Objectively measured physical activity is associated with vertebral size in mid-life

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ABSTRACT

Background: Vertebral fractures reduce the quality of life and are a major burden to the health care sector. Small vertebral size is associated with increased vertebral fracture risk. Previous studies have investigated the relationship between physical activity and vertebral size, but their results seem somewhat contradictory. In this population-based birth cohort study, we aimed to evaluate the relationship between objectively measured physical activity (PA) and vertebral size.

Methods: The study population consisted of 1202 cohort participants who underwent PA and vertebral size measurements at the age of 46–48. Moderate-to-vigorous physical activity (MVPA, ≥ 3.5 METs) was measured by a wrist-worn accelerometer (Polar Active, Polar Electro, Finland) for 14 days. The vertebral axial cross-sectional area (CSA) of the L4 vertebra was measured and calculated from lumbar magnetic resonance imaging (MRI) scans at 46–48 years. We analyzed the association between the daily amount of MVPA (min/day) and vertebral CSA using multivariable linear regression analysis.

Results: The daily amount of MVPA was significantly and positively associated with CSA in both sexes. For every minute/day of MVPA, men had 0.71 mm^2 (95% CI 0.36–1.06) and women 0.90 mm^2 (95% CI 0.58–1.21) larger CSA.

Conclusion: PA of at least moderate intensity is positively associated with vertebral size and may thus prevent future vertebral fractures.

Keywords: MVPA, Vertebrae, Lumbar spine, Osteoporosis, Fractures, Cohort study

INTRODUCTION

Fall incidents and osteoporosis increase in older age, leading to a higher incidence of vertebral fractures. Vertebral fractures reduce the quality of life and increase morbidity and mortality, which cause enormous social costs (1). A recent systematic literature review concluded that small vertebral dimensions may be associated with a higher vertebral fracture risk (2). Identifying the factors that influence possible future vertebral fractures can help prevent and reduce the risk of these fractures.

Bone strength is defined by many skeletal characteristics, including bone mineral density (BMD), bone microarchitecture and macroarchitecture, bone cross-sectional size, trabecular and cortical shape and geometry, the rate of bone turnover, and microdamage accumulation (3,4). Bone modeling is known to continue until the epiphyseal fusion of bone, whereas remodeling continues throughout the lifespan (3–5). Periosteal apposition continues with ageing and bone cross-sections become larger (6). Maximum bone strength is usually reached between 20 and 30 years of age. After this, age-related changes slowly reduce skeletal strength and thus also vertebral strength (4,7). There is also evidence that sex differences play a role in bone formation and skeletal strength (8).

Skeletal loading is known to influence bone strength: there is strong evidence that regular physical activity (PA) has a positive effect on bone mass, mineral density, geometry and structure, and decelerates bone loss, also decreasing the incidence of fragility fractures and preventing osteoporosis (4,9–12). However, some studies have also found no association between bone strength parameters and PA (13,14).

It is widely believed that PA is crucial for skeletal health, but there has also been discussion about which kind of PA and which level of PA is most effective (12,15). Recommendations propose that exercise should be regular for many years, performed three to four times per week, and include moderate- to high-magnitude impact from varying loading directions (9,10). We recently showed in the Northern Finland Birth Cohort 1966 (NFBC 1966) that high lifelong leisure-time PA was associated with large vertebral axial cross-sectional area (CSA) among women, but not among men. High-impact exercise in particular seemed to increase vertebral CSA, which is a major determinant of vertebral strength (16,17). Other recent evidence also strengthens our understanding that even PA at a moderate level, when performed regularly, has a positive influence on bone size and BMD (11,18).

The aim of this population-based birth cohort study was to evaluate the relationship between objectively measured PA and vertebral size using accelerometers and lumbar magnetic resonance imaging (MRI) scans. We hypothesized that higher levels of moderate to vigorous PA would be associated with larger vertebral CSA.

METHODS

This research used a population-based birth cohort study design to examine the relationship between objectively measured PA and vertebral size. The study population consisted of Finnish pregnant women and their children born in a specific time period. PA was measured by accelerometers, and the spines of the cohort members were scanned by magnetic resonance imaging (MRI), from which the CSA of the L4 vertebra were calculated. The accurate study setting is described below.

Study population and clinical examination

The Northern Finland Birth Cohort 1966 (NFBC1966) (http://www.oulu.fi/nfbc/) is a prospective population-based birth cohort. Originally, NFBC1966 data were collected from two provinces of Finland, Oulu and Lapland. Pregnant women in Finland visit maternity clinics regularly from the beginning of their pregnancy. All pregnant women living in Oulu and Lapland who visited the maternity clinic in 1965 were asked to take part in the NFBC1966, if the expected date of birth of their child was between January 1st and December 31st, 1966. These mothers (n= 12 068) and children (n= 12 231) have been followed ever since, and data have been collected on their health, lifestyle and social status via postal questionnaires and clinical examinations (19).

At the age of 46–48 (2012–2014), all cohort members whose addresses were known (n= 10 321) received postal questionnaires enquiring about their health status and lifestyle, and 66% responded (n= 6825). Cohort members living in Finland were also invited to clinical examinations, which 5861 (57%) attended. Height and weight measurements from which we calculated body mass index (BMI, kg/m2), were performed by a trained study nurse. In addition, the socioeconomic status of the participants was rated on the basis of the number of years spent at school (≤ 9 years, 9–12 years, > 12 years) and questions on basic education, with the following response alternatives: 1) Less than nine years of elementary school, 2) comprehensive school, or 3) matriculation examination. Smoking status was elicited by asking: 1) "Have you ever smoked cigarettes (yes/no)?" and 2) "Do you currently smoke (yes/no)?" Three categories were formed on the basis of the answers: 1) non-smoker, 2) former smoker, and 3) current smoker. General diet was elicited and categorized as vegetarian, lactose free, gluten free, weight-loss, other and no special diet.

Those who participated in the clinical examination and lived no more than 100 km from the city of Oulu (n=1 988), were invited to lumbar MRI, and 1540 attended. From this study population we excluded participants taking bone-affecting medication, including calcium supplements and osteoporosis medication (n= 42); and those for whom measuring vertebral dimensions was difficult due to anatomical reasons including vertebral fractures, spondylodesis, severe disc degeneration, Schmorl's nodes, segmentation errors and endplate erosions or reasons related to measuring equipment such as L4 not fully shown in scan, low image accuracy and failure to locate L4 (n= 159) or who had missing covariate or PA data (n= 137). Thus, the final study population consisted of 1202 participants.

Measurement of physical activity

PA was measured by a waterproof wrist-worn accelerometer, Polar Active (Polar Electro, Kempele, Finland), which has a 21-day memory (20,21). Accelerometers were chosen because they are widely regarded as reliable and sensitive for measuring PA (22,23,24). The Polar Active provides metabolic equivalent (MET) values with an epoch length of 30 seconds using sex, age, weight, and height as inputs (20). The Polar Active has been shown to correlate ($R^2 = 0.74$) with the double-labeled water technique while assessing energy expenditure (EE) during exercise training (21,25).

The participants carried the accelerometer 24 hours per day on their non-dominant wrist for at least 14 days. We included in our analysis those with at least four valid days of data excluding the day on which they received the accelerometer. A valid day was determined as at least 600 min/day monitoring time during waking hours (20,22,26–28). We calculated the Daily averages of duration (min/day) at five activity levels (very light: 1–2 MET, light: 2–3.5 MET, moderate: 3.5–5 MET, vigorous: 5–8 MET and very vigorous: ≥ 8 MET) on the basis of the threshold values used by the manufacturer (20).

Lumbar MRI

At the age of 46–48 (2012–2014) participants' spines were imaged through 1.5-T MRI (Signa HDxt, General Electric, Milwaukee, WI) using NeaView Radiology software (Neagen Oy, Oulu, Finland) version 2.31 at the University Hospital of Oulu. All the MR images were obtained by the staff of the department of radiology, Oulu University Hospital. The imaging was carried out in adherence with routine lumbar spine protocol, which consists of T2-weighted fast-recovery fast spin-echo (frFSE) images in sagittal (TR/effTE 3500/112 ms, 4 averages, FOV 280 × 280 mm, acquisition matrix 448 × 224, slice thickness 3 mm with 1 mm interslice gap) and transverse planes (TR/effTE 3600/118 ms, 4 averages, FOV 180 × 180 mm, acquisition matrix

256 × 224, slice thickness 4 mm with 1 mm interslice gap). The same researcher performed all the MRI measurements (Petteri Oura, P.O.).

We calculated the CSA and mean height of the L4 vertebra by measuring eight dimensions (three height dimensions: minimum, anterior, posterior, and two width dimensions: minimum, maximum, and three depth dimensions: superior, inferior, halfway) from the corpus of L4 (Figure 1). These measurements are accurately described in our previous article (17). The level of intra-rater reliability was high (intraclass correlation = 0.963) and relative measurement errors (%) were minor, the values distributing around the mean of 0.0 with a standard deviation (SD) of 4.9 (17). Using these measurements, we calculated CSA using the formula CSA = $\pi * a * b$, where a = vertebral width/2 and b = vertebral depth/2. Vertebral width and depth, used in a and b, were assessed using the mean value calculated from several slices of L4 (29). Vertebral height dimension was calculated as the mean of the three height dimensions mentioned above, and we used it as a covariate in the analysis.

Ethics

The study was conducted according to the Declaration of Helsinki and approved by the Ethical Committee of the Northern Ostrobothnia Hospital District. Participation was voluntary; cohort members signed their informed consent at each stage of the study. All personal details were replaced by identification codes so that it was impossible to recognize any individual from the data. This provided full anonymity for all the participants.

Statistical analyses

The data were analyzed using SPSS version 24 (IBM, Armonk, New York, USA). The level of statistical significance was set at P= 0.05. The general characteristics of the sample were calculated using means and SD for continuous variables and frequencies and percentages for categorical variables.

The association between vertebral CSA (mm^2, continuous outcome with normal distribution among each sex) and MVPA (min/day, continuous predictor) was analyzed using linear regression. In order to assess the robustness of our results, we constructed both unadjusted (i.e. simple) and adjusted (i.e. multivariable) models. The models were adjusted for height of the L4 vertebra (mm, continuous variable), weight at 46–48 years, socioeconomic status determined by education years (categorical variable), and lifetime smoking status determined at 46–48 years (categorical variable) (16,17). All analyses were stratified by sex due to the major differences in vertebral size between men and women. We collected beta estimates (B) and their 95% confidence intervals (CI) from the data output.

RESULTS

Study population

The final study population consisted of 1202 participants, 557 men and 645 women. The mean imaging age was 46.8 (SD 0.4) years. The mean weight of men was 86.0 kg (SD 12.5) and women 71.2 kg (SD 13.8) and the BMI was 27.0 (SD 3.7) and 26.2 (SD 5.0) among men and women, respectively. The majority of both men and women had more than nine years of education and most of them did not have any special diet (men 72%, women 66%). More than half of the participants were non-smokers (men 51%, women 60%). The mean CSA of men's L4 was 13.2 cm^2 (SD 1.7) and of women's 10.6 cm^2 (SD 1.3) (Table 1).

Level of physical activity

The mean wearing time of the accelerometer was 985 min/day (SD 65.7) for men and 968 min/day (SD 58.0) for women (16 hours/day on average among both sexes). The mean amount of moderate intensity PA was 49 min/day among men and 28 min/day among women, whereas the amount of vigorous PA was 18 min/day and 27 min/day, and very vigorous PA 12 min/day and 6 min/day among men and women, respectively (Table 1).

Association between moderate to vigorous physical activity and vertebral size

The daily amount of moderate to vigorous physical activity was positively and significantly associated with vertebral CSA among both sexes (Table 2). The results of both the unadjusted and adjusted analyses were similar. According to the β estimates of the adjusted models, for each minute/day of MVPA, men had 0.71 mm2 (95% CI 0.36–1.06) and women 0.90 mm2 (95% CI 0.58–1.21) larger CSA.

DISCUSSION

To our knowledge, this is the first population-based birth cohort study to evaluate the association between objectively measured PA and vertebral CSA using blinded accelerometers. This study showed a positive association between moderate to vigorous PA and vertebral size in both genders. Our results suggest that physical activity reaching at least a moderate activity level could offer a means of preventing future vertebral fractures.

Very few studies have examined the effects of objectively measured PA on vertebral size. In our earlier studies of the same NFBC1966 cohort, we have investigated the relationship of PA and CSA with self-reported PA data and discovered that high lifelong PA is associated with large vertebral size, at least among women (16,17). The lack of a distinct association among men may be due to, for example, hormonal or other sex differences in the effect of PA (7), or the use of self-reported PA data (30,31). In this study, we also assessed the models adjusting for self-reported PA in adolescence. As this had no effect on the models, the self-reported PA data were left out from the final models. Our present results, as well as those of a few other recent studies in this field (18,32,33), strengthen the understanding that PA has beneficial effects on vertebral size and bone health.

One recent cross-sectional study (18) examined the association between objectively measured PA, using accelerometers and bone health, by measuring the BMD and CSA of the tibia and the radius, as well as the BMD of the lumbar spine, vertebrae L1–L4. The study population in this research was similar to ours and included over 1200 men and women. The finding was that total PA was positively associated with the BMD and trabecular CSA of the tibia, but not with the BMD and CSA of the radius or the BMD of vertebrae L1–L4. Nevertheless, the conclusion was that MVPA may influence bone properties (18), which is congruent with our results.

Another up-to-date cross-sectional study has also concluded that PA may benefit skeletal health in adulthood: more than 1400 participants used pedometers and the researchers analyzed the associations between daily steps and bone values of the calcaneus and tibia, which are also weight-bearing bones like vertebrae (34). The results showed significant positive associations between daily steps and bone values in women, which was in line with the research group's earlier findings that PA seems to have beneficial effects on tibial bone size and geometry (35).

A further cross-sectional study (32) evaluated the relationship between objectively measured PA and the BMD of the hip and spine. The results of the study suggest that objectively measured PA is a prognostic factor of the differences in BMD of the hip and spine (32). In addition, the association between PA measured by accelerometers and bone mineral content (BMC), comparing vigorous-intensity PA (VPA) and MVPA, has been recently studied among children and adolescents (33). The conclusions are that MVPA and VPA are positively associated with spine and hip BMC among males, whereas among females the associations are between spine and hip BMC and VPA, and hip BMC and MVPA (33). Our study contributes to these findings, though the association between MVPA and lumbar spine BMD remained slightly indistinct in one of the studies (18). Researchers consider that PA must be more intense if it is to affect lumbar spine BMD. They also point out the significance of high-intensity vertical impacts when considering bone health (18).

Other studies have demonstrated similar results concerning the positive effect of PA on bone health, though they have mostly concentrated on the relationship between self-reported PA and BMD (15,36,37). A previous systematic literature review (12) concluded that PA can reduce the speed of bone loss in the spine of postmenopausal women and also have a positive effect on the bone mass of the lumbar spine of premenopausal women. Two more recent systematic reviews (38,39) analyzed studies on the relationship between self-reported PA and BMD. The conclusion was in line with our results, suggesting that among postmenopausal women, high-impact exercise may have a positive effect on bone mass and geometry, depending on its regularity and intensity (38). In addition, when performed regularly, PA may reduce bone loss by maintaining cortical and trabecular volumetric BMD (39). However, the authors admit that the large variation in types of exercise complicated the comparison of studies (38,39).

Other previous studies on the association between PA and BMD also support our finding that MVPA can have a positive effect on bone size (11,40). One population-based five-year prospective cohort study (40) investigated the relationship between self-reported PA and the areal BMD of total hip and lumbar spine, vertebrae L1–L4. The conclusion was that changes in PA have a positive effect on total hip BMD. Among men, this effect was also seen in lumbar spine BMD. Another population-based cross-sectional study investigated cortical bone size and the bone strength of the tibia and the radius, and measured the BMD of the spine and hip. The study revealed an independent association between current PA and cortical bone size at the distal tibia. The researchers believed that PA may lead to a decrement of cortical bone loss in weight-bearing bones, and that MVPA can have a positive effect on bone size (11), which is in line with our new results.

This study has several strengths. The population-based sample size was large compared to previous studies (2), including over 1200 birth cohort participants of both sexes. The study population was a representative sample of the Northern Finnish population (41), and the results are applicable at the population level.

Another strength of this study is its objective measurement of PA (22-24). It is well recognized that objective rather than self-reported methods of measuring physical activity should be favored, because subjective evaluation of PA induces bias originating from over- or underestimation of true physical activity, recall and response bias, and the inability to capture the absolute level of physical activity (22-24). Accelerometers have been regarded as sensitive, reliable, and practical for measuring PA (22-24). We evaluated the relationship between objectively measured PA and vertebral size using blinded accelerometers. Thus, the participants were not given any feedback on their activity.

Thirdly, we chose the fourth lumbar vertebra (L4) for CSA measurements: Although both lumbar vertebrae L4 and L5 carry most of the weight due to their caudal position in the vertebral column, L4 is considered more stable than L5 (42). In our previous studies we have demonstrated the high accuracy of MRI in measuring vertebral size and predicted minor measurement errors related to used lumbar vertebra (17,43).

Nevertheless, this study also has some limitations. The differences observed in vertebral size were moderate but statistically significant. Thus, clinical significance is not definite. However, there is evidence that even mild differences in vertebral CSA might be relevant and significant when comparing individuals with vertebral fractures to those without (2). The knowledge that CSA affects the weight-bearing capacity of a vertebra (44) supports our hypothesis that PA effects might be a preventive factor of future vertebral fractures.

Cross-sectional data cannot be used to infer causality because temporality is not known (15). We measured PA and vertebral CSA once at the age of 46–48, which allowed us to study only associations, not effects. Another limitation concerns utilizing the L4: We are aware that the varying orientation of L4 due to anatomical variation among the study participants may have affected our orientation of the MRI slices, increasing potential measurement error. Using one vertebra as the predictor of the strength of all vertebrae may also be seen as a potential cause of measurement error. On the other hand, evidence exists that measurements of one vertebra can be applied to all thoracolumbar vertebrae with high accuracy (44).

A wrist-worn monitor was selected in this study due to its higher wearing compliance than that of waist-worn monitors. The recent NHANES studies, for example, also used the wrist as sensor placement (45). However, the wrist-worn accelerometer could be seen as limitation, because the acceleration signal obtained from the sensor reflects the acceleration of the movements from that part of the body, making under- or overestimation of energy expenditure of specific movement patterns possible. However, the reported differences between these hip and wrist locations in bone loading rates have been rather small (46). The accelerometer was validated against the doubly labelled water technique and provided good correlation for measuring energy expenditure during exercise training (R=0.86).

Vertebral fractures reduce the quality of life: Immobility and incapability to survive without help at home lead to the hospitalization and institutionalization of elder people. As a result, morbidity and mortality increase, causing enormous social cost (1), not to mention personal distress. Thus, studying other factors that influence vertebral size, in addition to PA, is an essential aspect of enhancing the prevention of vertebral fractures. These contribute to enabling independent lives among the elderly and delaying hospitalization. Furthermore, knowledge regarding the effectiveness of various sports on vertebrae and bone health is significant for future research. Most importantly, because skeletal response to loading is slow, long-term prospective studies are needed in order to demonstrate and clarify findings and associations. In addition, knowledge regarding the positive effects and outcomes of PA performed already at middle age is crucial, as it can verify global recommendations for lifelong physical activity and motivate individuals to follow active lifestyles.

CONCLUSION

In this population-based birth cohort study we investigated the relationship between objectively measured PA and vertebral size. Among both sexes, physical activity reaching at least moderate intensity at the age of 46 was positively associated with vertebral size. Since vertebral size has been associated with vertebral strength and risk of fracture, MVPA might be considered a preventive factor of future vertebral fractures. These findings are mostly in line with previous literature, though differences in study designs and participants prevent direct comparison of studies. Further studies are needed to increase our understanding of the relationship between objectively measured PA and bone health.

REFERENCES

1. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. *Lancet.* 2011;377(9773):1276-87.
2. Ruyssen-Witrand A, Gossec L, Kolta S, Dougados M, Roux C. Vertebral dimensions as risk factor of vertebral fracture in osteoporotic patients: a systematic literature review. *Osteoporos Int.* 2007;18(9):1271-8.
3. Sambrook P, Cooper C. Osteoporosis. *Lancet.* 2006;367(9527):2010-8.
4. Weaver CM, Gordon CM, Janz KF, et al. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. *Osteoporos Int*. 2016; 27(4):1281-1386.
5. Seeman E, Delmas PD. Bone Quality — The Material and Structural Basis of Bone Strength and Fragility. *N Engl J Med.* 2006;354(21):2250-61.
6. Bouxsein M, Karasik D. Bone Geometry and Skeletal Fragility. *Curr Osteoporos Rep*. 2006;4(2):49-56.
7. Ebbesen EN, Thomsen JS, Beck-Nielsen H, Nepper-Rasmussen HJ, Mosekilde L. Age- and gender-related differences in vertebral bone mass, density, and strength. *J Bone Miner Res.* 1999;14(8):1394-403.
8. Duan Y, Turner CH, Kim BT, Seeman E. Sexual dimorphism in vertebral fragility is more the result of gender differences in age-related bone gain than bone loss. *J Bone Miner Res.* 2001;16(12):2267-75.
9. Gunter KB, Almstedt HC, Janz KF. Physical Activity in Childhood May Be the Key to Optimizing Lifespan Skeletal Health. *Exerc Sport Sci Rev.* 2012;40(1):13-21.

10. Nikander R, Sievänen H, Heinonen A, Daly RM, Uusi-Rasi K, Kannus P. Targeted exercise against osteoporosis: A systematic review and meta-analysis for optimising bone strength throughout life. *BMC Musculoskeletal Disorders* [Internet]. 2010 [cited 2018 May 31];8(47). Available from: http://www.biomedcentral.com/1741-7015/8/47. doi: 10.1186/1741-7015-8-47.

11. Nilsson M, Sundh D, Mellström D, Lorentzon M. Current Physical Activity Is Independently Associated With Cortical Bone Size and Bone Strength in Elderly Swedish Women. *J Bone Miner Res.* 2017;32(3):473-85.

12. Wallace BA, Cumming RG. Systematic Review of Randomized Trials of the Effect of Exercise on Bone Mass in Pre- and Postmenopausal Women. *Calcif Tissue Int.* 2000;67(1):10-8.

13. Junno JA, Paananen M, Karppinen J, et al. Influence of physical activity on vertebral strength during late adolescence. *Spine J.* 2013;13(2):184-9.

14. Whitfield GP, Kohrt WM, Pettee Gabriel KK, Rahbar MH, Kohl HW 3rd. Bone Mineral Density across a Range of Physical Activity Volumes: NHANES 2007–2010. *Med Sci Sports Exerc.* 2015;47(2):326-34.

15. Bielemann RM, Martinez-Mesa J, Gigante DP. Physical activity during life course and bone mass: a systematic review of methods and findings from cohort studies with young adults. *BMC Musculoskeletal Disorders* [Internet]. 2013 [cited 2018 May 31];14(77). Available from: http://www.biomedcentral.com/1471-2474/14/77. doi: 10.1186/1471-2474-14-77.

16. Oura P, Paananen M, Niinimäki J, et al. High-impact exercise in adulthood and vertebral dimensions in midlife - The Northern Finland Birth Cohort 1966 study. *BMC*

Musculoskeletal Disorders [Internet]. 2017 [cited 2018 May 31];18(1). Available from: https://doi.org/10.1186/s12891-017-1794-8. doi: 10.1186/s12891-017-1794-8.

17. Oura P, Paananen M, Niinimäki J, et al. Effects of Leisure-Time Physical Activity on Vertebral Dimensions in the Northern Finland Birth Cohort 1966. *Scientific Reports* [Internet]. 2016 [cited 2018 May 31];6(27844). Available from: www.nature.com/scientificreports. doi: 10.1038/srep27844.
18. Johansson J, Nordström A, Nordström P. Objectively measured physical activity is associated with parameters of bone in 70-year-old men and women. *Bone*. 2015;81:72-9.
19. Rantakallio P. The longitudinal study of the Northern Finland birth cohort of 1966. Paediatr Perinat Epidemiol. 1988;2(1):59-88.
20. Jauho AM, Pyky R, Ahola R, et al. Effect of wrist-worn activity monitor feedback on physical activity behavior: A randomized controlled trial in Finnish young men. *Prev Med Rep.* 2015;22(2):628-34.
21. Kinnunen H, Tanskanen M, Kyröläinen H, Westerterp KR. Wrist-worn accelerometers in assessment of energy expenditure during intensive training. *Physiol Meas.* 2012;33(11):1841-54.
22. Cain KL, Sallis JF, Conway TL, Van Dyck D, Calhoon L. Using accelerometers in youth physical activity studies: a review of methods. *J Phys Act Health.* 2013;10(3):437-50.
23. Slootmaker SM, Schuit AJ, Chinapaw MJ, Seidell JC, van Mechelen W. Disagreement in physical activity assessed by accelerometer and self-report in subgroups of age, gender, education and weight status. *Int J Behav Nutr Phys Act.* 2009;25(6):17.
24. Schaefer SE, Van Loan M, German JB. A feasibility study of wearable activity monitors for pre-adolescent school-age children. *Preventing Chronic Disease* [Internet]. 2014

[cited 2018 May 31];11(E85). Available from: https://www.cdc.gov/pcd/issues/2014/13_0262.htm. doi: 10.5888/pcd11.130262.

25. Brugniaux JV, Niva A, Pulkkinen I, Laukkanen RM, Richalet JP, Pichon AP. Polar Activity Watch 200: a new device to accurately assess energy expenditure. *Br J Sports Med.* 2010;44(4):245-9.
26. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of Physical Activities: an update of activity codes and MET intensities. Med Sci Sports Exerc. 2000;32(9):498-504.
27. Husu P, Suni J, Vähä-Ypyä H, et al. Objectively measured sedentary behavior and physical activity in a sample of Finnish adults: A cross-sectional study. *BMC Musculoskeletal Disorders* [Internet]. 2016 [cited 2018 May 31];16(920). Available from: https://doi.org/10.1186/s12889-016-3591-y. doi: 10.1186/s12889-016-3591-y.
28. Tudor-Locke C, Camhi SM, Troiano RP. A Catalog of Rules, Variables, and Definitions Applied to Accelerometer Data in the National Health and Nutrition Examination Survey, 2003-2006. *Preventing Chronic Disease* [Internet]. 2012 [cited 2018 May 31];9(E113). Available from: https://www.cdc.gov/pcd/issues/2012/11_0332.htm. doi: 10.5888/pcd9.110332.
29. Peel NF, Eastell R. Diagnostic value of estimated volumetric bone mineral density of the lumbar spine in osteoporosis. *J Bone Miner Res.* 1994;9(3):317-20.
30. Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of Self-reported versus Accelerometer-Measured Physical Activity. *Med Sci Sports Exerc.* 2014;46(1):99-106.
31. Gorzelitz J, Peppard PE, Malecki K, Gennuso K, Nieto FJ, Cadmus-Bertram L. Predictors of discordance in self-report versus device-measured physical activity measurement. *Ann Epidemiol.* 2018;28(7):427-31.

32. Hansen BM, Tucker LA. Fitness and bone density in women: The role of age, weight, calcium, vitamin D, and menopause. *J Sports Med Phys Fitness.* 2016;56(9):1047-59.

33. Janz KF, Letuchy EM, Francis SL, Metcalf KM, Burns TL, Levy SM. Objectively measured physical activity predicts hip and spine bone mineral content in children and adolescents ages 5-15 years: Iowa bone development study. Front Endocrinol. 2014;15(5):112.

34. Tolonen S, Sievänen H, Hirvensalo M, et al. Higher step count is associated with greater bone mass and strength in women but not in men. *Arch Osteoporos.* 2018;13(1):20.

35. Tolonen S, Sievänen H, Mikkilä V, et al. Adolescence physical activity is associated with higher tibial pQCT bone values in adulthood after 28-years of follow-up--the Cardiovascular Risk in Young Finns Study. *Bone*. 2015;75:77-83.

36. Bailey CA, Brooke-Wavell K. Exercise for optimising peak bone mass in women. *Proc Nutr Soc.* 2008;67(1):9-18.

37. Yeh ML, Liao RW, Hsu CC, Chung YC, Lin JG. Exercises improve body composition, cardiovascular risk factors and bone mineral density for menopausal women: A systematic review and meta-analysis of randomized controlled trials. *Appl Nurs Res.* 2018;40:90-8.

38. Hamilton CJ, Swan VJ, Jamal SA. The effects of exercise and physical activity participation on bone mass and geometry in postmenopausal women: a systematic review of pQCT studies. *Osteoporos Int.* 2010;21(1):11-23.

39. Polidoulis I, Beyene J, Cheung AM. The effect of exercise on pQCT parameters of bone structure and strength in postmenopausal women—a systematic review and meta-analysis of randomized controlled trials. *Osteoporos Int.* 2012;23(1):39-51.

40. Langsetmo L, Hitchcock CL, Kingwell EJ, et al. Physical activity, body mass index and bone mineral density-associations in a prospective population-based cohort of women and men: the Canadian Multicentre Osteoporosis Study (CaMos). *Bone*. 2012;50(1):401-8.
41. Oura P. Search for lifetime determinants of midlife vertebral size : Emphasis on lifetime physical activity and early-life physical growth [dissertation]. Acta Universitatis Ouluensis: University of Oulu; 2017.
42. Kiefer A, Shirazi-Adl A, Parnianpour M. Stability of the human spine in neutral postures. *Eur Spine J*. 1997;6(1):45-53.
43. Junno JA, Niskanen M, Nieminen MT, et al. Temporal trends in vertebral size and shape from medieval to modern-day. [Internet]. 2009 [cited 2018 May 31];4(e4836). Available from: https://doi.org/10.1371/journal.pone.0004836. doi: 10.1371/journal.pone.0004836.
44. Brinckmann P, Biggemann M, Hilweg D. Prediction of the Compressive Strength of Human Lumbar Vertebrae. *Spine*. 1989;14(6):606-10.
45. Troiano R, McClain J, Brychta R, et al. Evolution of accelerometer methods for physical activity research. *Br J Sports Med.* 2014; 48(13): 1019–1023.
46. Stiles V, Griew P, Rowlands A. Use of accelerometry to classify activity beneficial to bone in premenopausal women. *Med Sci Sports Exerc.* 2013;45(12):2353-61.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

FIGURE LEGENDS

Figure 1. MRI scans with vertebral measurements. 1 = Width (maximum and minimum widths were obtained from appropriate planes), 2 = Depth (cranial, midway and caudal depths were obtained from appropriate planes), 3 = Anterior height, 4 = Minimum height, 5 = Posterior height.

Table

Table 1. Characteristics of study participants (n= 1202).

	Men (N= 557)	Women (N= 645)
Age, years; mean (SD)	46.8 (0.4)	46.8 (0.4)
Height, cm; mean (SD)	178.6 (6.2)	164.8 (6.0)
Weight, kg; mean (SD)	86.0 (12.5)	71.2 (13.8)
BMI , mean (SD)	27.0 (3.7)	26.2 (5.0)
Education years		
≤ 9[1]	3.1 (17)	2.2 (14)
9–12[2]	73.4 (409)	71.6 (462)
> 12	23.5 (131)	26.2 (169)
Smoking		
Non-smoker	50.8 (283)	59.5 (384)
Former smoker	33.0 (184)	24.7 (159)
Current smoker	16.2 (90)	15.8 (102)
CSA of the L4 vertebra, cm^2; mean (SD)	13.2 (1.7)	10.6 (1.3)
Height of the L4 vertebra, cm; mean (SD)	2.8 (0.1)	2.7 (0.1)
PA		
Very light, min/d; mean (SD)	644.05 (95.7)	616.6 (86.5)
Light, min/d; mean (SD)	262.2 (67.2)	290.7 (70.3)
Moderate, min/d; mean (SD)	48.6 (24.8)	28.1 (14.9)
Vigorous, min/d; mean (SD)	18.2 (13.1)	27.2 (17.4)
Very vigorous, min/d; mean (SD)	12.1 (12.0)	5.7 (6.9)
Wear time, min/d; mean (SD)	985.1 (65.7)	968.3 (58.0)
Diet		

Lactose free (%)	8.4 (47)	7.9 (51)
Gluten free (%)	1.4 (8)	3.3 (21)
Weight loosing diet (%)	2.7 (15)	5.3 (34)
Vegetarian (%)	1.8 (10)	3.1 (20)
Other special diet (%)	14.0 (78)	14.1 (91)
No special diet (%)	71.6 (399)	66.4 (428)

[1]Compulsory comprehensive school in Finland lasts nine years.
[2]After comprehensive school, three years of high school are optional.

Table

Table 2. Association between moderate to vigorous physical activity (MVPA) and vertebral size according to linear regression models.

	Men			Women		
	Beta (mm^2)	95% CI	P	Beta (mm^2)	95% CI	P
MVPA						
Unadjusted	0.73	0.36, 1.09	< 0.001	0.70	0.37, 1.02	< 0.001
Adjusted[1]	0.71	0.36, 1.06	< 0.001	0.90	0.58, 1.21	< 0.001

[1]Adjusted for vertebral height, weight, diet, smoking, education years and wearing time.

Figure

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