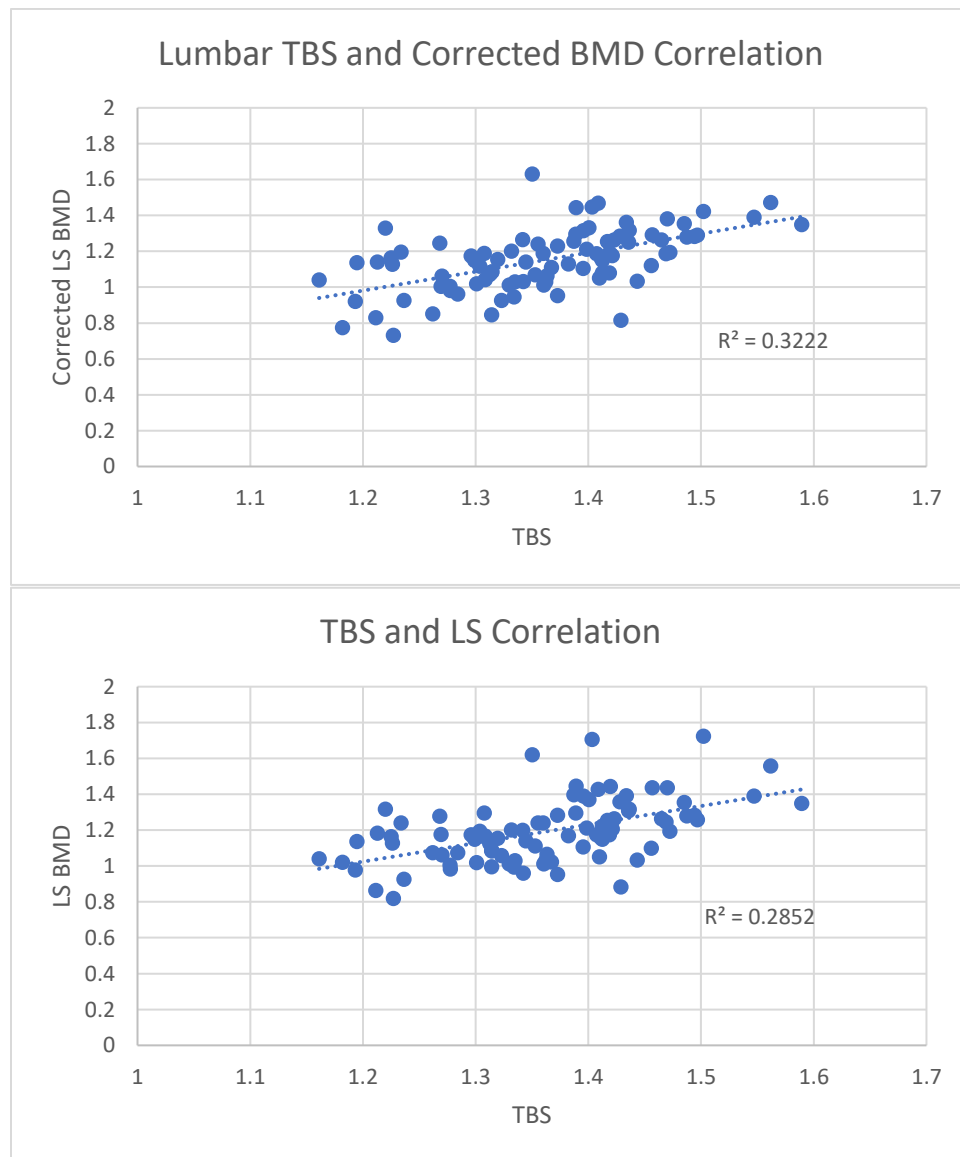


Figure A.4a and b: Pearson Correlation shows that TBS is positively correlated to both corrected and uncorrected BMD.

BMD, bone mineral density. LS, lumbar spine. TBS, trabecular bone score

**Objective:** To ascertain the correlation between trabecular bone score (TBS) and Fat (total and visceral adipose tissue, VAT) in the OWLE data (n=88).

**Hypothesis:** TBS will be inversely associated to VAT.

**Methods:** Pearson Correlation examining TBS and VAT and other soft tissue compartments.

**Results:** TBS is not correlated to VAT ( $r=.158$ ,  $p=.145$ ) or other soft tissue compartments.

**Conclusion:** TBS is not correlated to VAT or other soft tissue compartments (fat free soft tissue and total fat) in this subset of the current's study population.

VAT	TBS
<b>Pearson Correlation</b>	.158
<b>sig (2 tailed)</b>	.145
<b>N</b>	88

Fat Mass	TBS
<b>Pearson Correlation</b>	-.013
<b>sig (2 tailed)</b>	.903
<b>N</b>	88

Lean Mass	TBS
<b>Pearson Correlation</b>	.197
<b>sig (2 tailed)</b>	.067
<b>N</b>	88

Table A3a, b, c: Pearson correlation between TBS and visceral adipose tissue (VAT). TBS was not significantly correlated to any body composition. TBS, trabecular Bone Score. VAT, visceral adipose tissue

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