ORIGINAL ARTICLE

WU ET AL.

MVPA ASSOCIATED WITH MUSCULOSKELETAL HEALTH OUTCOMES

Moderate-to-Vigorous Physical Activity But Not Sedentary Time Is Associated With Musculoskeletal Health Outcomes in a Cohort of Australian Middle-Aged Women

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ABSTRACT

Associations between physical activity and time spent sedentary and musculoskeletal outcomes remain unclear in middle-aged adults. This study aimed to describe associations between objectively-measured physical activity and sedentary time and musculoskeletal health outcomes in middle-aged women. This cross-sectional study from a population-based sample of 309 women (age 36 to 57 years) examined associations of total physical activity (accelerometer counts/min of wear time), and time spent sedentary, in light physical activities and moderate-to-vigorous physical activities (MVPA) (by Actigraph GT1M accelerometer) with lumbar spine (LS) and femoral neck (FN) bone mineral density (BMD) (by dual-energy X-ray absorptiometry), lower limb muscle strength (LMS), and functional mobility and balance tests (timed up and go test [TUG], functional reach test [FRT], lateral reach test [LRT], and step test [ST]) using linear regression. Total physical activity was beneficially associated with FN BMD (values are β ; 95% CI) (0.011 g/cm²; 95% CI, 0.003 to 0.019 g/cm²), LMS (2.13 kg; 95% CI, 0.21 to 4.06 kg), and TUG (−0.080 s; 95% CI, −0.129 to −0.030 s), after adjustment for confounders. MVPA was also beneficially associated with FN BMD (0.0050 g/cm²; 95% CI, 0.0007 to 0.0094 g/cm²), LMS (1.48 kg; 95% CI, 0.45 to 2.52 kg), ST (0.12 steps; 95% CI, 0.02 to 0.23 steps), and TUG (−0.043 s; 95% CI, −0.070 to −0.016 s).

Associations between MVPA and LMS, TUG and ST persisted after further adjustment for sedentary time. Only TUG was associated with sedentary time, with a detrimental effect (0.075 s; 95% CI, 0.013 to 0.137 s) and this did not persist after further adjustment for MVPA. Light physical activity was not associated with any outcome. MVPA appears more important than light physical activity or sedentary time for many musculoskeletal outcomes in middle-aged women. This needs to be considered when developing interventions to improve habitual physical activity that aim to improve musculoskeletal health. © 2016 American Society for Bone and Mineral Research

KEY WORDS: PHYSICAL ACTIVITY; BONE DENSITY; MUSCLE STRENGTH; BALANCE; MIDDLE-AGED WOMEN

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Introduction

Bone mineral density (BMD), muscle strength, and balance are all important aspects of musculoskeletal health. Low BMD is a major risk factor for fractures⁽¹⁾ and age-related loss of muscle strength is associated with decreased balance and functional limitations in older people.^(2,3) Consequently, impaired balance and mobility increases risk of falls,⁽⁴⁾ conferring a high risk of fractures.⁽⁵⁾ Declines in muscle mass, strength,⁽⁶⁾ BMD and bone strength,^(7,8) mobility and balance start around 45 to 55 years of age,^(9,10) suggesting that prevention of functional limitation in older age should begin in early midlife.⁽¹¹⁾ In order to do so, ways to prevent age-related decline in BMD, muscle strength, mobility, and balance need to be identified.

The amount of physical activity recommended for adults age 18 to 64 years is 150

to 300 min of moderate-intensity aerobic physical activity or 75 to 150 min of vigorous-intensity aerobic physical activity weekly, or an equivalent combination.⁽¹²⁾ However, it is uncertain whether these recommendations are appropriate for musculoskeletal health in middle-aged adults because only a few studies have investigated the effects of physical activity using objective measures of duration and intensity of physical activity in this age group^(13–17) and only one has measured sedentary time.⁽¹⁷⁾ However, all those studies were of convenience samples, most had small sample sizes, and results differed by studies and outcomes. Two studies showed positive association of moderate-to-vigorous physical activities (MVPA) with broadband ultrasound attenuation at the heel⁽¹³⁾ and change in BMD at the proximal femur,⁽¹⁴⁾ but one showed that intensity of physical activity was not associated with hip BMD,⁽¹⁵⁾ which may be due to the different approach used to define intensities of physical activity and the difference in bone outcomes and measured sites. In contrast, results were generally consistent by demonstrating a positive association between MVPA and muscle strength or postural stability.^(13,16,17) However, whether these associations are independent of sedentary time and whether sedentary time also plays a role is poorly understood. Only one study of small sample size ($n = 49$) examined whether MVPA and sedentary time were independently associated with muscle strength and postural stability, showing that positive association of MVPA with muscle strength and postural stability was independent of sedentary time, but not vice versa.⁽¹⁷⁾ This data requires confirmation and, moreover, it is unknown whether MVPA and sedentary time exert independent effects on bone health outcomes. These information is important for developing physical activity interventions and public health guidelines for musculoskeletal health.

Therefore, the aims of this study were to: (1) describe associations of objectively-measured total physical activity, time spent at different intensities of physical activity and sedentary time with BMD, lower limb muscle strength (LMS), mobility and balance measures in middle-aged women; and (2) examine whether any associations with MVPA are independent of sedentary time, and vice versa. We hypothesized that both total physical activity and time spent at different intensities of physical activity are positively and sedentary time is negatively associated with these outcomes and that any associations of MVPA with these outcomes are independent of sedentary time, and vice versa.

Subjects and Methods

Participants

Participants were from a 10-year follow-up of a previously reported 2-year randomized controlled trial conducted in 2000 in Southern Tasmania, Australia. Details of the original trial have been reported elsewhere.⁽¹⁸⁾ Briefly, women age 25 to 44 years were randomly selected from the 2000 Tasmanian Electoral Roll. As reported, the population of southern Tasmania was predominantly white.⁽¹⁸⁾ Women were excluded if they had previous measurement of bone density, thyroid disease, renal failure, malignancy, or rheumatoid arthritis, a history of hysterectomy, were taking hormone replacement therapies, pregnant or planning pregnancy within 2 years of study entry, or lactating. At baseline, 470 women were randomly assigned to one of two osteoporosis educational interventions: group education using the Osteoporosis Prevention and Self-Management Course (OPSMC) or an information leaflet. Participants had their BMD measured at the spine and hip at baseline, 2 years, and 12 years. Their relative fracture risk in later life was provided as an additional intervention: at baseline, those with a mean spine and hip *T*-score <0 were informed that they were at a higher risk in later life, whereas those with a mean *T*-score of zero or greater were informed that they were not at higher risk. The present study is a cross-sectional analysis of data obtained an additional 10 years after the original 2-year trial was completed (ie, the 12-year follow-up), comprising 347 women (age 36 to 57 years). Participants were included in this analysis if they had at least one of the outcome measures performed and had at least 5 valid days of physical activity recorded at 12 years (see below). Ethics approval was obtained from the Royal Hobart Hospital Ethics Committee, and all participants gave written informed consent.

Measurement of physical activity and sedentary time

Accelerometers (ActiGraph GT1M) were used to measure ambulatory physical activity for 7 consecutive days. Participants were asked to wear the accelerometer over the right hip. Accelerometer counts were recorded in 60-s epochs. Participants were included in the analysis if they wore the accelerometer for at least 10 hours per day for 5 days in the week. Participants recorded start and finish times each day in a diary, as well as the duration and reason for any time where they took the accelerometer off and circumstances potentially affecting accelerometer readings (ie, driving on uneven

ground). Total physical activity was expressed as total accelerometer counts divided by total monitoring time per day (counts/min of wear time [CPM]). A cutoff of <150 CPM was used to define time spent sedentary.^(19,20) Cutoffs for light physical activity and MVPA were 151 to 1748 CPM and ≥ 1749 CPM, respectively.⁽²¹⁾ Total sedentary time and time spent in light physical activity and MVPA was divided by the number of valid days of accelerometer wear to produce an average time spent per day at each intensity.

BMD

BMD was measured at the lumbar spine (LS) and femoral neck (FN) by dual-energy X-ray absorptiometry (DXA) using fan beam setting on a Hologic Delphi bone densitometer (Hologic QDR2000; Hologic, Waltham, MA, USA), calibrated daily with coefficient of variation (CV) of 1%.

LMS

LMS was measured to the nearest kilogram using a dynamometer (TTM Muscular Meter; Gloria, Tokyo, Japan). This test examines isometric strength, predominantly of the quadriceps and hip extensors. The examiner demonstrated the correct technique to the participant before testing. Participants stood on the back of the dynamometer platform, with back straight against a wall and knees flexed to an angle of 115 degrees. A bar connected by a chain to the dynamometer was held on the front of the thighs with both hands. They were then instructed to lift the bar upward using maximum force using their legs only, with the back and neck straight. A published figure illustrates the assessment.⁽²²⁾ The mean of two readings was calculated for analysis. The intraclass correlation coefficient for LMS was 0.94 (95% CI, 0.92 to 0.95) in this study (from two-way random-effects model⁽²³⁾).

Functional mobility and balance measurements

Functional mobility and balance was assessed using four clinical tests: the timed up and go test (TUG), the step test (ST), the functional reach test (FRT), and the lateral reach test (LRT), with details described elsewhere.⁽²⁴⁾ For each test, an average value of all measures taken was calculated for use in analyses.

Functional mobility

For the TUG participants sat in a normal armchair (45 cm high) with their back against the chair. The length of time required to stand up, walk a distance of 3 m, turn around,

walk back, and sit down again with their back against the chair was recorded. Two measures were performed.

Balance

For the ST, participants stood on one leg 5 cm from an 8.5-cm-high block positioned against a wall and placed the whole foot of the other leg onto the block and returned it to the floor repeatedly as fast as possible for 15 s, with the number of steps recorded. Both legs were tested.

For the FRT, participants stood with their feet behind a line perpendicular and adjacent to a wall. The arm closest to the wall was raised to shoulder height and the position of the knuckle of the middle finger marked. Keeping the feet flat, participants leaned forward as far as possible and the position of the knuckle was recorded at the point of farthest reach. FRT was the difference between the two measures. Each side was measured three times.

For the LRT, participants stood with their backs near but not touching a wall with the heels 10 cm apart. Participants raised both arms to shoulder height and maintained equal weight bearing while the position of the third finger's tip on the side being measured was marked on the wall. Participants then lowered the arm not being measured and reached sideways as far as possible with the arm being measured and the position of farthest reach marked. The difference between the two marks was calculated. Each side was measured three times.

Serum 25-hydroxy vitamin D levels

Venous blood samples were taken. Serum 25-hydroxy vitamin D (25OHD) level was assayed using liquid chromatography (LC)-tandem mass spectrometry (LC-MS/MS). The assay measures 25OHD₂ and 25OHD₃ separately with a CV 3% to 6%, using an internal standard.

Dietary intake

We estimated habitual dietary intake by using a food frequency questionnaire (Anti-Cancer Council of Victoria), which has been validated against 7-day food diaries with energy-adjusted correlation coefficients for nutrient intakes ranging from 0.28 for vitamin A to 0.78 for carbohydrate.⁽²²⁾ Intakes of calcium, energy, fat, protein, carbohydrate, cholesterol, iron, magnesium, phosphorus, sodium, vitamin C, vitamin E, and zinc were

calculated using Nutrient tables for use in Australia (NUTTAB) 2010.

Anthropometry and other factors

Height was measured by stadiometer (The Leicester height measure; Invicta Plastics Ltd, Oadby, UK), weight by a single set of calibrated scales (Heine, Dover, NH, USA). Body mass index (BMI) was calculated (kg/m^2). Other items were assessed using questionnaires: education level, employment status of main financial provider in the household, smoking history (current/former/never), marital status, number of children, breastfeeding history, menopausal status, personal history of fracture, and family history of osteoporosis and/or fracture.

Statistical analysis

Mean $\pm$ SD and median (interquartile range) were used to describe continuous variables as appropriate; n (%) was used to describe categorical variables.

A weighted estimating equation method^(25,26) was used to take into account missing data, where data were assumed to be missing at random. A logistic regression model was used to estimate the probability of a participant being retained in the analysis (ie, to be “not missing”). Baseline characteristics from the original study (ie, age, height, education level, current smoking status, and marital status), for which complete data were available were used as explanatory variables. In subsequent analyses, complete cases were weighted by the inverse of their estimated probabilities of being observed; ie, of being “not missing.” Unweighted data of complete cases were also analyzed as a sensitivity analysis.

Univariable and multivariable linear regression models were used to describe associations between total physical activity (CPM), time spent sedentary (min/day) and in light physical activity (min/day) and in MVPA (min/day) with each of the outcomes, adjusting for potential confounders (age, weight, height, and menopausal status, calcium intake, serum 25OHD levels, and history of fracture).

To explore independent associations between sedentary time and time spent in light physical activity and MVPA with each outcome, we included MVPA time and sedentary time together in one adjusted model, and investigated potential interactions between MVPA and sedentary time by including a cross-product interaction term for continuous variables of MVPA and sedentary time ($\text{MVPA} \times \text{sedentary time}$) in

multivariable regression models for each outcome). The potential interactions between MVPA and serum 25OHD levels were also examined in the same approach. Similarly, we included light physical activity and MVPA time together in an adjusted model. However, we did not include sedentary time with light physical activity in any model because of substantial collinearity between these variables, as indicated in other literature.⁽²⁷⁾ Sensitivity analyses were performed by fitting models using different cut-points taken from the literature in younger adults for different physical activity intensities.^(19,28–30) These were: sedentary time (<250 CPM); light physical activity (150–1951 CPM, 150–2191 CPM when 150 CPM was used for sedentary time; 250–1748, 250–1951, and 250–2191 CPM when 250 was used for sedentary time) and MVPA (>1951 CPM or 2191 CPM as appropriate according to the cut-point for light physical activity).

All analyses were performed in Stata version 12 (Stata Corp., College Station, TX, USA). A two-tailed *p* value <0.05 was considered statistically significant.

Results

Of the 347 women who participated in the 10-year follow up, 37 had fewer than 5 valid days of accelerometer results and one did not have any outcome measured, thus 309 women were included in this analysis. Compared to their counterparts, women who were lost to follow-up or had no accelerometer data or outcome measures were younger and shorter, had higher education level, and were more likely to be current smokers while less likely to be married or in a de facto relationship. Characteristics of participants included in the present study are shown in Table 1. The mean of total physical activity was 376 CPM. The median for total accelerometer wear time, sedentary time, and time spent in MVPA were 851, 535, and 37 min/day, respectively (Table 1). The prevalence of low 25OHD was 7.1% (<30 nmol/L) and 26.5% (<50 nmol/L).

<Insert Table 1>

After adjustment for confounders (Table 2), total physical activity (per 100 CPM) was positively associated with FN BMD (β 0.013 g/cm²; 95% CI, 0.004 to 0.021 g/cm²) and LMS (β 2.28 kg; 95% CI, 0.50 to 4.07 kg), while negatively but beneficially associated with TUG (β -0.079 s; 95% CI, -0.131 to -0.028 s). These associations equate to differences from the sample mean of approximately 1.6% for FN BMD, 3.0% for

LMS, and 1.5% for TUG. There were no associations between total physical activity and LS BMD, ST, FRT, and LRT.

<Insert Table 2>

There were no statistically significant interactions between MVPA, sedentary time, and serum 25OHD levels ($p > 0.05$ for all outcomes). After adjustment for potential confounders (Table 3: Model 2), MVPA (per 10 min) was beneficially associated with FN BMD (β 0.0055 g/cm²; 95% CI, 0.0012 to 0.0098 g/cm²), LMS (β 1.44 kg; 95% CI, 0.54 to 2.33 kg), ST (β 0.12 steps; 95% CI, 0.01 to 0.22 steps), and TUG (β -0.041 s; 95% CI, -0.069 to -0.014) (Table 3: Model 2); this equates to differences from the sample mean of approximately 0.7% for FN BMD, 1.9% for LMS, 0.7% for ST, and 0.8% for TUG. Time spent in light physical activity was not associated with any outcome (Table 3). An increase in sedentary time of 60 min/day was detrimentally associated with FN BMD (β -0.0120 g/cm²; 95% CI, -0.0226 to -0.0014 g/cm²) and TUG (β 0.077 s; 95% CI, 0.015 to 0.138 s), equating to differences from the sample mean of around 1.4% for FN BMD and 1.5% for TUG. There were no statistically significant associations with any other outcomes.

<Insert Table 3>

After additionally adjusting for sedentary time, the association between MVPA and FN BMD was attenuated (β 0.0038 g/cm²; 95% CI, -0.0012 to 0.0089 g/cm²). The association with TUG was also attenuated (β -0.032 s; 95% CI, -0.064 to -0.001 s). In contrast, adjusting for sedentary time strengthened associations of MVPA with LMS (β 1.45 kg; 95% CI, 0.42 to 2.48 kg) and ST (β 0.15 steps; 95% CI, 0.04 to 0.27 steps) (Table 3: Model 3). The associations between sedentary time and FN BMD and TUG did not persist after adjustment for MVPA (Table 3: Model 3).

In sensitivity analyses, using unweighted complete cases or different cut-points for physical activity intensity levels did not affect the results (data not shown).

Discussion

To our knowledge, this is the first study to describe the independent associations between objectively-measured physical activity and time spent sedentary with musculoskeletal health outcomes in a population-based sample of middle-aged women. Each additional 100 CPM of total physical activity was associated with 1.6% greater FN BMD, 3.0%

greater LMS, and 1.5% shorter TUG time. Intensity of physical activity was also important: MVPA was beneficially associated with FN BMD, LMS, TUG, and ST, but light physical activity was not associated with any outcomes. After adjustment for potential confounders, each 60-min increase in sedentary time was associated with 1.2% lower FN BMD and 1.4% longer TUG time. Importantly, associations of MVPA with LMS, TUG, and ST, but not FN BMD were independent of sedentary time, but not vice versa. However, there were no interactions between MVPA and sedentary time. These findings suggest that greater total physical activity is important for musculoskeletal health in middle-aged women, but increasing time spent in MVPA may be more important than decreasing sedentary time or increasing light physical activity.

The effects observed are of sufficient magnitude to potentially be clinically meaningful. For example, there is an average loss of 1.0% per year for total hip BMD in the late perimenopausal period,⁽³¹⁾ and in our study, a relatively modest 10-min increase in MVPA was associated with FN BMD improvement equivalent to approximately 0.6%. Similarly, the effect sizes for LMS (2.0%), ST (0.7%), and TUG (0.9%) compare favorably to annualized decline of 2.2% and 2.5% for grip strength, 0.3% and 1.6% for balance (the standard Romberg test), and 0.19% and 0.25% for gait velocity observed in women aged 50 and 60 years at baseline, respectively.⁽³²⁾ Moreover, if increases in BMD accrue over time, the potential for clinically important impacts are even higher. For example, modeling by Hernandez and colleagues⁽³³⁾ suggests that a 10% increase in peak bone mass could translate to an estimated 50% reduction in the relative risk of hip fracture.⁽³⁴⁾ Similarly, estimates are that in older women, for every 5% loss in FN BMD in risk of all fractures and of hip fracture increases by 40% and 90%, respectively.⁽³⁵⁾ For this reason, robust longitudinal data are required to determine how much the benefits of MVPA accrue over time.

Existing data on associations between objectively-measured physical activity and BMD are sparse in middle-aged women.^(13–15) In line with our study, two small studies found that activities of higher intensity producing higher loading were significantly associated with broadband ultrasound attenuation at the heel⁽¹³⁾ ($n = 34$) and change in BMD at the proximal femur⁽¹⁴⁾ ($n = 64$) in middle-aged women. However, a 6-year longitudinal study in 244 women age 35 to 45 years reported that total physical activity

was associated with change in hip BMD, but intensity was not,⁽¹⁵⁾ but only small numbers of women were classified as having moderate and vigorous intensity (27 and 17 participants, respectively) limiting the study's power. The role of sedentary time in BMD in middle-aged women is even less well understood. Chastin and colleagues⁽²⁷⁾ reported a negative association between sedentary behavior and total femur BMD in women aged 23 to 90+ years, and that the association was independent of MVPA. However, they did not report specifically on effects in middle-aged women. It is possible that there could be age-related differences in the response of bone to sedentary behavior or in the types and patterns of sedentary behavior that might explain this difference in our study findings. Neither Chastin and colleagues' study⁽²⁷⁾ nor ours observed any association between sedentary time and LS BMD. Although the reason for the site-specific difference in the association between sedentary time and BMD is unknown, one potential explanation could be variations in postures across different in sedentary behaviors. For example, the joint forces of upper and lower erector spinae muscle groups are increased when sitting compared with standing whereas the quadriceps and hamstring muscles are rarely activated.⁽³⁶⁾ However, further research in which either greater detail on types of sedentary behaviors or additional data from use of inclinometers would be needed to confirm this theory. Overall, the importance of the impact of sedentary time on BMD in middle-aged women remains poorly understood.

Similarly, the site-specific response of BMD to MVPA may be due to the site dependency of the BMD in response to different activities.^(18,37) It has been shown that BMD at femoral neck in older women was more likely to be increased by the exercise program that introduced stress to the skeleton via ground reaction forces (GRF) (eg, walking, jogging) but not joint reaction forces (eg, weight lifting, rowing).⁽³⁷⁾ Indeed, a meta-analysis of clinical trials and randomized controlled trials (RCTs) examining the effects of aerobic, high-intensity resistance training have reported an increase of about 1% per year in BMD at lumbar spine in premenopausal women⁽³⁸⁾ but no effects on FN BMD was observed. In contrast, high-impact aerobic exercise such as jumping and jogging⁽³⁹⁾ and programs that combine weight-bearing aerobic and strength training have been reported to be effective at increasing FN BMD.⁽⁴⁰⁾ Although it is suggested that a threshold of mechanical strain magnitude should be reached before osteogenic stimulus is

initiated,⁽⁴¹⁾ our capacity to examine the association between vigorous physical activity and BMD was limited by the very few limited time spent in vigorous physical activity in our study sample (90.6% did not have any vigorous physical activity, median = 0.38 min/day for those who had vigorous physical activity). Physical activity produces dynamic mechanical loads that influence bones through ground reaction forces and by the contractile activity of muscles.⁽⁴²⁾ Although the intensity is likely to reflect the GRF, our measure is of ambulatory physical activity and we cannot be certain of how osteogenic the different intensities were. This is because that the same intensity can be captured in totally different exercise environments, which can dramatically affect the vertical GRF. For example, it has been shown that the peak vertical GRF of various head-out aquatic exercises were significantly reduced in the aquatic environment, up to 41% to 72% lower than those obtained on dry land.⁽⁴³⁾ Therefore, direct evidence is still needed to determine the role of objectively-measured time spent in vigorous physical activity in BMD in middle-aged women.

Data on other musculoskeletal outcomes are sparse but generally consistent with our results. Willoughby and Copeland⁽¹⁷⁾ showed that in a convenience sample of 49 women age 50 to 67 years greater MVPA was associated with greater peak torque of knee extensors (standardized $\beta = 0.325$, $p = 0.022$) and better postural stability assessed using computerized dynamic posturography (standardized $\beta = 0.362$, $p = 0.012$), which were independent of time spent sedentary; in contrast, the deleterious effects of sedentary time on postural stability and relative peak torque of the knee flexors were not independent of MVPA. Together with our findings, this highlights the potential importance of increasing MVPA for maintaining muscle strength and balance, regardless of the amount of time spent sedentary. Two other studies also showed positive associations between MVPA or moderate and vigorous physical activity with muscle function but did not examine whether those associations were independent of sedentary time. Specifically, in 60 middle-aged postmenopausal women (mean $\pm$ SD age: 58.9 ± 3.9 years), Straight and colleagues⁽¹⁶⁾ showed that high MVPA was associated with greater isokinetic knee torque (standardized $\beta = 0.38$ and 0.41 for 60 degrees/s and 180 degrees/s, respectively; $p < 0.01$ for both) and lower-extremity muscle power (standardized $\beta = 0.31$, $p = 0.02$). Chahal and colleagues⁽¹³⁾ found that light ($r = 0.32$, $p <$

0.01), moderate ($r = 0.45$, $p < 0.001$), and vigorous ($r = 0.45$, $p < 0.001$) physical activities were all associated with knee extension torque in a convenience sample of 34 middle-aged women from a local fitness center (mean $\pm$ SD age: 49.8 ± 7.5 years), but because light physical activity in their study included fast walking which is often considered as moderate physical activity, their findings are essentially consistent with ours.

Despite the potential synergistic association between vitamin D and physical activity on musculoskeletal outcomes,^(44,45) there was no interaction between 25OHD levels and any outcomes in our study. This might be partly explained the relatively low prevalence of low serum 25OHD, which could be due to the high proportion of women taking vitamin D supplements (36%) given that the participants were originally from an osteoporosis education intervention trial. Indeed, we have recently published cross-sectional data suggesting the effects of vitamin D on bone density and balance may only be apparent when vitamin D levels are quite low (around 30 nmol/L).⁽⁴⁶⁾ Therefore, the interactions between MVPA and vitamin D status with musculoskeletal health should be further examined in younger populations with a wide range of 25OHD levels, particularly covering people with low vitamin D levels. Our study has some limitations. Causality cannot be inferred due to the cross-sectional design—we cannot exclude the possibility that those who have poorer BMD, muscle strength, and balance are less likely to be physically active. However, intervention studies have shown that high-impact activity with high-magnitude resistance training are effective for improving BMD in premenopausal and postmenopausal women,^(38,47) suggesting that some degree of causation is likely. In addition, as the study is cross-sectional, we cannot show if any musculoskeletal benefits accrue if physical activity and/or sedentary time is maintained over time. Longitudinal studies are required for this but RCTs of different intensities of ambulatory physical activity for bone density, LMS, and balance are also needed to definitively determine the optimal physical activity advice to give younger women for improving these musculoskeletal outcomes and before community interventions are implemented. This cohort of women had previously participated in a behavioral intervention to improve osteoporosis-preventive behaviors, including physical activity, thus the levels of physical activity measured at 12 years might be higher than the general

population of women of this age. However, the time spent in MVPA of about 259 min/week in our study at 12 years was not dissimilar to self-reported time spent in physical activity (about 239 min/week of MVPA, walking for fitness and transport) among adults age 45 to 54 years reported in the 2011–2012 Australian Health Survey⁽⁴⁸⁾ and at the end of the original trial, the levels of strenuous physical activity were similar between intervention groups,⁽¹⁸⁾ suggesting that this is not a major issue for the generalizability of results. Moreover, the cutoffs used for sedentary time, and physical activity intensities could influence the results; however, in sensitivity analyses using a range of published cutoffs the results remained largely unchanged, suggesting this is not a significant issue. Finally, although our original study used population-based sampling,⁽⁴⁹⁾ the generalizability of this analysis might be reduced due to the fact that it is a cross-sectional analysis of data from the 74% of the cohort retained after 12 years. However, we took into account missing data by using inverse probability weighting and the results were similar whether this method was used or not. Moreover, although there were some differences in smoking status and sociodemographic variables,⁽⁵⁰⁾ the wide spread of education levels at baseline and employment rate at 12 years approximates the overall population figures for these socioeconomic factors. Therefore, the likelihood of loss to follow-up influencing our findings is low and our findings are still likely to apply to healthy middle-aged women across a range of sociodemographic characteristics.

In summary, our study showed that in middle-aged women, greater total physical activity (CPM) was associated with better musculoskeletal health. MVPA appears more important than light physical activity or sedentary time for many musculoskeletal outcomes in middle-aged women. These findings are important for developing interventions to improve habitual physical activity that are targeted at improving musculoskeletal health among women in midlife when an accelerated process of decline in BMD, muscle strength, and balance begins. However, RCTs are needed before community interventions are implemented.

Disclosures

All authors state that they have no conflicts of interest.

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