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Self-reported physical functional health predicts future bone mineral density in EPIC-Norfolk cohort

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Abstract:	Purpose Self-reported physical functional health may predict bone mineral density (BMD) and thus provide a method to identify people at risk of low BMD. In this study, the association between the 36-item short-form questionnaire (SF-36) physical component summary (PCS) score and future BMD in participants aged 40-79 years enrolled in the European Prospective Investigation of Cancer-Norfolk study was investigated. Methods Associations between a participant's SF-36 PCS score, measured 18 months after baseline health check, and broadband ultrasound attenuation (BUA – a measure of BMD), measured 2-5 years after baseline, were examined using sex-specific linear and logistic regression analyses adjusting for age, BMI, medical co-morbidities, lifestyle and socioeconomic factors. Results Data from 10,203 participants, mean (standard deviation (SD)) age 61.5 (8.9) years (57.4% women) were analysed from 1993-2000. For every five points lower PCS score in men and women, there was approximately a 0.5 dB/MHz lower mean BUA. In women, a PCS score of less than one standard deviation (1SD) below the sex-specific mean was associated with having a low BUA (< 1SD below sex-specific mean) and very low BUA (< 2.5SD below the sex specific mean); odds ratio (OR) (95% confidence interval) 1.53 (1.24, 1.88) and 8.28 (2.67, 25.69), respectively. The relationship was lesser so in men; corresponding OR (95%CI) were 1.34 (0.91, 1.98) and 2.57 (0.72, 9.20), respectively. Conclusions Self-reported physical functioning predicts BMD in an apparently healthy population, particularly in women. This could potentially provide an inexpensive, simple screening tool to identify individuals at risk of osteoporosis.
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Self-reported physical functional health predicts future bone mineral density in EPIC-Norfolk cohort

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Synopsis

Using a large population sample from the UK, we found that self-reported physical functional health may be used to predict future bone mineral density especially in women. It may be a useful and inexpensive way to identify individuals before further decline in bone mineral density and the risk of fracture.

Abstract

Purpose Self-reported physical functional health may predict bone mineral density (BMD) and thus provide a method to identify people at risk of low BMD. In this study, the association between the 36-item short-form questionnaire (SF-36) physical component summary (PCS) score and future BMD in participants aged 40-79 years enrolled in the European Prospective Investigation of Cancer-Norfolk study was investigated.

Methods Associations between a participant's SF-36 PCS score, measured 18 months after baseline health check, and broadband ultrasound attenuation (BUA – a measure of BMD), measured 2-5 years after baseline, were examined using sex-specific linear and logistic regression analyses adjusting for age, BMI, medical co-morbidities, lifestyle and socioeconomic factors.

Results Data from 10,203 participants, mean (standard deviation (SD)) age 61.5 (8.9) years (57.4% women) were analysed from 1993-2000. For every five points lower PCS score in men and women, there was approximately a 0.5 dB/MHz lower mean BUA. In women, a PCS score of less than one standard deviation (1SD) below the sex-specific mean was associated with having a low BUA (< 1SD below sex-specific mean) and very low BUA (< 2.5SD below the sex specific mean); odds ratio (OR) (95% confidence interval) 1.53 (1.24, 1.88) and 8.28 (2.67, 25.69), respectively. The relationship was lesser so in men; corresponding OR (95%CI) were 1.34 (0.91, 1.98) and 2.57 (0.72, 9.20), respectively.

Conclusions Self-reported physical functioning predicts BMD in an apparently healthy population, particularly in women. This could potentially provide an inexpensive, simple screening tool to identify individuals at risk of osteoporosis.

Keywords physical functioning, bone mineral density, older adults, SF-36

Abbreviations: BMD, bone mineral density; BMI; body mass index; BUA, broadband ultrasound attenuation; CI, confidence interval; COAD, chronic obstructive airways disease; CUBA, calcaneal ultrasound broadband attenuation; DEXA, dual energy X-ray absorptiometry; EPIC, European

Prospective Investigation into Cancer; FRAX, fracture risk assessment tool; HLEQ, health and life experiences questionnaire; HRQL, health-related quality of life; HRT, hormone replacement therapy; OR, odds ratio; PCS, physical component summary; SD, standard deviation; SE, standard error; SF-36, short-form 36; TDI, Townsend Deprivation Index; WHO, World Health Organisation; 2HC, second health check.

Declarations

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Conflicts of interest Sarah Perrott, Kathryn Martin, Victoria L Keevil, Nicholas J Wareham, Kay-Tee Khaw, and Phyo Kyaw Myint declare that they have no conflict of interest.

Availability of data and materials There are no linked research data sets for this paper. Data will be made available on request to the steering committee of EPIC-Norfolk.

Authors' contributions KM, VK and PKM contributed to the study conception and KM and PKM supervised SP. SP performed literature review and statistical analysis. KTK and NJW are PIs of EPIC-Norfolk. The first draft of the manuscript was written by SP and all authors read and reviewed the final manuscript.

Ethics approval The EPIC-Norfolk study was approved by the Norwich Research Ethics Committee.

1. Introduction

Osteoporosis is a major public health issue[1]; with one in three women experiencing an osteoporotic fracture in their lifetime[2]. Osteoporosis is a silent disease until fracture occurrence, the latter associated with poor outcomes in the ageing population[1, 3]. Besides limiting mobility and independence, the disability caused by osteoporosis is a substantial economic burden and contributor to healthcare system pressures, estimated to annually cost up to $25.3 billion in the USA[4–6]. Early detection of poor bone health and prevention of osteoporosis is more effective than relying on pharmaceutical intervention in later life[3].

Various health-related quality of life (HRQL) measures have been used to predict future health outcomes. Self-reported functional health measured by the short-form 36-item questionnaire (SF-36) is used to assess HRQL, and previous studies have shown scores to be predictive of many outcomes – including mortality and stroke risk[7–10]. Weight-bearing physical activity is a sustainable method to enhance bone health, preserve bone mineral density (BMD) and enable bone regeneration[1, 3, 6]. Since lifestyle is a determining factor of SF-36, self-reported physical functioning measures could prove a simple and inexpensive method to identify people at risk of low BMD.

Bone mass is generated in adolescence; failure to reach and maintain peak BMD during adulthood is a crucial factor in determining future osteoporosis risk[1, 3, 6]. Women are disproportionately impacted by osteoporosis due to hormonal changes at menopause, with osteoporotic fractures being more common than stroke, myocardial infarction and breast cancer combined[11, 12]. Exercise can maintain BMD in those aged over 60 years, although beyonf this age BMD is harder to regain[3, 13]. One in eight men will have an osteoporotic fracture in their lifetime; despite less rapid bone deterioration compared to women, fracture-related mortality can be twice as high[14, 15].

The relationship between physical function and BMD is well-established[16]; multiple physical performance measures (e.g. walking speed, grip strength) have proven to be of high predictive value regarding future fracture risk[17]. Identifying poor BMD before further decline and fracture occurrence is imperative, therefore indicators of poorer BMD provided by self-reported physical functional health could help counter this public health issue.

Low self-reported health-related quality of life measures have previously been associated with osteoporosis[18, 19]. In this study, physical functional health assessed using SF-36 was used to predict future BMD in men and women aged 40-79 years.

2. Material and Methods

2.1 Population

This study population consists of 12,071 participants who took part in the European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) cohort study who had their BMD evaluated. EPIC-Norfolk participant recruitment and methodology has previously been described[20]. In brief, participants were identified from general practice age-sex registers and invited to participate in a baseline questionnaire, health check, nutrition evaluation and biospecimen collection from 1993-1997. The cohort was followed up over 25 years with health checks at regular intervals. The EPIC-Norfolk cohort are representative of the UK population, albeit with lower proportion of smokers[20].

2.2 Predictor variables

Participants were asked to complete a Health and Life Experiences Questionnaire (HLEQ) 18 months after baseline. This questionnaire included the anglicised Short-Form 36 (UK SF-36), which measures self-reported health across eight domains: perceptions of general health; social functioning; physical functioning; role limitation due to physical issues; role limitation due to emotional issues; mental health; pain; energy and vitality[21]. Overall scores were calculated for each domain and then converted to a 0-100 scale, where 0 represents poor and 100 represents best possible health[21, 22]. The Physical Component Summary (PCS) score is derived using all eight SF-36 domains[21]. In this study, PCS was used as a continuous predictor variable (every five-point decrease in PCS) and as a categorical variable. Participants were categorised into those with poor physical functioning, a PCS score of less than one standard deviation (SD) below the sex-specific mean, and those with good physical functioning, a PCS score greater than this.

2.3 Outcome variables

BMD was assessed using broadband (i.e. calcaneal) ultrasound attenuation (BUA) measured at the second health check (2HC) from 1998-2000, at least three years after baseline, using a contact ultrasound bone analyser (CUBA) device[23]. Cross-sectional analysis approach was employed since the outcome is a measurement as opposed to an incident event such as heart attack and thus not appropriate for Cox-regression models. BUA can can discriminate patients with low BMD equally as well as dual-energy X-ray absorptiometry (DEXA)[24]. BUA measures were taken at least twice in each foot and the mean BUA from left and right were used for analysis. A greater BUA reading is indicative of higher BMD. Each CUBA device was calibrated daily and calibration between all devices used for this study were checked monthly[25].

Participants with a mean BUA less than 1SD below the sex-specific mean were considered to have low BMD. Participants with a mean BUA less than 2.5SD below the sex-specific mean were considered to have very low BMD. These cut-offs were based on evidence which suggests for each SD decrease below the young-adult mean, fracture risk doubles[12, 26, 27]. Although our study uses the means of older rather than young adults, this measure should identify individuals with at least osteopenia (BMD <1SD below young-adult mean), as per the World Health Organisation (WHO) definition[27]. Participants with a BUA less than 2.5SD below the sex-specific mean, classified as having very low BMD, were likely to have osteoporosis based on the WHO definition of osteoporosis (BMD <2.5SD below young-adult mean)[27].

2.4 Covariates

Age, sex, weight and height were recorded and body mass index (BMI) was calculated at 2HC using a standardised protocol[28]. Cigarette smoking status was obtained and recorded as ‘current’, ‘former’ or ‘never’ smoker, which was reclassified into ‘former or current smoker’ and ‘never smoker’ for the purpose of this study. Similarly, average weekly alcohol consumption was recorded, and re-classified into ‘consumes alcohol regularly’ (at least one drink a week) or ‘minimal or non-drinker’.

Participant socioeconomic status were evaluated by three measures: social class; education status; and Townsend Deprivation Index (TDI). Social class was categorised into five groups according to participant’s own or partner’s occupation, where social class I consisted of professionals, and social class V included unskilled manual workers[20]. Educational status was split into four groups based on highest qualification achieved (i.e. degree or equivalent; A-level or equivalent; O-level or equivalent; and less than O-level). O-level usually indicates academic achievement to the minimum UK school leaving age. TDI is a multi-factor scoring system used to determine deprivation, where 0 is the national mean, with positive scores representing greater deprivation and negative scores representing low deprivation[29]. Social class was reclassified into 'semi/unskilled workers' (social classes IV and V) and 'skilled workers' (social classes I, II and III). Highest education level achieved was reclassified into 'none or O-level' and 'A-level or degree', and TDI was classified into '0 or less' and 'above 0'. These reclassifications were made as deprivation, low social class and education status tend to be associated with suboptimal BMD[30, 31].

Participants were asked in the baseline health questionnaire to self-report any medically-diagnosed illnesses (e.g., cancer, diabetes mellitus, depression requiring treatment, stroke and myocardial infarction). Use of hormone replacement therapy (HRT) at any time, and steroid use at 2HC were also recorded.

2.5 Statistical analyses

Analyses were performed using SPSS version 26.0 (IBM, New York, USA). Participants with prevalent cancer and who did not have either a BUA reading or PCS score were excluded. Only participants with data for all the covariates required for the models were included. All analyses were stratified by sex as previous studies show sex-specific differences in BMD[26].

Participant characteristics were described using proportions, means and medians. Differences between men and women were compared using the t-test or Mann-Whitney test for continuous variables, or the Pearson Chi-squared test for categorical variables.

Sex-specific linear regression models were used to explore associations between PCS score (every 5 point decrease) and BUA as a continuous outcome measure. Multivariate models were used to examine whether potential confounders may attenuate any relationships observed. In men, we first adjusted for: ever smoked; steroid use at 2HC; education level below A-levels; social class; alcohol consumption; depression requiring treatment; BMI; and age. In women, we adjusted for the same confounders as men, but also HRT use. Confounders were identified using the Pearson Chi-squared test and selected if they showed association with BUA and PCS score. The unstandardised ß-coefficients were calculated with the standard of error (SE) for each 5 points decrease in PCS score and presented with p-values.

Relationships between poor physical functioning, defined as participants with a PCS score <1SD below the sex-specific mean, and low BUA (<1SD below the sex-specific mean) and very low BUA (<2.5SD below the sex specific mean) were also explored using logistic regression, adjusting for the same confounders as in the linear regression models. Odds ratios (OR) were presented with 95% confidence intervals (95% CI) and associated p-values.

Although the relationship between PCS score and BUA is longitudinal, we used cross-sectional analysis (OR) as both predictor and outcome were not discrete episodes, but measurements which could remain stable and more likely to deteriorate subtly over time.

3. Results

3.1 Main findings

Of the 15,786 participants who attended 2HC, 11,995 had BUA measured. Of these, 536 were missing SF-36 PCS scores and remaining participants with a cancer diagnosis (n=747) were excluded. Missing data were more likely in women and in those aged over 65 years; 5.1% of participants had missing data in at least one covariable: smoking status (n=83), highest education level attained (n=5), BMI (n=20), social class (n=5), alcohol consumption status (n=209), ever taken HRT (n=132), self-reported depression (n=896). The final sample included 10,203 participants (57.1% women), mean (SD) age 61.5 (8.9) years, who had a complete dataset, detailed in table 1.

Table 1 shows the distribution of sample characteristics by sex. The population is predominantly non-deprived, of high educational and occupational status, and non-obese. PCS score was on average 0.4 points lower in women compared to men (p=0.015), with BUA greater in men (p<0.001), with mean (SD) BUA 90.2 (17.3) dB/MHz and 72.5 (16.4) dB/MHz, respectively.

3.2 PCS score as a continuous predictor of BUA

Table 2 shows the sex-specific linear regression models for PCS score as a predictor of BUA. In the unadjusted analysis in men, a 5-point lower PCS score corresponds with 0.52 dB/MHz lower mean BUA. The adjusted model for confounders had β-coefficient (SE) 0.47 (0.03) (p=0.001). In women, similar changes in BUA for every 5-point lower PCS score were observed in the unadjusted analyses, but associations weakened in the multivariate model (β-coefficients (SE) 0.59 (0.02) and 0.19 (0.02), respectively).

3.3 PCS score as a categorical predictor of low and very low BUA

Table 3 shows the OR and 95% CI representing associations between poor physical functioning (PCS score <1SD below sex-specific mean) and low BUA, indicative of at least osteopenia[27]. The same variables were controlled for as in the linear regression model. There were 425 women and 235 men with low BUA, compared to 5400 women and 4143 men with normal BUA. In women, consistent associations between poor physical functioning and higher odds of low BUA were found across unadjusted and adjusted models, with an OR (95% CI) of 1.53 (1.24, 1.88) in the multivariable model. In men, the same direction of association was observed between poor physical functioning and low BUA, but associations were not significant (multivariable model: OR 1.34 95% CI 0.91, 1.98).

Similarly, Table 4 shows the OR and 95% CI representing relationships between poor PCS and very low BUA, indicative of osteoporosis[27]. In this analysis, there were 11 women and 5 men classified as having very low BUA. Strong associations between poor physical functioning and higher odds of very low BUA were observed in women, although CIs were wide, with an OR (95% CI) of 8.28 (2.67, 25.69) in the adjusted model. The association was less pronounced in men and, although the same trends were observed, results did not reach statistical significance (fully adjusted model OR: 2.57, 95% CI 0.72, 9.20).

4. Discussion

4.1 Main findings

We found that among EPIC-Norfolk cohort participants, lower PCS scores were associated with poorer future BUA, an indicator of BMD, independent of age, BMI, and other confounding factors (i.e., cigarette smoking, steroid use, lower education level, higher alcohol consumption, depression requiring treatment, and HRT usage among women). However, even after adjustment for these, clear differences in BUA between those with higher and lower PCS scores remained. These findings coincide with evidence that higher physical activity in middle-late adulthood is protective against rapid deterioration in bone health[3, 6]. Another study of EPIC-Norfolk participants found that more time spent doing high-impact physical activity was strongly and positively associated with superior BUA – independent of confounding variables[25]. Several other cohort studies have found physical capability to be a strong indicator of BMD[1, 6, 32–34].

Our results suggested differences in the relationship between low PCS and BUA in men compared to women. When both PCS and BUA were considered as continuous predictor and outcome variables, a strong association between PCS and BUA was evident in men but less so in women. Conversely, when both were considered as categorical variables, and relationships between self-reported physical functioning and low or very low BUA were considered, relationships were stronger in women. Changes in physical functioning in men may be a stronger marker of osteoporosis than in women, however in this cohort few men had low or very low BUA and results were thus underpowered. As a group, women are more likely to have low BMD, hence categorical outcomes showed a stronger relationship for women. Other studies investigating physical function measures and BUA have noticed a stark difference between sex[25, 35]. Jakes et al. found high physical activity in men conferred a BUA of around 9.5% higher than that of those who reported low physical activity. However, in women this was only 3.4% higher, and similar in size to that of a four-year age-difference[25]. This is likely to be attributed to higher BMI in women with a sedentary lifestyle, which is protective against rapid BMD deterioration after menopause due to increased oestrogens production by adipose tissue and greater mechanical loading[25, 36]. A Brazilian study found the impact of prolonged sedentary time and lower physical activity on BMD varied greatly between men and women; with benefits of shorter bouts of sedentary behaviour only observed in women[35].

Our findings suggest a PCS score of less than 1SD below the sex-specific mean was a weak to moderate predictor of low BUA, indicative of at least osteopenia. Osteopenia is BMD of 1 to 2.5SD below mean peak levels (i.e. young-adult BMD) and describes low, but not yet critical, bone mass[27, 37]. Early detection and management of osteopenia, including increased weight-bearing exercise and increasing calcium and vitamin D intake, has been demonstrated to reduce fracture risk and improve quality of life[27, 37]. When the outcome was low or very low BUA, indicative of osteopenia or osteoporosis, low PCS was demonstrated to be a strong predictor, although more so in women. This is likely to be due to increased chance of low BMD among women compared to men in the cohort. The number of individuals with very low BUA, particularly in men, was small which resulted in underpowered results.

4.2 Clinical relevance

Older adults constitute the world's fastest growing population, making osteoporosis a significant social and economic burden[12]. Therefore risk assessing this population is crucial, and although Fracture Risk Assessment Tool (FRAX) is an effective tool for older white women, it is less effective among men and non-Caucasians[38]. Furthermore, FRAX assesses fracture risk, not overall bone health status[38]. Indicators of poorer BMD provided by self-reported physical functional health could make a significant contribution to tackle this public health issue. Furthermore, the SF-36 can potentially predict numerous measures besides BMD status, from surgical outcomes[7, 8] to risk of death from heart disease and stroke[9, 10], emphasising the versatility of the tool as a measure of health status and risk.

4.3 Strengths

To our knowledge, this study is the first to investigate self-reported physical functional health as a predictor of future BMD in older adults, allowing for early identification of people at risk of suboptimal BMD potentially earlier than FRAX can[38]. We used a large population-based cohort with validated follow-up methods[20], with the ability to control for a range of confounders including sociodemographic and lifestyle factors. Data were collected prospectively, minimising potential for recall bias, and follow-up was over a critical period of time in the participants' lives when BMD typically deteriorates. This highlighted the effectiveness of PCS score as an early, inexpensive, and non-invasive indicator of BMD and therefore risk of future osteopenia and osteoporosis.

4.4 Limitations

The existence of healthy volunteer bias is possible given that EPIC-Norfolk is a volunteer study consisting of predominantly white, middle-class, and health-conscious individuals. However, previous literature suggest EPIC-Norfolk sample characteristics are representative of the UK population[20] and mean SF-36 scores are comparable to mean scores in other population-based studies[39]. As a secondary data analysis of an observational study, there may be unknown confounders that were not adjusted for. Potential confounders measured at baseline or 2HC may vary during follow-up, e.g. alcohol consumption. The WHO osteopenia and osteoporosis criteria considers spine, hip, or forearm BMD measures by DEXA, and compares this to the young-adult BMD mean[37]. Here we assessed BMD using CUBA which is a cheaper, safer and relatively precise alternative to DEXA, although can be limited by poor foot positioning[24, 40]. We compared the sex-specific mean which was in older, rather than younger, adults where peak BMD will have already deteriorated, potentially underestimating the number of participants with low or very low BMD[3, 41]. Furthermore, use of CUBA estimates BMD in the calcaneus, rather than the spine, hip or forearm[37]. Although calibration of devices were regularly checked and measurements taken at least twice in each foot[25], random measurement error is possible. Despite these limitations, using a CUBA devise is an inexpensive and accurate method to evaluate BMD, without any radiation exposure[12]. Time between PCS and BUA assessment varied among participants, with the shortest interval being 18-months. This relatively short time interval in some participants will result in an estimation of what current/near future BMD is, rather than predicting BMD status several years in advance.

4.5 Further research

The use of PCS score as a predictor of BMD in later life warrants further investigation. Despite having a different function to the FRAX tool, direct comparison between PCS score and FRAX is required to evaluate the effectiveness of each. SF-36 has the potential to predict many health outcomes, therefore may prove to be a useful tool in clinical practice.

4.6 Conclusion

Study findings indicate that self-reported physical functioning is a tool capable of predicting future BMD and identifying at-risk individuals in an apparently healthy population, especially in women. In the current climate, where increased sedentary activity and a reduction of routine medical appointments due to COVID-19 will have implications on bone health, self-reported functional health may prove a useful and inexpensive indicator to stratify populations by risk of low BMD. Further validation is required to gain insight into the role of PCS score in clinical practice.

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Self-reported physical functional health predicts future bone mineral density in EPIC-Norfolk cohort

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Synopsis

Using a large population sample from the UK, we found that self-reported physical functional health may be used to predict future bone mineral density especially in women. It may be a useful and inexpensive way to identify individuals before further decline in bone mineral density and the risk of fracture.

Abstract

Purpose Self-reported physical functional health may predict bone mineral density (BMD) and thus provide a method to identify people at risk of low BMD. In this study, the association between the 36-item short-form questionnaire (SF-36) physical component summary (PCS) score and future BMD in participants aged 40-79 years enrolled in the European Prospective Investigation of Cancer-Norfolk study was investigated.

Methods Associations between a participant's SF-36 PCS score, measured 18 months after baseline health check, and broadband ultrasound attenuation (BUA – a measure of BMD), measured 2-5 years after baseline, were examined using sex-specific linear and logistic regression analyses adjusting for age, BMI, medical co-morbidities, lifestyle and socioeconomic factors.

Results Data from 10,203 participants, mean (standard deviation (SD)) age 61.5 (8.9) years (57.4% women) were analysed from 1993-2000. For every five points ~~decrease~~ lower ~~in~~ PCS score in men and women, there was approximately a 0.5 dB/MHz ~~decrease~~ lower~~in~~ mean BUA. In women, a PCS score of less than one standard deviation (1SD) below the sex-specific mean was associated with having a low BUA (< 1SD below sex-specific mean) and very low BUA (< 2.5SD below the sex specific mean); odds ratio (OR) (95% confidence interval) 1.53 (1.24, 1.88) and 8.28 (2.67, 25.69), respectively. The relationship was lesser so in men; corresponding OR (95%CI) were 1.34 (0.91, 1.98) and 2.57 (0.72, 9.20), respectively.

Conclusions Self-reported physical functioning predicts BMD in an apparently healthy population, particularly in women. This could potentially provide an inexpensive, simple screening tool to identify individuals at risk of osteoporosis.

Keywords physical functioning, bone mineral density, older adults, SF-36

Abbreviations: BMD, bone mineral density; BMI; body mass index; BUA, broadband ultrasound attenuation; CI, confidence interval; COAD, chronic obstructive airways disease; CUBA, calcaneal ultrasound broadband attenuation; DEXA, dual energy X-ray absorptiometry; EPIC, European Prospective Investigation into Cancer; FRAX, fracture risk assessment tool; HLEQ, health and life experiences questionnaire; HRQL, health-related quality of life; HRT, hormone replacement therapy; OR, odds ratio; PCS, physical component summary; SD, standard deviation; SE, standard error; SF-36, short-form 36; TDI, Townsend Deprivation Index; WHO, World Health Organisation; 2HC, second health check.

Declarations

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Conflicts of interest Sarah Perrott, Kathryn Martin, Victoria L Keevil, Nicholas J Wareham, Kay-Tee Khaw, and Phyo Kyaw Myint declare that they have no conflict of interest.

Availability of data and materials There are no linked research data sets for this paper. Data will be made available on request to the steering committee of EPIC-Norfolk.

Authors' contributions KM, VK and PKM contributed to the study conception and KM and PKM supervised SP. SP performed literature review and statistical analysis. KTK and NJW are PIs of EPIC-Norfolk. The first draft of the manuscript was written by SP and all authors read and reviewed the final manuscript.

Ethics approval The EPIC-Norfolk study was approved by the Norwich Research Ethics Committee.

1. Introduction

Osteoporosis is a major public health issue[1]; with one in three women experiencing an osteoporotic fracture in their lifetime[2]. ~~Until fracture occurrence, O~~Oosteoporosis is a silent disease until fracture occurrence, the latter associated with poor outcomes in the ageing population[1, 3]. Besides limiting mobility and independence, the disability caused by osteoporosis is a substantial economic burden and contributor to healthcare system pressures, estimated to annually cost up to $25.3 billion in the USA[4–6]. Early detection of poor bone health and prevention of osteoporosis is more effective than relying on pharmaceutical intervention in later life[3].

Various health-related quality of life (HRQL) measures have been used to predict future health outcomes. Self-reported functional health measured by the short-form 36-item questionnaire (SF-36) is used to assess HRQL, and previous studies have shown scores to be predictive of many outcomes – including mortality and stroke risk[7–10]. Weight-bearing physical activity is a sustainable method to enhance bone health, preserve bone mineral density (BMD) and enable bone regeneration[1, 3, 6]. Since lifestyle is a determining factor of SF-36, self-reported physical functioning measures could prove a simple and inexpensive method to identify people at risk of low BMD.

Bone mass is generated in adolescence; failure to reach and maintain peak BMD during adulthood is a crucial factor in determining future osteoporosis risk[1, 3, 6]. Women are disproportionately impacted by osteoporosis due to hormonal changes at menopause, with osteoporotic fractures being more common than stroke, myocardial infarction and breast cancer combined[11, 12]. Exercise can maintain BMD in those aged over 60 years, although beyonf this age BMD is harder to regain[3, 13]. One in eight men will have an osteoporotic fracture in their lifetime; despite less rapid bone deterioration compared to women, fracture-related mortality can be twice as high[14, 15].

The relationship between physical function and BMD is well-established[16]; multiple physical performance measures (e.g. walking speed, grip strength) have proven to be of high predictive value regarding future fracture risk[17]. Identifying poor BMD before further decline and fracture occurrence is imperative, therefore indicators of poorer BMD provided by self-reported physical functional health could help counter this public health issue.

Low self-reported health-related quality of life measures have previously been associated with osteoporosis[18, 19]. In this study, physical functional health assessed using SF-36 was used to predict future BMD in men and women aged 40-79 years.

2. Material and Methods

2.1 Population

This study population consists of 12,071 participants who took part in the European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) cohort study who had their BMD evaluated. EPIC-Norfolk participant recruitment and methodology has previously been described[20]. In brief, participants were identified from general practice age-sex registers and invited to participate in a baseline questionnaire, health check, nutrition evaluation and biospecimen collection from 1993-1997. The cohort was followed up over 25 years with health checks at regular intervals. The EPIC-Norfolk cohort are representative of the UK population, albeit with lower proportion of smokers[20].

2.2 Predictor variables

Participants were asked to complete a Health and Life Experiences Questionnaire (HLEQ) 18 months after baseline. This questionnaire included the anglicised Short-Form 36 (UK SF-36), which measures self-reported health across eight domains: perceptions of general health; social functioning; physical functioning; role limitation due to physical issues; role limitation due to emotional issues; mental health; pain; energy and vitality[21]. Overall scores were calculated for each domain and then converted to a 0-100 scale, where 0 represents poor and 100 represents best possible health[21, 22]. The Physical Component Summary (PCS) score is derived using all eight SF-36 domains[21]. In this study, PCS was used as a continuous predictor variable (every five-point decrease in PCS) and as a categorical variable. Participants were categorised into those with poor physical functioning, a PCS score of less than one standard deviation (SD) below the sex-specific mean, and those with good physical functioning, a PCS score greater than this.

2.3 Outcome variables

BMD was assessed using broadband (i.e. calcaneal) ultrasound attenuation (BUA) measured at the second health check (2HC) from 1998-2000, at least three years after baseline, using a contact ultrasound bone analyser (CUBA) device[23]. Cross-sectional analysis approach was employed since the outcome is a measurement as opposed to an incident event such as heart attack and thus not appropriate for Cox-regression models. BUA can can discriminate patients with low BMD equally as well as dual-energy X-ray absorptiometry (DEXA)[24]. BUA measures were taken at least twice in each foot and the mean BUA from left and right were used for analysis. A greater BUA reading is indicative of higher BMD. Each CUBA device was calibrated daily and calibration between all devices used for this study were checked monthly[25].

Participants with a mean BUA less than 1SD below the sex-specific mean were considered to have low BMD. Participants with a mean BUA less than 2.5SD below the sex-specific mean were considered to have very low BMD. These cut-offs were based on evidence which suggests for each SD decrease below the young-adult mean, fracture risk doubles[12, 26, 27]. Although our study uses the means of older rather than young adults, this measure should identify individuals with at least osteopenia (BMD <1SD below young-adult mean), as per the World Health Organisation (WHO) definition[27]. Participants with a BUA less than 2.5SD below the sex-specific mean, classified as having very low BMD, were likely to have osteoporosis based on the WHO definition of osteoporosis (BMD <2.5SD below young-adult mean)[27].

2.4 Covariates

Age, sex, weight and height were recorded and body mass index (BMI) was calculated at 2HC using a standardised protocol[28]. Cigarette smoking status was obtained and recorded as 'current', 'former' or 'never' smoker, which was reclassified into 'former or current smoker' and 'never smoker' for the purpose of this study. Similarly, average weekly alcohol consumption was recorded, and re-classified into 'consumes alcohol regularly' (at least one drink a week) or 'minimal or non-drinker'.

Participant socioeconomic status were evaluated by three measures: social class; education status; and Townsend Deprivation Index (TDI). Social class was categorised into five groups according to participant's own or partner's occupation, where social class I consisted of professionals, and social class V included unskilled manual workers[20]. Educational status was split into four groups based on highest qualification achieved (i.e. degree or equivalent; A-level or equivalent; O-level or equivalent; and less than O-level). O-level usually indicates academic achievement to the minimum UK school leaving age. TDI is a multi-factor scoring system used to determine deprivation, where 0 is the national mean, with positive scores representing greater deprivation and negative scores representing low deprivation[29]. Social class was reclassified into 'semi/unskilled workers' (social classes IV and V) and 'skilled workers' (social classes I, II and III). Highest education level achieved was reclassified into 'none or O-level' and 'A-level or degree', and TDI was classified into '0 or less' and 'above 0'. These reclassifications were made as deprivation, low social class and education status tend to be associated with suboptimal BMD[30, 31].

Participants were asked in the baseline health questionnaire to self-report any medically-diagnosed illnesses (e.g., cancer, diabetes mellitus, depression requiring treatment, stroke and myocardial infarction). Use of hormone replacement therapy (HRT) at any time, and steroid use at 2HC were also recorded.

2.5 Statistical analyses

Analyses were performed using SPSS version 26.0 (IBM, New York, USA). Participants with prevalent cancer and who did not have either a BUA reading or PCS score were excluded. Only participants with data for all the covariates required for the models were included. All analyses were stratified by sex as previous studies show sex-specific differences in BMD[26].

Participant characteristics were described using proportions, means and medians. Differences between men and women were compared using the t-test or Mann-Whitney test for continuous variables, or the Pearson Chi-squared test for categorical variables.

Sex-specific linear regression models were used to explore associations between PCS score (every 5 point decrease) and BUA as a continuous outcome measure. Multivariate models were used to examine whether potential confounders may attenuate any relationships observed. In men, we first adjusted for: ever smoked; steroid use at 2HC; education level below A-levels; social class; alcohol consumption; depression requiring treatment; BMI; and age. In women, we adjusted for the same confounders as men, but also HRT use. Confounders were identified using the Pearson Chi-squared test and selected if they showed association with BUA and PCS score. The unstandardised ß-coefficients were calculated with the standard of error (SE) for each 5 points decrease in PCS score and presented with p-values.

Relationships between poor physical functioning, defined as participants with a PCS score <1SD below the sex-specific mean, and low BUA (<1SD below the sex-specific mean) and very low BUA (<2.5SD below the sex specific mean) were also explored using logistic regression, adjusting for the same confounders as in the linear regression models. Odds ratios (OR) were presented with 95% confidence intervals (95% CI) and associated p-values.

Although the relationship between PCS score and BUA is longitudinal, we used cross-sectional analysis (OR) as both predictor and outcome were not discrete episodes, but measurements which could remain stable and more likely to deteriorate subtly over time.

3. Results

3.1 Main findings

Of the 15,786 participants who attended 2HC, 11,995 had BUA measured. Of these, 536 were missing SF-36 PCS scores and remaining participants with a cancer diagnosis (n=747) were excluded. Missing data were more likely in women and in those aged over 65 years; 5.1% of participants had missing data in at least one covariable: smoking status (n=83), highest education level attained (n=5), BMI (n=20), social class (n=5), alcohol consumption status (n=209), ever taken HRT (n=132), self-reported depression (n=896). The final sample included 10,203 participants (57.1% women), mean (SD) age 61.5 (8.9) years, who had a complete dataset, detailed in table 1.

Table 1 shows the distribution of sample characteristics by sex. The population is predominantly non-deprived, of high educational and occupational status, and non-obese. PCS score was on average 0.4 points lower in women compared to men (p=0.015), with BUA greater in men (p<0.001), with mean (SD) BUA 90.2 (17.3) dB/MHz and 72.5 (16.4) dB/MHz, respectively.

3.2 PCS score as a continuous predictor of BUA

Table 2 shows the sex-specific linear regression models for PCS score as a predictor of BUA. In the unadjusted analysis in men, a 5-point ~~decrease~~ lower ~~in~~ PCS score corresponds with 0.52 dB/MHz ~~decrease~~ lower ~~in~~ mean BUA. The adjusted model for confounders had β-coefficient (SE) 0.47 (0.03) (p=0.001). In women, similar changes in BUA for every 5-point ~~decrease~~ lower~~in~~ PCS score were observed in the unadjusted analyses, but associations weakened in the multivariate model (β-coefficients (SE) 0.59 (0.02) and 0.19 (0.02), respectively).

3.3 PCS score as a categorical predictor of low and very low BUA

Table 3 shows the OR and 95% CI representing associations between poor physical functioning (PCS score <1SD below sex-specific mean) and low BUA, indicative of at least osteopenia[27]. The same variables were controlled for as in the linear regression model. There were 425 women and 235 men with low BUA, compared to 5400 women and 4143 men with normal BUA. In women, consistent associations between poor physical functioning and higher odds of low BUA were found across unadjusted and adjusted models, with an OR (95% CI) of 1.53 (1.24, 1.88) in the multivariable model. In men, the same direction of association was observed between poor physical functioning and low BUA, but associations were not significant (multivariable model: OR 1.34 95% CI 0.91, 1.98).

Similarly, Table 4 shows the OR and 95% CI representing relationships between poor PCS and very low BUA, indicative of osteoporosis[27]. In this analysis, there were 11 women and 5 men classified as having very low BUA. Strong associations between poor physical functioning and higher odds of very low BUA were observed in women, although CIs were wide, with an OR (95% CI) of 8.28 (2.67, 25.69) in the adjusted model. The association was less pronounced in men and, although the same trends were observed, results did not reach statistical significance (fully adjusted model OR: 2.57, 95% CI 0.72, 9.20).

4. Discussion

4.1 Main findings

We found that among EPIC-Norfolk cohort participants, lower PCS scores were associated with poorer future BUA, an indicator of BMD, independent of age, BMI, and other confounding factors (i.e., cigarette smoking, steroid use, lower education level, higher alcohol consumption, depression requiring treatment, and HRT usage among women). However, even after adjustment for these, clear differences in BUA between those with higher and lower PCS scores remained. These findings coincide with evidence that higher physical activity in middle-late adulthood is protective against rapid deterioration in bone health[3, 6]. Another study of EPIC-Norfolk participants found that more time spent doing high-impact physical activity was strongly and positively associated with superior BUA – independent of confounding variables[25]. Several other cohort studies have found physical capability to be a strong indicator of BMD[1, 6, 32–34].

Our results suggested differences in the relationship between low PCS and BUA in men compared to women. When both PCS and BUA were considered as continuous predictor and outcome variables, a strong association between PCS and BUA was evident in men but less so in women. Conversely, when both were considered as categorical variables, and relationships between self-reported physical functioning and low or very low BUA were considered, relationships were stronger in women. Changes in physical functioning in men may be a stronger marker of osteoporosis than in women, however in this cohort few men had low or very low BUA and results were thus underpowered. As a group, women are more likely to have low BMD, hence categorical outcomes showed a stronger relationship for women. Other studies investigating physical function measures and BUA have noticed a stark difference between sex[25, 35]. Jakes et al. found high physical activity in men conferred a BUA of around 9.5% higher than that of those who reported low physical activity. However, in women this was only 3.4% higher, and similar in size to that of a four-year age-difference[25]. This is likely to be attributed to higher BMI in women with a sedentary lifestyle, which is protective against rapid BMD deterioration after menopause due to increased oestrogens production by adipose tissue and greater mechanical loading[25, 36]. A Brazilian study found the impact of prolonged sedentary time and lower physical activity on BMD varied greatly between men and women; with benefits of shorter bouts of sedentary behaviour only observed in women[35].

Our findings suggest a PCS score of less than 1SD below the sex-specific mean was a weak to moderate predictor of low BUA, indicative of at least osteopenia. Osteopenia is BMD of 1 to 2.5SD below mean peak levels (i.e. young-adult BMD) and describes low, but not yet critical, bone mass[27, 37]. Early detection and management of osteopenia, including increased weight-bearing exercise and increasing calcium and vitamin D intake, has been demonstrated to reduce fracture risk and improve quality of life[27, 37]. When the outcome was low or very low BUA, indicative of osteopenia or osteoporosis, low PCS was demonstrated to be a strong predictor, although more so in women. This is likely to be due to increased chance of low BMD among women compared to men in the cohort. The number of individuals with very low BUA, particularly in men, was small which resulted in underpowered results.

4.2 Clinical relevance

Older adults constitute the world's fastest growing population, making osteoporosis a significant social and economic burden[12]. Therefore risk assessing this population is crucial, and although Fracture Risk Assessment Tool (FRAX) is an effective tool for older white women, it is less effective among men and non-Caucasians[38]. Furthermore, FRAX assesses fracture risk, not overall bone health status[38]. Indicators of poorer BMD provided by self-reported physical functional health could make a significant contribution to tackle this public health issue. Furthermore, the SF-36 can potentially predict numerous measures besides BMD status, from surgical outcomes[7, 8] to risk of death from heart disease and stroke[9, 10], emphasising the versatility of the tool as a measure of health status and risk.

4.3 Strengths

To our knowledge, this study is the first to investigate self-reported physical functional health as a predictor of future BMD in older adults, allowing for early identification of people at risk of suboptimal BMD potentially earlier than FRAX can[38]. We used a large population-based cohort with validated follow-up methods[20], with the ability to control for a range of confounders including sociodemographic and lifestyle factors. Data were collected prospectively, minimising potential for recall bias, and follow-up was over a critical period of time in the participants' lives when BMD typically deteriorates. This highlighted the effectiveness of PCS score as an early, inexpensive, and non-invasive indicator of BMD and therefore risk of future osteopenia and osteoporosis.

4.4 Limitations

The existence of healthy volunteer bias is possible given that EPIC-Norfolk is a volunteer study consisting of predominantly white, middle-class, and health-conscious individuals. However, previous literature suggest EPIC-Norfolk sample characteristics are representative of the UK population[20] and mean SF-36 scores are comparable to mean scores in other population-based studies[39]. As a secondary data analysis of an observational study, there may be unknown confounders that were not adjusted for. Potential confounders measured at baseline or 2HC may vary during follow-up, e.g. alcohol consumption. The WHO osteopenia and osteoporosis criteria considers spine, hip, or forearm BMD measures by DEXA, and compares this to the young-adult BMD mean[37]. Here we assessed BMD using CUBA which is a cheaper, safer and relatively precise alternative to DEXA, although can be limited by poor foot positioning[24, 40]. We compared the sex-specific mean which was in older, rather than younger, adults where peak BMD will have already deteriorated, potentially underestimating the number of participants with low or very low BMD[3, 41]. Furthermore, use of CUBA estimates BMD in the calcaneus, rather than the spine, hip or forearm[37]. Although calibration of devices were regularly checked and measurements taken at least twice in each foot[25], random measurement error is possible. Despite these limitations, using a CUBA devise is an inexpensive and accurate method to evaluate BMD, without any radiation exposure[12]. Time between PCS and BUA assessment varied among participants, with the shortest interval being 18-months. This relatively short time interval in some participants will result in an estimation of what current/near future BMD is, rather than predicting BMD status several years in advance.

4.5 Further research

The use of PCS score as a predictor of BMD in later life warrants further investigation. Despite having a different function to the FRAX tool, direct comparison between PCS score and FRAX is required to evaluate the effectiveness of each. SF-36 has the potential to predict many health outcomes, therefore may prove to be a useful tool in clinical practice.

4.6 Conclusion

Study findings indicate that self-reported physical functioning is a tool capable of predicting future BMD and identifying at-risk individuals in an apparently healthy population, especially in women. In the current climate, where increased sedentary activity and a reduction of routine medical appointments due to COVID-19 will have implications on bone health, self-reported functional health may prove a useful and inexpensive indicator to stratify populations by risk of low BMD. Further validation is required to gain insight into the role of PCS score in clinical practice.

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Table 1: Characteristics of 4378 men and 5825 women EPIC-Norfolk participants at 2HC, with exception of SF-36 which was measured at HLEQ1.

Characteristics	**Men**	**Women**	***P*-value**
Number (%)	4378	5825	
Smoking status			
Current smoker	307 (7.0)	435 (7.5)	<0.001[a]
Former smoker	2384 (54.5)	1849 (31.7)	
Never smoker	1687 (38.5)	3541 (60.8)	
Occupation			
Unskilled/semi-skilled	1589 (36.3)	1994 (34.2)	0.026[a]
Skilled	2789 (63.7)	3831 (65.8)	
Highest education status			
Degree	785 (17.9)	792 (13.6)	<0.001[a]
A-levels	2082 (47.6)	2226 (38.2)	
O-levels or lower	1502 (34.3)	2800 (48.1)	
Deprivation (Townsend Index >0)	655 (15.0)	874 (15.0)	0.065[a]
Self-reported prevalent illness			
Any	1769 (40.4)	2554 (43.8)	<0.001[a]
Cardiovascular disease	328 (7.5)	177 (3.0)	
Diabetes	174 (4.0)	129 (2.2)	
COAD	771 (17.6)	1256 (21.6)	
Arthritis	1034 (23.6)	1920 (33.0)	
Depression requiring treatment	416 (9.5)	1078 (18.5)	
Consumes alcohol regularly			<0.001[a]
Yes	3872 (88.4)	4674 (80.2)	
No	434 (9.9)	1014 (17.4)	
Steroid use at 2HC	168 (3.8)	297 (5.1)	0.001[a]

Ever used HRT	-	2276 (39.1)	
Mean (SD)			
Age in years	62.3 (8.9)	61.0 (8.9)	0.867[b]
BMI in kg/m^2	26.8 (3.3)	26.5 (4.4)	<0.001[b]
BUA averaged over both heel bones in dB/MHz	90.2 (17.3)	72.5 (16.4)	<0.001[b]
Median (IQR)			
Alcohol consumption in units/week	6.5 (2.0, 14.0)	2.0 (1.0, 7.0)	<0.001[c]
SF-36 PCS score	51.5 (44.8, 55.2)	51.1 (43.6, 55.2)	0.015[c]
SF-36 MCS score	55.8 (50.3, 58.9)	54.7 (48.1, 58.4)	<0.001[c]

P-value as calculated by Chi-squared test [a], independent samples t-test[b] and Mann-Whitney test[c]

Abbreviations:

2HC: second health check, between 1997-2000

SF36: 36-item short-form questionnaire

HLEQ1: Heath and Lifestyle Questionnaire, taken 18-months after first health check between 1994-1998

COAD: Chronic obstructive airway disease

HRT: Hormone replacement therapy

SD: standard deviation

BMI: body mass index

BUA: broadband ultrasound attenuation; averaged over both heel bones at 2HC measured in dB/MHz

PCS: Physical component summary

MCS: Mental component summary

Table 2: The ß-coefficient (SE) of linear regression model for change in BMD measure by every 5-point decrease in SF-36 PCS score in 4378 men and 5825 women, with and without adjustment.

	ß-coefficient (SE)	***P*-value**
<u>Men</u>		
Unadjusted	-0.52 (0.03)	<0.001
Adjusted for confounders	-0.47 (0.03)	0.001
<u>Women</u>		
Unadjusted	-0.59 (0.02)	<0.001
Adjusted for confounders	-0.19 (0.02)	0.056

Confounders: ever smoked; steroid use at 2HC; education level below A-levels; social class based on skilled occupation; alcohol consumption; depression requiring treatment; ever used HRT (women only); BMI; age

Abbreviations:

PCS = physical capability score, part of SF-36 (36-item short-form questionnaire), score 0-100 - where 100 is peak physical health

SE = standard error

n = number included in analysis

BUA = broadband ultrasound attenuation, measured in dB/MHz, measure of bone mineral density

Table 3: The odds ratio (95% CI) of low BMD defined as BMD measure less than -1SD value below sex-specific mean for those with SF-36 PCS values less than -1 D, compared to their counterparts with higher SF-36 PCS score, in 4378 men and 5825 women, with and without adjustment.

	Odds ratio (95% CI)	***P*-value**
<u>Men</u>		
Mean (SD) BUA = 90.22 (17.29) dB/MHz		
Unadjusted	1.39 (0.96, 2.02)	0.083
Adjusted for confounders	1.34 (0.91, 1.98)	0.140
<u>Women</u>		
Mean (SD) BUA = 72.52 (16.42) dB/MHz		
Unadjusted	1.72 (1.42, 2.07)	<0.001
Adjusted for confounders	1.53 (1.24, 1.88)	<0.001

Confounders in men: ever smoked (p=0.283); steroid use at 2HC (p=0.496); education level below A-levels (p=0.532); social class based on skilled occupation (p=611); alcohol consumption (p=0.207); depression requiring treatment (p=0.855); BMI (p=0.036); age (p=0.052)

Confounders in women: ever smoked (p=0.385); steroid use at 2HC (p=0.125); education level below A-levels (p=0.011); social class based on skilled occupation (p=0.299); alcohol consumption (p=0.029); ever used HRT (p<0.001); depression requiring treatment (p=0.260); BMI (p<0.001); age (p<0.001)

<u>Abbreviations:</u>

SF-36 = 36-item short-form questionnaire

PCS = physical component summary

SD = standard deviation

CI = confidence interval

BUA = broadband ultrasound attenuation, measured in dB/MHz, measure of bone mineral density

Table 4: The odds ratio (95% CI) of very low BMD defined as BMD measure less than -2.5SD value below sex-specific mean for those with SF-36 PCS values less than -1SD, compared to their counterparts with higher SF-36 PCS score, in 4378 men and 5825 women, with and without adjustment.

	Odds ratio (95% CI)	***P*-value**
<u>Men</u>		
Mean (SD) BUA = 90.22 (17.29) dB/MHz		
Unadjusted	3.82 (1.32, 11.06)	0.013
Adjusted for confounders	2.57 (0.72, 9.20)	0.148
<u>Women</u>		
Mean (SD) BUA = 72.52 (16.42) dB/MHz		
Unadjusted	11.49 (3.92, 33.70)	<0.001
Adjusted for confounders	8.28 (2.67, 25.69)	<0.001

Confounders in men: ever smoked (p=0.807); steroid use at 2HC (p=0.092); education level below A-levels (p=0.187); social class based on skilled occupation (p=0.552); alcohol consumption (p=0.314); depression requiring treatment (p=0.994); BMI (p=0.478); age (p=0.035)

Confounders in women: ever smoked (p=0.962); steroid use at 2HC (p=0.025); education level below A-levels (p=0.711); social class based on skilled occupation (p=0.811); alcohol consumption (p=0.054); ever used HRT (p=0.745); depression requiring treatment (p=0.299); BMI (p=0.129); age (p=0.041)

<u>Abbreviations:</u>

SF-36 = 36-item short-form questionnaire

PCS = physical component summary

SD = standard deviation

CI = confidence interval

BUA = broadband ultrasound attenuation, measured in dB/MHz, measure of bone mineral density