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Sedentary behaviour and bone health in older adults: a systematic review

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Declarations

Conflict of Interest

Dawn A. Skelton is a Director of a not for profit training company, Later Life Training, which provides training to health and leisure professionals to deliver strength and balance training.

Lauren McMichan, Michael Dick, Sebastien F.M. Chastin, Neville Owen, David W. Dunstan, William D. Fraser, Jonathan C.Y. Tang, Carolyn A. Greig, Sandra Agyapong-Badu, Alexandra Mavroeidi declare no conflict of interests.

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Abstract:

Purpose:

Older adults spend more than 8 hours/day in sedentary behaviours. Detrimental effects of sedentary behaviour (SB) on health are established, yet little is known about SB and bone health (bone mineral density; BMD) in older adults. The purpose of this review is to examine associations of SB with BMD in older adults.

Methods:

Five electronic databases were searched: Web of Science (Core Collection); PubMed; EMBASE; Sports Medicine and Education; and PsycInfo. Inclusion criteria were: healthy older adults mean age ≥65 years; measured SB; measured BMD using dual-energy X-ray absorptiometry. Quality was assessed using National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

Results:

After excluding duplicates 17,813 papers were assessed; 17,757 were excluded on title/abstract, 49 at full text, resulting in two prospective and five cross-sectional observational studies reviewed. Four were rated 'good' and three were rated 'fair' using the quality assessment criteria. Findings varied across the studies and differed by gender. In women, four studies reported significant positive associations of SB with BMD at different sites, and two found significant negative associations. Five studies which examined both men and women, men reported negative or no associations of SB with femoral neck, pelvic, whole body, spine or leg BMD.

Conclusion:

While these findings suggest differences between men and women in the associations of SB with BMD, they may be due to the varying anatomical sections examined for BMD, the different methods used to measure SB, the varied quality of the studies included and the limited number of published findings.

Keywords:

Sedentary behaviour, older adults, bone health, bone mineral density

Abbreviations:

BMD = Bone Mineral Density

DXA = Dual-X-Ray Absorptiometry

FN = Femoral Neck

LPA = Light Physical Activity

LS = Lumbar Spine

MVPA = Moderate-to-Vigorous Physical Activity

PA = Physical Activity

SB = Sedentary Behaviour

ST = Sedentary Time

TB = Total Body

TF = Total Femur

TH = Total Hip

TS = Total Spine

Introduction

Sedentary behaviour (SB) can be defined as "any waking activity characterized by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture" [1]. High volumes of SB can be detrimental to health, particularly in people who do not undertake sufficient amounts of moderate-vigorous physical activity (MVPA) [2, 3]. Adverse health consequences include higher risk of cardiovascular disease [4], diabetes mellitus [5], and reduced cognitive function [6]. SB encompasses many behaviours performed routinely throughout the day, for example, sitting at a chair/sofa, driving to and from places, and watching television [7]. Older adults (aged 65+ years) can accumulate > 8 hours of time spent in SB daily [8, 9], with an average being 9.4 hours/day [10].

The beneficial effects of daily weight bearing physical activities on bone health are well established [11]. Aging is a natural process, within which bone mass deterioration occurs, including changes to the structure and composition [12] of bone tissue. Although some bone loss is typical of the aging process, osteoporosis is not an inevitable disease of the old, with many risk factors for osteoporosis and osteoporotic fracture being modifiable [13]; low levels of PA have long been recognised as such a risk factor. A published consensus statement on Exercise and Osteoporosis recommends meeting the PA guidelines (accumulation of 150 mins/week of moderate PA) for health and reducing prolonged SB alongside more specific recommendations for exercise (resistance training and impact) [14]. There is a high prevalence of fractures in those over the age of 50 years, with one in two women and one in five men fracturing a bone [15]. It is estimated that 500,000 fragility fractures occur in the United Kingdom every year [16], with hospital costs of hip fractures alone estimated at £1.1 billion [17].

Mechanical forces (through gravitation or muscular loading) are essential for the maintenance of bone health, therefore reducing these forces can have a detrimental effect [18]. Space flight and bed rest studies have shown that reducing mechanical forces leads to substantial reductions in bone strength [19]. Although the space-flight and bed-rest evidence is from extreme and unusual circumstances, SB also involves the reduction of mechanical forces, and could have a detrimental effect of bone health. A recent systematic review explored the effects of SB on bone health in children, adolescents and young adults [20]. The review yielded 17 studies. It was reported that there was a moderately negative association between SB and bone health in the lower extremities. It was also reported that one less hour of sedentary time mimics the positive effect of 18 minutes of MVPA in femoral neck bone mineral density (BMD); however, this finding was weighted heavily on one strong longitudinal study in boys [21].

Gender also appears to play an important role on bone quality, with men exhibiting up to 20% higher BMD compared to women [22]. This was evident in a study which analysed data from the National Health and Nutrition Examination Study where negative associations between SB and hip BMD in adult women, but not men, were identified [23].

Despite the emerging evidence on the potential detrimental influence that SB may have on skeletal health in younger populations, little is known about the associations of SB and bone health (specifically, BMD) in older adults. Therefore, the purpose of this study was to systematically review the evidence on associations of SB with BMD (total and site-specific) in older adults.

Methods

Protocol and Registration

147 The protocol for this systematic review was registered on Prospero
148 [CRD42019138999] in June 2019. The review was modelled using the PRISMA guidelines
149 [24, 25].

150

151 Eligibility Criteria

152 Studies which explored the associations of SB on BMD in healthy older adults (mean
153 age ≥ 65 years old) were included in the review. Other inclusion criteria were studies which
154 measured SB, and measured BMD using Dual-Energy X-ray Absorptiometry (DXA). Studies
155 were peer reviewed, and in the English language.

156

157 Information Sources

158 Five electronic databases were searched: Web of Science (Core Collection), PubMed,
159 EMBASE, Sports Medicine and Education, and PsycInfo. The search strategy was originally
160 conducted in March 2019. The search strategy was then repeated using additional search
161 terms to broaden the search results. This was conducted in June 2019.

162

163 Search

164 The search strategy used for the databases is shown in Table 1. Note adaptations to
165 truncations and limiting factors were made based on the individual databases.

166

167 **Table 1** Search Strategy

Population	(Adult* OR "Older Adult*" OR Elderly OR Geriatric OR Ageing OR Aged)
Search Operator	AND
Outcome	(Bone OR "Bone Health" OR "Bone Mineral Density" OR "Bone Mineral" OR "Bone Mass" OR "Bone Fracture*" OR "Bone Strength" OR Osteoporosis OR "Bone Mineral Content")
Search Operator	AND
Exposure	(Sedentar* OR "sedentary behavior" OR "Sedentary Behaviour" OR "Sedentary Time" OR "Sitting Time" OR Sitting OR "screen time" OR "television viewing" OR inactiv* OR "activity restriction" OR "Computer use" OR "stationary behaviour" OR "stationary behavior" OR lying OR reclining OR "non-screen based behaviour" OR "non-screen based behavior")
Limits	English only. Humans only.

168

169 Study Selection

170 Articles retrieved from the search strategy were imported into EndNote Reference
171 Manager, version X8.2 (Thomson Reuters, Philadelphia, PA) and duplicates were removed.

Articles were then exported to a Microsoft Excel, version 2016 (Microsoft Corp, Redmond, WA) spreadsheet where titles were screened. Articles included based on title screening were reviewed at abstract level, and then reviewed as full text. We also reviewed the bibliography of full text papers to identify any additional related papers. All articles were reviewed by the first author (LM) and a sample (10%) was double checked by another reviewer (AM) as per PROPSERO protocol. Any articles where there was uncertainty at abstract and full text level were also checked by the senior author (AM). If there were any discrepancies, a discussion between the two authors was conducted until an agreement was reached. Exclusion of articles were based on criteria and were excluded if they did not assess SB and BMD in older adults (mean age $\geq$ 65 years). Studies which included multiple age ranges but performed a sub-analysis on older adults were included in the review.

Data Collection Process and Data Items

Data were extracted and imported into a standardised Microsoft Word, version 2016 (Microsoft Corp, Redmond, WA) table. Data extracted were: author(s)/year of publication; study design; sample size; gender; age range; SB measurement method and outcomes; BMD measurement methods and outcomes; overall results. Were pivotal data was missing we aimed to contact the authors and request such data.

Quality Assessment

Quality of studies included in the review was assessed using the 'Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [26]. The tool consists of a 14-item checklist: clearly stated research question; specific study population; rate of participation of eligible persons; subject selection process; justification of sample size;

exposure measured prior to outcome(s); suitable timeframe between exposure and outcome; levels of exposure; exposure measures clearly defined; exposure(s) assessed more than once over time; outcome measures defined valid, reliable and consistent; blinding of outcome assessors; loss to follow-up; and, adjustment for key confounders. Studies were then awarded a rating of good, fair or poor. Quality was assessed by the first and last authors (LM/AM) to ensure agreement. It should be noted that one of the co-authors (SFMC) was the co-author of 3 of the included studies.

Summary of Measures

Primary exposure measures were SB (self-reported by questionnaire or objectively measured) and BMD measures were the outcomes. Studies included objective and subjective methods of assessing SB. The anatomical sites that were evaluated were grouped into three separate categories; lower extremities (including the femoral neck (FN), total femur (TF), hip, legs), trunk (including ribs, lumbar spine (LS)) and total body (TB). Markers of bone health were measured using DXA in all included studies since comparison of bone health is not possible if different assessments methods are used.

Results

Study Selection

The initial search strategy yielded 19,194 potentially relevant studies (Figure 1.). Following deduplication, this number was reduced to 17,813. Seventeen thousand seven hundred fifty seven articles were excluded based on title and abstract. Forty-nine articles were excluded at full text (see supplementary material for complete list of excluded studies),

leaving seven included for review [23, 27-32]. One of those studies (Chastin et al [23]) did not present data for the over 65s separately in their published manuscript. However, as SFMC is a co-author in the current review, he was able to repeat the main paper analysis from the NHANES database refining it to those aged over 65 years; this sub analysis was included in the current review.

Study Characteristics

Five studies were cross-sectional [23, 27, 29-32] and two were longitudinal [28, 29]. Sample size ranged from 112 [30] to 1134 [29] participants. Two studies included women only [27, 29]. Mean age of participants ranged from 64.5 ± 7.2 years [28] to 76.9 ± 5.3 years (men) and 76.7 ± 4.7 years (women) [31]. A full summary of study characteristics and results are shown in Table 2. Four studies were rated good [23, 28-30] for quality, whilst three were rated fair [27, 31, 32].

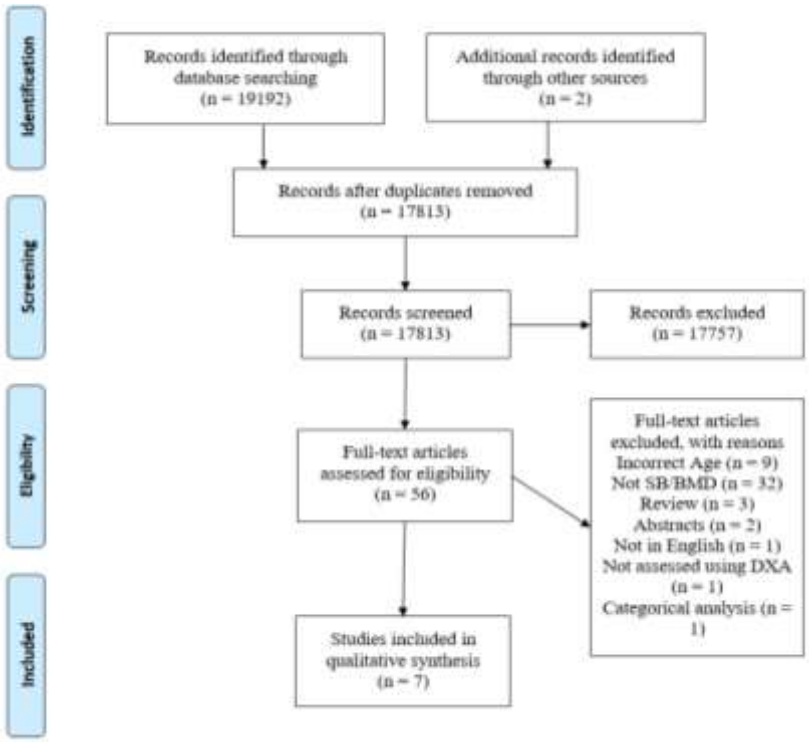

Fig 1 PRISMA diagram [25] of the screening process

233

234 Measurement of BMD and SB

235 All studies measured BMD using DXA. Six studies used Hologic models [23, 27, 28, 30-32],
236 whilst one used a Lunar model [29]. Measures of SB differed between studies. Two studies
237 used questionnaires to assess SB [27, 29]. The questionnaires asked how many hours per day
238 participants were sedentary. Five studies assessed SB using objective measures
239 (accelerometry) [23, 28, 30-32]. Two studies [31, 32] used ActiTrainer/ActiGraph wGT3X-
240 BT, two used used ActiGraph GT1M [23, 28], and one used GENEActiv Action
241 [30].Accelerometer placement was different between studies, with the majority of the studies
242 [23, 31, 32] using hip mounded accelerometers and one study [30] using a leg mounded
243 accelerometer. All studies asked participants to wear their accelerometers for 6-7 consecutive
244 days but some participants had to remove their accelerometer during waking hours when
245 engaging in water based activities [23, 31, 32]. Every study had its own unique wear-time
246 protocol. For example, data were excluded from the analysis if participants did not wear
247 device for at least 5 days and wore the device for less than 10 hours per day [23, 28] but these
248 criteria were different for the studies by Rodrigues- Gomez et al who included only results
249 with at least 4 valid days that included at least 8h/day of wear time [31, 32].

250

251 Total Body BMD

252 Four studies measured total BMD [28, 30-32]. McMillan et al [28] found no significant
253 associations over time between SB and total BMD in either men or women, using prospective
254 linear regression analyses.

255 Rodriguez-Gomez et al [31] reported a borderline significant positive association
256 between SB and total body BMD when both genders were analysed together. There were

gender differences when analyses were separated. There were no significant associations between SB and total body BMD for men. For women, significant positive associations were found between SB and total body BMD ($\gamma = 0.022$; $p = 0.00$). Gender differences were also reported in Rodriguez-Gomez et al [32] who found a significantly negative association between SB and total body BMD ($\gamma = -0.015$; $p = 0.041$) in robust healthy men, but reported significant positive associations between SB and total body BMD ($\gamma = 0.020$; $p = 0.003$) in robust healthy women. It is important to note that the two Rodriguez-Gomez [31, 32] analyses are based on the same cohort and models from both studies were adjusted for age, gender, BMI, fat and lean mass, alcohol, smoking, nutrition, calcium, education, level of income, marital status, frailty, arthritis, and thyroid disease.

Onambele-Pearson et al [30] also found differences between men and women. For daily SB, there were no significant associations with total BMD for men, whilst there was a significant positive association ($r = 0.317$, $p < 0.01$) for women. However, when analyses were adjusted (age, total fat mass, general anthropometry) this was non-significant. Onambele-Pearson et al [30] also explored the association between SB bouts and BMD. Whilst breaks in SB did not have a significant impact on total BMD in women, there was a positive association in men ($r = 0.330$, $p < 0.01$). There was also positive association in men when SB bouts were ≥ 5 mins ($r = 0.373$, $p < 0.01$).

Lower Extremities

In a prospective study, Nguyen et al [29] reported that, over time, sedentary lifestyle significantly reduced BMD in the femoral neck (FN) ($-1.5 \pm 0.2\%$, $p < 0.001$) in women. Adjusted analyses (accounting for age, PA, baseline weight, weight change over time and baseline BMD) also suggested a significant reduction in femoral neck BMD ($-1.35 \pm 0.8\%$, p

< 0.05).The other longitudinal study included in the review (McMillan et al [28]) also conducted analyses separately by gender. .Their adjusted (model 2) prospective multivariate linear regression analyses, showed a significantly positive association between SB and total hip BMD ($\beta = 0.199$, $p = 0.046$) in women. For adjusted (model 2) prospective multivariate linear regression analyses in men, there were significantly negative associations between SB and femoral neck BMD ($\beta = -0.232$, $p = 0.047$). Model 2 analyses were adjusted for age, height, lean mass and smoking.

Onambele-Pearson et al [30] reported no significant associations for daily SB for men and BMD ; in women, there were significant positive associations between daily SB and lower limb BMD ($r = 0.272$, $r_{adj}^{n} = 0.260$, $p < 0.05$). Similar findings were reported for breaks in SB ($r = 0.299$, r_{adj}^{n} = non-significant, $p < 0.05$), and for bouts of SB < 5 mins ($r = 0.334$, r_{adj}^{n} = non-significant, $p < 0.01$). There was also a positive association between breaks in SB and pelvic BMD in women only ($r = 0.232$, r_{adj}^{n} = non-significant, $p < 0.05$).

Braun et al [27] reported a negative association in older women between ST and femoral BMD (b (SE) = -0.0028 (0.0001);$p = 0.027$). These analyses were adjusted for race/ethnicity, milk consumption or supplement use, BMI, smoking, osteoporosis history, prednisone or cortisone use, and menopausal status.

Rodriguez-Gomez et al [31] reported significant positive associations between SB and leg leg BMD ($\gamma = 0.028$, $p = 0.00$). There were no significant associations reported for any femoral region assessed. When men and women were examined separately, there were no associations between SB and leg/femoral region BMD in men. In women, there were significantly positive associations for leg BMD ($\gamma = 0.063$, $p = 0.00$), but no associations for femoral regions. In the pelvic region, a significant negative association was reported between SB and BMD ($\gamma = -0.027$, $p = 0.05$) in men only.

Rodriguez-Gomez et al [32] reported significant positive associations between SB and leg BMD ($\gamma = 0.035$, $p = 0.000$) in robust (those who do not exhibit any of the frailty criteria set out by Fried et al [33]) older adults. No associations were reported for femoral neck. When analyses were conducted separately for men and women, men were found to have negative associations for leg BMD ($\gamma = -0.018$, $p = 0.036$). However, in women there were positive associations between SB and leg BMD ($\gamma = 0.066$, $p = 0.000$). No associations were reported for femoral neck in either gender.

Trunk

Only two studies reported significant associations between SB and areas of the trunk [23, 30]. In women, Onambele-Pearson et al [30] reported significant positive association between daily SB and spine BMD ($r = 0.233$, $p < 0.05$), although this was non-significant when adjusted for confounders. There were significant positive associations between SB breaks and SB bouts of < 5 minutes, and BMD of the ribs ($r = 0.266$, $p < 0.05$; $r = 0.328$, $p < 0.01$, respectively). The association between breaks in SB and BMD were non-significant when adjusted for confounders. There was a negative association between W50% min (defined as "the bout duration below which half of all sedentary time is accrued" [30]) and rib BMD ($r = -0.224$, $p < 0.05$; non-significant after adjusting). For men, breaks in SB and SB bouts ≥ 5 minutes were positively associated with rib BMD ($r = 0.282$, $p < 0.05$; $r = 0.349$, $p < 0.01$, respectively).

A significant negative association with sedentary time (ST – total duration of daily SB bouts) and spine BMD with ($p = 0.05$) and a significant positive association between fragmented ST and spine BMD ($p = 0.05$) were reported for the unpublished sub-analysis of the NHANES data by Chastin et al [23], yet there were non-significant differences between

328 women and men. Analyses were adjusted for age, BMI, ethnicity, parathyroid hormones,
329 smoking, alcohol (men only) and prednisone use (women only). (Table 2).

330

331 Quality Assessment

332 Of the seven studies included in the review, four were rated good [23, 28-30] and
333 three were rated fair [27, 31, 32]. Table 3 provides a full summary of each study and the
334 criteria which the assessment was based on.

335 **Table 2** Overview of study attributes and findings on sedentary behaviour with bone outcomes

Author	Sample size, gender (♂/♀), age (years)	SB outcomes measured	SB assessment method	Bone assessment method	Sites of anatomical assessment	Conclusions/results
			CROSS-SECTIONAL STUDIES			
Chastin et al (sub analysis of ref [23]	591 (n =259 ♀) Age = 75.2 ± 6.7	Total ST (Daily) Bouts of SB	Accelerometry (ActiGraph GT1M)	DXA	TF, FN, Trochanter Ward triangle, Intertrochanter, Spine	No significant association for men or women between ST or bouts of SB with TF, FN, Trochanter Ward triangle, Intertrochanter BMD. Significant negative association with spine BMD for ST (p =0.05), sub analysis per gender leads to non-significant results. Significant positive association between more fragmented ST (shorter bout duration) and spine BMD (p=0.05), sub analysis per gender leads to non-significant results.
Onambele-Pearson et al [30]	112 (n = 61 ♀) Age = 72.5 ± 6.4	ST (hours/day), Bouts of SB	Accelerometry (GENEActiv Action)	DXA	Ribs, Spine, Pelvis, Upper Limbs, Lower Limbs, Total Body	♂ = Significant positive association between breaks in SB and BMD for ribs ($p < 0.05$) and total BMD ($p < 0.01$). SB bouts > 5 minutes were positively associated with lower limbs ($p < 0.05$), ribs and total BMD ($p < 0.01$). No significant associations reported for total ST. ♀ = Significantly positive association between total ST and spine, lower limb ($p < 0.05$) and total ($p < 0.01$) BMD. Significant positive correlation between breaks in SB and ribs, pelvis and lower limbs ($p < 0.05$). For bouts < 5 minutes, there were positive associations for ribs and lower limbs ($p < 0.01$). There was a negative association between W50% and rib BMD ($p < 0.05$).
Rodriguez-Gomez et al [31]	871 (n =476 ♀) ♂ age = 76.9 ± 5.3 ♀ age = 76.7 ± 4.7	Total ST, separately for ♂ and ♀	Accelerometry (ActiTrainer & Actigraph wGT3X-BT)	DXA	TB, LS (L1-L4), FN, TH (greater trochanter, inter trochanter, Ward's triangle) and FN), BMD &	♂♀: SB positively associated with leg /BMD ($p = 0.00$) and whole body BMD ($p = 0.05$). ♂: SB negatively associated with pelvic BMD ($p = 0.05$) ♀: SB was positively associated with whole body /BMD (;$p = 0.00$) and leg /BMD ($p = 0.00$). ♀: Reduce time spent in SB to reduce fracture risk.

Rodriguez-Gomez et al [32]	540 (n = 289 ♀), ♂&♀ Age = 76.0 ± 4.4 (robust individuals only)	Total ST	Accelerometry (ActiTrainer & Actigraph wGT3X-BT)	DXA	TB, LS (L1-L4), FN, TH, Leg BMD &	SB significantly positively associated with leg BMD/ ($p = 0.000$) for whole sample. ♂SB significantly negatively associated with TB BMD ($p = 0.041$) and leg BMD/ ($p = 0.036$) in robust men. ♀SB significantly positively associated with TB BMD/ ($p = 0.000$) and leg BMD/ ($p = 0.000$) in robust women.
Braun et al [27]	327 ♀ only Age ≥ 65	SB (mins/day)	Questionnaire	DXA	FN, LS (L1-L4) (trochanter, inter trochanter, Ward's triangle, TF, TS)	SB significant predictor of decreased Femoral BMD ($p = 0.027$), yet not a significant association in spinal BMD ($p > 0.05$).
LONGITUDINAL PERSPECTIVE STUDIES						
McMillan et al [28]	209, (n =111 ♀), Age = 64.5 ± 7.2	SB (mins/day), separately for ♂and♀	Accelerometry (ActiGraph GT1M)	DXA	TH, LS, FN, Pelvis, Legs & TB	♂: Negative association between SB and FN /BMD ($p = 0.047$) over 2.2 years. ♀: SB was positively associated with TH /BMD (; $p = 0.046$) over 2.2 years.
Nguyen et al [29]	1134 ♀ only n = 366 sedentary Age = 69.9 ± 7.4† (N=1134; N = 827 at follow up)	ST (hours/day)	Questionnaire	DXA	FN	ST was significantly associated with reduced BMD (-1.5 ± 0.2%, $p < 0.001$). 47% of individual's with significant bone loss (n = 163) were categorised within the sedentary group.

Abbreviations: BMD bone mineral density, DXA dual-X-ray-absorptiometry, FN femoral neck, LPA light physical activity, LS lumbar spine, MVPA moderate-to-vigorous physical activity, PA physical activity, SB sedentary behaviour, ST sedentary time, TB total body, TF total femur, TH total hip, TS total spine. † Mean age was calculated by as follows ((age of sedentary group x n sedentary group) + (age of moderately active group x n moderately active group) + (age active group x n active group)/(total N of participants)).

340 **Table 3** Summary of the quality assessment for each study using the National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional
341 Studies*.

	Chastin et al [23]	Braun et al [27]	McMillan et al [28]	Nguyen et al [29]	Onambele-Pearson et al [30]	Rodriguez-Gomez et al [31]	Rodriguez-Gomez et al [32]
1) Was the research question or objective in this paper clearly stated?	Y	Y	Y	Y	Y	Y	Y
2) Was the study population clearly specified and defined?	Y	Y	Y	Y	Y	Y	Y
3) Was the participation rate of eligible persons at least 50%?	Y	Y	Y	Y	CD	CD	CD
4) Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Y	Y	Y	Y	Y	Y	Y
5) Was a sample size justification, power description, or variances and effect estimates provided?	N	N	N	N	Y	N	N
6) For the analyses in the paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	CD	CD	CD	CD	NA	NA	NA
7) Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	NA	NA	Y	Y	NA	NA	NA
8) For exposures that can vary in amount or level, did the study examine different levels of exposure as related to the outcome (e.g. categories of exposure, or exposure measured as continuous variable)?	Y	N	NA	NA	Y	Y	Y
9) Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y
10) Was the exposure(s) assessed more than once over time?	NA	N	Y	Y	NA	NA	NA
11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y
12) Were the outcome assessors blinded to the exposure status of participants?	NA	NA	NA	NA	NA	NA	NA
13) Was loss to follow up after baseline 20% or less?	NA	NA	Y	N	NA	NA	NA
14) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Y	Y	Y	Y	Y	Y	Y
Rating	Good	Fair	Good	Good	Good	Fair	Fair

342 * Y = Yes, N = No, CD = Cannot Determine, NA = Not Applicable

Discussion

This review examined the associations between sedentary behaviour (SB) and BMD in older adults (mean age ≥ 65 years). Following the screening of potentially relevant articles, seven were included for review. Studies varied with respect to: measurement of SB (subjective vs objective measures); anatomical measures of BMD; and whether they were cross-sectional or longitudinal in nature. All studies used DXA as a method to assess BMD.

Summary of Evidence

Longitudinal studies [28, 29] that explored the associations of SB on BMD over time, reported negative associations between higher levels of SB with BMD for both sexes and at all sites measured (except for total hip BMD in the female subgroup of the McMillan study [28]). Disparities may have arisen due to the larger sample size of women in Nguyen's [29] study in comparison to McMillan et al [28] and both studies measured SB differently (subjectively vs objectively, respectively).

The results from the cross-sectional studies however revealed a different pattern between men and women. Some verified the deleterious associations of higher levels of SB on BMD [27] in women, while others failed to identify a significant association when sub analysis by gender took place [23] (possibly due to the smaller numbers of participants in each subgroup). However; the majority of the studies [30-32] found a disparity in results between men and women. In women, positive associations were observed between SB and BMD (at different measuring sites) while the opposite was true for their male counterparts. It appears that, as discussed by Rodriguez-Gomez et al [31], other movement behaviours could have an impact on the SB and BMD association. It is common to find concomitant higher SB and higher MVPA levels, thus the MVPA could have a positive association on BMD in the presence of high levels of SB [31]. In addition, it was also highlighted that greater sedentary

time could result in more frequent breaks in sitting time. More frequent postural changes could result in higher volumes of mechanical load bearing, thus resulting in a positive association on BMD [31].

Likewise, Onambele-Pearson et al [30] reported higher BMD in women who reported more frequent sedentary bouts and identified that this frequency of interruption to SB could contribute the higher BMD. This is consistent with other research in post-menopausal women, whereby a greater number of breaks in SB resulted in a 10% reduction in the odds of being diagnosed with osteoporosis/osteopenia [35]. A small study in frailer older adults found that breaking SB on a roughly hourly basis throughout the day improved physical function (timed up and go and 30 second chair stand) over a 10-week period, with no significant change in total ST or PA [36]. Similarly, Aunger et al [37] reported clinically significant improvement in physical function with non-significant increases in daily steps and time spent upright, despite non-significant decreases in SB. This modest body of emerging evidence suggests that regular interruptions to ST may be beneficial to bone health in older adults. Further investigation is warranted, with a particular emphasis being on the wider application of thigh-worn accelerometers which have been shown to have higher accuracy for detecting postural changes than wrist and waist-worn accelerometers.

Measurement of SB also varied between the studies included in this review. The two studies that measured SB subjectively using questionnaires, reported negative associations between femoral BMD and SB [27, 29] in women, which appears to contradict the findings of objectively measured studies. This could be attributed to the underestimation of SB and overestimation of PA; a bias which is commonly acknowledged when subjectively measuring PA [39]. It is reported that a random error of 2.5 hours per day is observed in subjective assessment of total SB and that subjective measures are not valid in assessing SB bouts [40]. Studies that used objective measures of SB reported more positive associations between SB

and BMD in women [28, 30-32]. It has been recently suggested, that moving to a single SB question assessing the whole day (via means of a visual analogue scale) might be worth considering for future studies, in cases where the use of a device-based measurement of PA is not practically possible [41].

Strengths and Limitations

This is the first review to explore the associations between SB and BMD in healthy older adults. However, there are a number of limitations influencing interpretation of the study findings. We appreciate that in order to reduce the risk of bias ideally two independent reviewers should have carried out all the steps of study selection and data extraction. In this study and due to time and resource limits the primary author (LM) screened the titles and abstracts, and excluded any irrelevant articles and only a sample (10%) of the studies were checked by one other reviewer (AM). As per PROSPERO protocol, when there were discrepancies in the inclusion or exclusion criteria discussion took place until an agreement was made.

Of the studies reviewed, two were prospective, and five were cross-sectional in design, as such any associations found here are not of a causal inference, and the possibility of bi-directional associations in the cross sectional studies cannot be ruled out. It should also be noted that the reported significant associations between SB and BMD, do not necessarily translate to clinically important associations and thus caution should be applied when interpreting these for such use. The generalisability of the results from this study should also be considered in light to the moderate quality of the studies included in the review, and the low numbers of participants in the subgroup (gender specific) analysis. In addition only healthy adults were assessed (clinical population were excluded from this review), therefore

there was no analysis on different populations and different health status in older adults. This included omitting the analysis of those who were deemed as 'frail' [32].

Likewise, the role of body weight as a confounder was not analysed in detail as part of this review. There is extensive body of findings suggesting that a higher body weight or body mass index can be associated with higher BMD [42, 43, 44] and reduced fracture risk [45]. These associations are probably attributable to the accentuated mechanical loading on the skeleton due to the increase in body mass although the exact mechanism is still not fully understood [46]. Indeed future studies should interpret data in the context of a number of confounders (including body weight and/or BMI) but also comorbidities, which are common in this older population and can induce sedentary behaviour.

There were various anatomical sites assessed using DXA and various methods of monitoring objectively and subjectively SB (different accelerometer types and questionnaires); in the absence of standardised assessments what may be concluded from the findings of the studies is limited. Although BMD measurement remains the most useful diagnostic tool for identifying patients with osteoporosis other technologies (e.g. ultra-high-resolution peripheral QCT, and 3D magnetic resonance imaging [MRI]) could noninvasively assess bone cross-sectional geometry and trabecular architecture. The combination of these, as well the assessment of number of fractures, may provide a more comprehensive picture of bone strength/health, compared with 2-dimensional BMD measurements in future studies. In addition this review included studies that used different densitometers to assess BMD, which is inevitably a limitation due to the well-established inherent measurement differences between scanners. In order to make progress in this field, we need well-designed longitudinal studies in this age group, with objective measures of SB and PA, and assessment of bone outcomes beyond just DXA.

Conclusion

This systematic review aimed to determine the associations between SB and BMD in healthy older adults (mean age ≥ 65 years). In conclusion, the research suggests there are gender difference in the associations of SB with BMD, with SB seemingly positive association on BMD in older women, but having a negative or no association in older men. However, there were only seven studies included in the review, with men being assessed in five of those studies, thus limiting the conclusions that can be drawn and thus these gender specific results should be treated with caution though due to the inherited issues with the relative small numbers of participants in subgroup analyses In order to better understand the associations of SB on BMD in older adults, there is a particular need to examine variations in patterns of sedentary time, using objective measures, including sit-stand transitions and how these might vary between men and women.

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