Physical Activity for Bone Health: How Much and/or How Hard?

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[1]Assessment of Movement Behaviours Group (AMBer), Leicester Lifestyle and Health Research Group, Diabetes Research Centre, University of Leicester, Leicester, UNITED KINGDOM; [2]NIHR Leicester Biomedical Research Centre, UNITED KINGDOM; [3]Alliance for Research in Exercise, Nutrition and Activity (ARENA), Sansom Institute for Health Research, Division of Health Sciences, University of South Australia, Adelaide, AUSTRALIA; [4]Department of Health and Human Physiology, The University of Iowa, Iowa City, IA; and [5]Department of Epidemiology, The University of Iowa, Iowa City, IA

ABSTRACT

ROWLANDS, A. V., C. L. EDWARDSON, N. P. DAWKINS, B. D. MAYLOR, K. M. METCALF, and K. F. JANZ. Physical Activity for Bone Health: How Much and/or How Hard? *Med. Sci. Sports Exerc.*, Vol. 52, No. 11, pp. 2331–2341, 2020. **Purpose:** High-impact physical activity is associated with bone health, but higher volumes of lower-intensity activity may also be important. The aims of this study were to: 1) investigate the relative importance of volume and intensity of physical activity accumulated during late adolescence for bone health at age 23 yr; and 2) illustrate interpretation of the results. **Methods:** This is a secondary analysis of data from the Iowa Bone Development Study, a longitudinal study of bone health from childhood through to young adulthood. The volume (average acceleration) and intensity distribution (intensity gradient) of activity at age 17, 19, 21, and 23 yr were calculated from raw acceleration ActiGraph data and averaged across ages. Hip areal bone mineral density (aBMD), total body bone mineral content (BMC), spine aBMD, and hip structural geometry (dual-energy X-ray absorptiometry, Hologic QDR4500A) were assessed at age 23 yr. Valid data, available for 220 participants (124 girls), were analyzed with multiple regression. To elucidate significant effects, we predicted bone outcomes when activity volume and intensity were high (+1SD), medium (mean), and low (−1SD). **Results:** There were additive associations of volume and intensity with hip aBMD and total body BMC (low-intensity/low-volume cf. high-intensity/high-volume = Δ0.082 $g \cdot cm^{-2}$ and Δ169.8 g, respectively). For males only, spine aBMD intensity was associated independently of volume (low-intensity cf. high-intensity = Δ0.049 $g \cdot cm^{-2}$). For hip structural geometry, volume was associated independently of intensity (low-volume cf. high-volume = Δ4.8–6.6%). **Conclusions:** The activity profile associated with optimal bone outcomes was high in intensity and volume. The variation in bone health across the activity volume and intensity distribution suggests intensity is key for aBMD and BMC, whereas high volumes of lower intensity activity may be beneficial for hip structural geometry. **Key Words:** BMC, aBMD, HIP STRUCTURAL GEOMETRY, ACCELEROMETER, INTENSITY GRADIENT

Movement is accumulated across the entire day and across a continuous spectrum of physical activity intensity. In practice, this means that movement accumulated at a specific intensity should not be considered in isolation, but in the context of physical activity accumulated across the remaining spectrum of intensity (1,2). Focusing on physical activity accumulated in one-intensity category, for example, moderate-to-vigorous physical activity (MVPA), may limit: (a) insight into mechanisms underlying the associations between health and physical activity; and (b) development of optimal prescriptions of physical activity for health. This is because it presupposes the intensity (or intensities) assumed to be beneficial to health. Further, it relies on these intensities being present in the data and ignores the rest of the physical activity profile which may act in synergy with the investigated intensity.

Ideally, both the daily volume of physical activity and its intensity distribution should be captured. Depending on the health outcome, the volume of physical activity may be more important than the intensity (e.g., [3–5]), intensity may be key (e.g., [6,7]), or intensity and volume may have a cumulative effect (e.g., [8]). This can be investigated using two metrics derived directly from the data stored in raw acceleration activity monitors: the average acceleration (indicative of volume) and

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the intensity gradient (intensity distribution) (2). However, these metrics do not lend themselves to easy interpretation or translation. To address this, the intensity above which the most active X minutes/time are accumulated, can be used to illustrate the volume and intensity of the physical activity profile. For example, the M120, M60, M30, M15, M10, M5 and M2 illustrate the intensity of the most active accumulated 120 min, 60 min, 30 min, 15 min, 10 min, 5 min and 2 min of the day and the $M\frac{1}{3}_{DAY}$ the intensity of the most active 8 h (1/3) of the day. The intensity (magnitude of the acceleration) for each of the MX metrics can be interpreted *post hoc* to inform physical activity recommendations in terms of activity intensity (e.g., MVPA) and/or the acceleration associated with indicative activities (9).

For example, we recently showed that intensity and volume of physical activity were additively associated with body fat in adults. It was optimal to have relatively high-volume and high-intensity physical activity. However, high volumes of low-intensity physical activity (e.g., several hours per day of slow walking and intermittent low-intensity physical activity, such as pottering around) were also associated with lower body fat (8). Similarly, low volumes of high-intensity physical activity (e.g., 30 $min{\cdot}d^{-1}$ MVPA), including 5 to 15 $min{\cdot}d^{-1}$ of fast walking, were associated with lower body fat (8). Conversely, in children, the intensity of physical activity was key. While most children obtained 60 $min{\cdot}d^{-1}$ of MVPA, accumulating 5 to 15 min of sprinting and vigorous physical activity within that 60 min was associated with lower body fat (8–10). For physical function in adults with type 2 diabetes, an interactive association was evident. When activity intensity was low, higher volume was associated with better physical function. However, when activity intensity was high, function was relatively high, irrespective of activity volume (8).

It is known that high-impact physical activity is associated with bone health (11), but it is also suggested that higher volumes of lower-impact physical activity may be important (12–14), especially when high-impact physical activity is absent. In support of this, we recently showed a borderline additive association of volume and intensity of physical activity with bone health in premenopausal women from UK Biobank (8). Previous analyses with the same data have confirmed the importance of accumulated physical activity equivalent to running for a total of 1 to 2 $min{\cdot}d^{-1}$ (15).

The Iowa Bone Development Study (IBDS) is an ongoing study of lifestyle and bone health; the participants are now adults but have been tracked from the age of 5 yr. Since age 17 yr, raw acceleration accelerometers were used to assess physical activity allowing calculation of metrics derived directly from the measured acceleration (e.g., average acceleration, intensity gradient and MX metrics). This well-phenotyped longitudinal data set facilitates investigation of associations between physical activity accumulated during late adolescence and young adulthood on adult bone health.

AIMS

Our primary aim was to investigate the relative importance of volume and intensity of physical activity accumulated during late adolescence and young adulthood (age, 17–23 yr) for markers of bone health (hip, spine and whole body) at age 23 yr.

Our secondary aims were to (a) describe how bone health varies across the physical activity volume and intensity distribution and (b) to illustrate how metrics that focus on the most active periods of the day can be used to interpret results.

METHODS

This is a secondary analysis of data from the IBDS, an ongoing longitudinal study of bone health from childhood through adolescence and young adulthood. The IBDS began in 1998, when participants were age 5 yr (wave 1) and tracked participants' bone development in relation to physical fitness and lifestyle measures (16,17). Data collection occurred in waves of approximately 400 to 500 participants, with wave 1 at age 5 yr, wave 2 at age 8 yr, wave 3 at age 11 yr, then every 2 yr. Additional information about the IBDS and demographic information of participants is presented elsewhere (16). This secondary analysis focuses on physical activity measured using raw acceleration accelerometers. These data are available for approximately 60% of assessment wave 6 (age, 17 yr) and assessment waves 7 to 9 (19, 21, and 23 yr). Physical activity exposures were averaged across waves 6 to 9 to give an estimate of physical activity across late adolescence and young adulthood. Anthropometric measures and bone outcomes were taken from wave 9 (age, 23 yr). The IBDS was approved by the University of Iowa Institutional Review Board (human subjects). Participants younger than 18 yr provided written informed assent, legal caregivers, and participants older than 18 yr provided written informed consent.

Body Height, Mass, and Peak Height Velocity (Wave 9, Age 23 yr)

Participants' body height (cm) was measured using a Harpenden stadiometer (Holtain Ltd., Crosswell, UK), and body weight (kg) using a Healthometer physician's scale (Continental, Bridgeview, IL). In each of waves 3 to 5 (ages, 11–15 yr) of the IBDS, biological maturity was estimated as the number of years from age at peak height velocity (PHV). This is predicted from height, sitting height, leg length, and age using the Mirwald equation (18). This equation is most precise when the measures the estimate is based on are taken close to the actual PHV age (18). Therefore, for each participant, the estimate of PHV age that was closest to the actual assessment age was used. If only one PHV estimate was available, it was used. In the current study, years since PHV was used as a measure of biological age.

Bone Outcomes (Wave 9, Age 23 yr)

Whole body and hip dual-energy X-ray absorptiometry (DXA) scans were conducted using the Hologic QDR 4500A DXA (Delphi upgrade) with software V.12.3 in the fan-beam mode, as described previously (17). Total body (less the head) bone mineral content (BMC, g), areal bone mineral density (aBMD) ($g{\cdot}cm^{-2}$) of the left hip and spine were measured using standardized protocols as previously described (17,19,20). In brief, the general boundaries of the hip and spine images were designated using software-specific Global Regions of Interest (ROI). The bone within the ROI box was reviewed and edited to ensure appropriate bone-edge detection and aBMD ($g \cdot cm^{-2}$) was determined.

The Hip Structure Analysis program (Hologic Apex 3.0 software) was used to estimate structural geometry from hip DXA images as described in Ward et al. (19). In brief, the Hologic software program located the narrowest point of the femoral neck where bone cross-sectional area (CSA, cm^2) and cross-sectional moment of inertia (cm^4) for bending in the image plane were calculated, from which the femoral neck section modulus (hip FN Z, cm^3), an indicator of bending resistance in cross-section (19) was derived.

All scans were acquired by one of three International Society of Clinical Densitometry–certified technicians. Quality control scans were performed daily using the Hologic spine phantom (DXA). The precision error for BMC measurements is low (coefficient of variation of <1% for quality control scans using the phantom).

Physical Activity (Waves 6 to 9, Ages 17 to 23 yr)

Physical activity was measured using ActiGraph GT3X+ (ActiGraph, Pensacola, FL) accelerometers worn at the hip. Participants were requested to wear the monitors for five consecutive days including both weekend days. For waves 6 to 7, the protocol specified waking hours only; for waves 8 to 9, participants were given the option of 24 h wear. The sampling frequency was 30 Hz for all waves, except for approximately one third of files in wave 7 where the sampling frequency was 100 Hz. There is high agreement between physical activity outcomes derived from acceleration data collected at 30 and 100 Hz (21).

Accelerometer processing. ActiGraphs were initialized and downloaded using the latest release of ActiLife available at the wave of data collection (versions 6.0.0-6.13.3; ActiGraph, Pensacola, FL). Data were saved in raw format as GT3X files, before being converted to raw csv file format for signal processing. Accelerometer files were processed and analyzed with R-package GGIR version 1.9-4 (http://cran.r-project.org) (22). Signal processing in GGIR includes autocalibration using local gravity as a reference (23), detection of sustained abnormally high values; detection of nonwear, and calculation of the average magnitude of dynamic acceleration corrected for gravity (Euclidean Norm minus 1g, ENMO). These were averaged over 5-s epochs. All were expressed in milligravitational units (mg). Nonwear was imputed using the default setting in GGIR, that is, invalid data were imputed by the average at similar time-points on different days of the week. For calculation of the intensity gradient data for the entire 24-h cycle are required (2); therefore nonwear during the night was imputed as zeros. See Text, Supplemental Digital Content 1: Additional methodological detail, http://links.lww.com/MSS/B983.

Participants were excluded if their accelerometer files showed: postcalibration error greater than 0.01g (10 mg), fewer than 3 d of valid wear (defined as >16 $h \cdot d^{-1}$ after imputation for nonwear during the night), or wear data (24) wasn't present for each 15-min period of the 24-h cycle (after imputation of nonwear during the night, see Text, Supplemental Digital Content 1: Additional methodological detail, http://links.lww.com/MSS/B983).

Accelerometer outcome variables. The following outcomes were generated and averaged across all valid days: average acceleration (mg); intensity gradient (2); acceleration above which a person's most active fraction of the day or X minutes (MX) are accumulated: $M\frac{1}{3}_{DAY}$ (mg), M120 (mg), M60 (mg), M30 (mg), M15 (mg), M10 (mg), M5 (mg), M2 (mg) (within the GGIR package, these metrics are obtained in part 2 using: qlevels (0, 24 h): 960/1440, 1320/1440, 1380/1440, 1410/1440, 1425/1440, 1430/1440, 1435/1440, and 1438/1440. These MX statistics rank the acceleration for each epoch during the day in descending order to obtain the acceleration above which the person's most active X minutes are accumulated (25).

Average acceleration reflects the volume of physical activity. The intensity gradient reflects the distribution of acceleration intensity across the 24 $h \cdot d^{-1}$ and has been described elsewhere (2); in brief, it describes the negative curvilinear relationship between physical activity intensity and the time accumulated at that intensity during the 24 $h \cdot d^{-1}$. The intensity gradient is always negative, reflecting the drop in time accumulated as intensity increases; a more negative (lower) gradient reflects a steeper drop with little time accumulated at midrange and higher intensities, whereas a less negative (higher) gradient reflects a shallower drop with more time spread across the intensity range. It was calculated as previously described (2) and generated in GGIR (argument iglevels = TRUE).

To characterize the patterns of physical activity over waves 6 to 9, all physical activity outcome variables were averaged over waves 6, 7, 8, and 9. Under the assumption that data were missing at random, participants were included providing at least one measurement per participant was available from the four waves. Mean age of the included physical activity waves was calculated and included as a covariate in analyses.

Statistical Analysis

Descriptive statistics were calculated for each variable using mean (SD). The average acceleration and intensity gradient of boys and girls were compared using regression, with the following covariates: proportion of the 24-h cycle the monitor was worn, wear duration, age at bone scan in wave 9, and mean age of the included physical activity waves. Pearson's correlation coefficients were used to investigate the intercorrelations between the average acceleration and the intensity gradient to determine the extent to which they contained independent information on the physical activity profile (2).

Analyses were carried out for the following dependent variables (all taken from wave 9): hip aBMD ($g \cdot cm^{-2}$), hip bone CSA (hip CSA, cm^2), hip femoral neck section modulus (hip FN Z, cm^3), total body BMC (minus head, g), spine aBMD ($g \cdot cm^{-2}$). Covariates for associations with physical activity were: sex, age at scan in wave 9, height, mass, years from PHV (all from wave 9), the $24h_{CYCLE}$ (the proportion of the 24-h cycle the monitor was worn), and mean age of the included physical activity waves.

Primary aim. To address our primary aim, multiple linear regression analyses were used to explore the relative contributions of physical activity intensity distribution (intensity gradient) and volume (average acceleration) for markers of bone health. Model 1 was adjusted for sex and mass only, and model 2 was adjusted for all covariates. Model 3 was further adjusted for the alternate activity metric to test whether associations were independent, and the product term of average acceleration and the intensity gradient entered to determine whether there was an interactive effect of volume and intensity of physical activity. To test whether sex had a moderating effect on association between physical activity and bone, Model 2 was also run with a sex–activity term. If this was significant, all analyses were run separately by sex for that dependent variable.

By entering both metrics and their product term into regression analyses, it is possible to determine whether: primarily intensity OR volume is important (main effect of one independent of the other, but no additive or interactive effect); there are additive effects of volume and intensity (main effects of intensity and volume independent of each other, but no interaction); or the effect of volume differs by intensity, for example, at high intensities, there is little added benefit from increasing volume, but at low intensities adding volume is beneficial (interactive effect). Continuous variables were centered before entry into the analyses. Centering entailed subtracting the mean from each individual score; therefore, the mean of the centered variable was zero. The product terms of average acceleration and the intensity gradient were calculated from the centered scores.

Secondary aims. To elucidate the form of significant independent, additive, and/or interactive effects, we graphed the relationship between physical activity volume and the dependent variable when the intensity gradient was medium (at its mean), high (1 SD above the mean), and low (1 SD below the mean), as described by Jaccard and Turrisi (26). These illustrate the predicted bone outcome for a female participant (or as specified for sex-specific analyses) with mean values for all the covariates.

Finally, we used MX metrics (8,9) to illustrate translation of the optimal intensity gradient and average acceleration for a given marker of bone health. To do this, we split the sample into low/medium/high tertiles for average acceleration and/or low/medium/high tertiles for intensity gradient and selected the intensity gradient/volume combinations that related to poorer and better markers of bone health based on the results of the regression analyses. We described these physical activity patterns by plotting eight MX metrics covering approximately half of the waking day ($M^1\!/\!_{3\,DAY}$, M120, M60, M30, M15, M10, M5, M2) on a radar plot.

The MX metrics are plotted on the radii of the plot, one radii for each metric. The points are joined, resulting in a shape for each group; the greater the surface area of the plotted shape on the left of the radar plot (where the shorter duration MX metrics (M2, M5, M10, M15) are situated), the higher the intensity gradient. The dotted/dashed gray circles show approximate accelerations associated with slow walking (70 m*g*), brisk walking (160 m*g*), and vigorous physical activity (260 m*g*) from a laboratory calibration study (26); these can be used to translate the MX metrics. For example, if the M30 exceeds the dotted gray line depicting the acceleration associated with brisk walking, then, on average, the participants accumulated 30 min of brisk walking. Based on the accelerations reported by Hildebrand et al. (27), acceleration ranges were further categorized as: pottering (intermittent slow walking/low-intensity lifestyle) (≅10–70 m*g*) and running (≅>450 m*g*).

To clearly illustrate relative differences between each of the MX metrics for the given combinations of intensity gradient and volume a standardized version of each plot is also presented, where the MX metrics are standardized within metric. As each MX metric is standardized the mean is 0 (marked by the dashed gray line) and the SD is ±1.

Two sensitivity analyses were carried out repeating all analyses above: 1) calculating the intensity gradient with no imputation for nonwear during the night and a valid day defined as 10 h of waking wear; 2) imputing zeros for nonwear during the night for average acceleration as well as the intensity gradient.

All analyses were conducted in STATA (v15.1). Alpha was set at 0.05. Significance values between 0.05 and 0.1 were considered borderline.

RESULTS

Valid accelerometer files were available for 179 (54%), 255 (54%), 291 (67%), and 223 (61%) participants for waves 6, 7, 8, and 9, respectively. There were 220 participants (124 women) with at least one valid accelerometer assessment across the four measurement waves and bone outcomes for wave 9. At wave 9, the hip FN CSA and hip FN *Z* were significantly lower in the included participants ($P < 0.05$). Otherwise, the sex, height, mass, age, and bone outcomes at wave 9 of these participants did not differ from the participants with bone outcomes at wave 9, but no valid accelerometer data.

Descriptive statistics are presented in Table 1 for the whole sample and for males and females separately. Participant characteristics are from wave 9, whereas physical activity outcomes are the average of waves 6 to 9; 15% of participants had physical activity data from one wave, 38% from two waves, 35% from three waves, and 12% from four waves. Males had a significantly higher average acceleration than females, but the intensity gradient did not differ (Table 1). See Figure, Supplemental Digital Content 2: Comparison of physical activity patterns between males and females, http://links.lww.com/MSS/B984.

The correlation between the average acceleration and the intensity gradient was moderate at 0.41, shared variance 17% (data not displayed in tables), indicating the two metrics provided complementary information.

TABLE 1. Descriptive characteristics of the five data sets.

	All (N = 220)	Females (n = 124)	Males (n = 96)
[a]Age (yr)	23.4 (0.5)	23.4 (0.5)	23.4 (0.6)
[a]Years from PHV	10.7 (1.3)	11.5 (0.8)	9.7 (1.0)
[a]Body size			
Height (cm)	171.9 (9.8)	166.0 (7.0)	179.5 (7.5)
Mass (kg)	81.5 (22.6)	74.0 (20.0)	91.3 (33.2)
Body mass index (BMI) ($kg \cdot m^{-2}$)	27.4 (6.7)	26.8 (6.9)	28.3 (6.3)
Percent body fat	33.1 (8.7)	37.2 (7.1)	27.7 (7.7)
[a]Bone mass			
Total body BMC (minus head) (g)	2100.1 (480.6)	1826.0 (310.6)	2454.1 (427.5)
Spine aBMD ($g \cdot cm^{-2}$)	1.085 (0.120)	1.069 (0.127)	1.105 (0.108)
Hip aBMD ($g \cdot cm^{-2}$)	1.080 (0.151)	1.031 (0.128)	1.143 (0.157)
[a]Hip structure analysis			
Hip FN CSA (cm^2)	3.63 (0.77)	3.26 (0.58)	4.11 (0.72)
Hip FN section modulus (cm^3)	1.80 (0.53)	1.49 (0.35)	2.20 (0.46)
[b]Physical activity (24 h)			
Average acceleration (m*g*)	15.5 (3.9)	15.0 (3.8)	16.1 (3.9)
Intensity gradient	−2.62 (0.21)	−2.62 (0.22)	−2.62 (0.19)
[b]Physical activity MX metrics (m*g*)			
$M^1/_{3DAY}$	9.4 (3.3)	9.1 (3.1)	9.8 (3.6)
M120	44.6 (15.1)	42.7 (13.2)	47.1 (17.0)
M60	84.3 (26.0)	81.5 (25.0)	88.1 (26.9)
M30	127.1 (38.8)	125.8 (43.0)	128.7 (51.5)
M15	171.2 (58.1)	170.3 (63.0)	172.3 (51.5)
M10	197.4 (69.7)	196.3 (73.8)	198.9 (64.3)
M5	236.4 (82.3)	232.1 (82.2)	242.1 (82.5)
M2	282.2 (93.7)	275.0 (92.4)	291.4 (95.0)
Accelerometer wear			
Proportion of the 24 h cycle monitor was worn	0.85 (0.07)	0.86 (0.07)	0.85 (0.07)
No. valid days	4.3 (0.7)	4.3 (0.7)	4.3 (0.7)
No. waves	2.4 (0.9)	2.5 (0.9)	2.4 (0.9)

Values are mean (SD).
[a]Wave 9.
[b]Mean of waves available.

Primary Aim

Relative importance of volume and intensity of physical activity with markers of bone health.

Table 2 shows the associations of volume and intensity distribution of physical activity with markers of bone health. There was a sex–activity interaction for spine aBMD so males and females were analyzed separately. For all other bone markers there was no sex–activity interaction so males and females were combined for analysis.

When entered into separate regression models, both average acceleration and the intensity gradient were positively associated with all bone outcomes, with the exception of spine aBMD in females (model 1). Significant associations were maintained after accounting for covariates (model 2).

When entered into the same regression model (model 3), average acceleration and intensity gradient were both independently associated with hip aBMD and total body BMC. This suggests that volume and intensity distribution of physical activity have an additive effect for hip aBMD and total body BMC.

For spine aBMD, there was a main effect for intensity, independent of average acceleration, for spine aBMD, but not *vice versa* (model 3). This suggests that intensity of physical activity is more important than volume for spine aBMD.

In contrast, for the hip structure analysis outcomes (hip FN CSA and FN *Z*), there were significant associations with average acceleration, independent of intensity gradient, but not *vice versa* (model 3). This suggests that volume of physical activity is more important than intensity for hip geometry.

No significant product terms were evident, suggesting that the effect of volume did not vary by intensity distribution. Sensitivity analyses showed the pattern of results was similar when analyses were repeated with nonimputed data (see Table, Supplemental Digital Content 3: Associations of the two physical activity metrics with markers of bone health with no imputing of zeros during nighttime nonwear, http://links.lww.com/MSS/B985) and data with imputing of zeros for nonwear during the night for both intensity gradient and average acceleration (see Table, Supplemental Digital Content 4: Associations of the two physical activity metrics with markers of bone health with nonwear during the night imputed as zeros for both intensity gradient and average acceleration, http://links.lww.com/MSS/B986).

Secondary Aims

The variation of bone health across activity physical activity volume and intensity distribution is described for each bone outcome in the subsections below and illustrated in Figures 1A and 1B (hip aBMD, total body BMC, respectively), Figure 2A (spine aBMD, males only), and Figures 3A and 3B (hip FN CSA and hip FN *Z*, respectively).

The physical activity patterns indicative of the intensity gradient/average acceleration combinations associated with poorer and better markers of bone health are described for each bone outcome in the subsections below and illustrated in Figure 1C (hip aBMD, total body BMC), Figure 2B (spine aBMD, males only), and Figure 3C (hip geometry).

The shades of green and red/orange in Figure 1C correspond with the color of the column borders in Figures 1A

TABLE 2. Associations of the two physical activity metrics[a] with markers of bone health (wave 9, N = 220).

	Model 1		Model 2		Model 3		
	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI	Result
Hip aBMD							
Average acceleration (m*g*)	**0.007**	**0.003 to 0.011**	**0.007**	**0.003 to 0.012**	**0.006**	**0.001 to 0.011**	Independent effect of volume
[b]Intensity gradient	**0.120**	**0.044 to 0.196**	**0.128**	**0.053 to 0.203**	**0.091**	**0.007 to 0.175**	Independent effect of intensity
Average acceleration X intensity gradient					−0.005	−0.025 to 0.014	
Total body BMC (minus head)							
Average acceleration (m*g*)	**14.092**	**4.431 to 23.753**	**16.156**	**8.485 to 23.827**	**12.990**	**20.059 to 29.191**	Independent effect of volume
[b]Intensity gradient	**218.337**	**39.374 to 397.301**	**256.107**	**126.278 to 385.937**	**162.767**	**14.804 to 310.727**	Independent effect of intensity
Average acceleration X intensity gradient					−10.651	−39.047 to 17.746	
[c]Spine aBMD							
Males (n = 96)							
Average acceleration (m*g*)	**0.007**	**0.002 to 0.012**	**0.007**	**0.002 to 0.012**	0.005	−0.000 to 0.011	
[b]Intensity gradient	**0.137**	**0.034 to 0.239**	**0.153**	**0.055 to 0.251**	**0.127**	**0.020 to 0.233**	Independent effect of intensity
Average acceleration X intensity gradient					−0.001	−0.021 to 0.019	
Females (n = 124)							
Average acceleration (m*g*)	0.003	−0.003 to 0.008	0.003	−0.003 to 0.008	0.002	−0.004 to 0.007	
[b]Intensity gradient	0.045	−0.048 to 0.138	0.063	−0.036 to 0.162	0.055	−0.042 to 0.152	
Average acceleration X intensity gradient					−0.010	−0.034 to 0.014	
Hip femoral neck cross-sectional area							
Average acceleration (m*g*)	**0.025**	**0.009 to 0.042**	**0.027**	**0.012 to 0.042**	**0.021**	**0.003 to 0.039**	Independent effect of volume
[b]Intensity gradient	**0.410**	**0.104 to 0.716**	**0.449**	**0.186 to 0.712**	0.288	−0.021 to 0.597	
Average acceleration X intensity gradient					−0.007	−0.068 to 0.054	
Hip femoral neck section modulus							
Average acceleration (m*g*)	**0.015**	**0.004 to 0.026**	**0.017**	**0.008 to 0.027**	**0.014**	**0.003 to 0.025**	Independent effect of volume
[b]Intensity gradient	**0.224**	**0.021 to 0.426**	**0.231**	**0.056 to 0.406**	0.106	−0.094 to 0.306	
Average acceleration X intensity gradient					0.010	−0.026 to 0.048	

[a]Activity metrics (average of waves 6–9): intensity gradient (calculated with imputing of zeros for nonwear during the night), average acceleration (across wear-time).
[b]Intensity gradient: Gradient of the regression line from log-log plot of intensity (x) and minutes accumulated (y).
[c]Analyses run separately by sex due to a significant sex–activity interaction term. For the sex-specific analyses only, consistently nonsignificant covariates (height and age) were dropped.
Model 1 adjusted for sex and mass only. Model 2 adjusted for sex, age, height, mass, years from PHV (all from wave 9), the proportion of the 24 h cycle the monitor was worn and mean age for physical activity measures. Model 3 further adjusted for alternate activity metric and the product term (average acceleration X intensity gradient) entered to investigate interactive effects 95% CI, 95% confidence interval.
Scores were centered before entry into the analysis. Physical activity interaction terms were calculated from the centered scores.
Significant associations are denoted in bold.

and 1B to identify the corresponding average acceleration/ intensity gradient combination and associated bone health outcome. Similarly, Figure 2B corresponds with the color of the column borders in Figure 2A, and Figure 3C with the column borders in Figures 3A and 3B. Red equates to the worse bone outcomes, through orange to green for improving outcomes.

Additive effect of volume and intensity (hip aBMD and total body BMC). Figures 1A and 1B illustrate this additive effect on hip aBMD and total body BMC, respectively. Hip aBMD and total body BMC are highest when both intensity gradient and average acceleration are high (column outlined in green) and worst when both average acceleration and intensity gradient are low (column outlined in red). In both cases, midrange bone outcomes are evident with high acceleration (1 SD above the mean) even when intensity gradient is low (1 SD below the mean) (columns outlined in dark orange), or with high-intensity gradient (1 SD above the mean) even when average acceleration is low (columns outlined in light orange).

Figure 1C contrasts the physical activity profile associated with optimal bone outcomes (high in both average acceleration and intensity gradient—green), the profile associated with the worst outcomes (low in both and intensity gradient—red), and two profiles associated with midrange outcomes (high average acceleration, low-intensity gradient (dark orange); low average acceleration, high-intensity gradient (light orange)). The optimal physical activity profile (green) consisted of large volumes of low-intensity activity including around 1 to 2 h of slow walking of which 30 min is equivalent to brisk walking, and approximately 15 min is vigorous activity (1, Fig. 1C, left panel). Midrange hip aBMD and total body BMC were associated with EITHER accumulation of either high volumes of lower intensity activity (dark orange) (2, Fig. 1C, right panel) OR lower volumes of more intense activity (light orange) (3, Fig. 1C, right panel). High volumes of low intensity could be accumulated through 1–2 h of slow walking including 10 min equivalent to at least brisk walking (2, Fig. 1C, left panel). Lower volumes of more intense activity included less time in slow walking (60 min), including 15 min of brisk walking of which 2 min was vigorous (3, Fig. 1C, left panel).

Main effect of intensity distribution (spine aBMD, males only). Figure 2A illustrates the main effect for intensity gradient on spine aBMD. When the intensity gradient is high (1 SD above the mean, e.g., column outlined in green), the spine aBMD is high. When the intensity gradient is lower (mean or 1 SD below the mean, e.g., columns outlined in orange and red, respectively), the spine aBMD is lower. The observations for the intensity gradient hold, somewhat irrespective of the average acceleration; the highlighted columns indicate the effect when average acceleration is similar (at the mean). There is a borderline significant association for the average acceleration (P = 0.053), suggesting intensity and volume are additively associated with higher spine aBMD. This explains the similar predicted spine aBMD for a participant with low-intensity gradient/high average acceleration and high-intensity gradient/ low average acceleration.

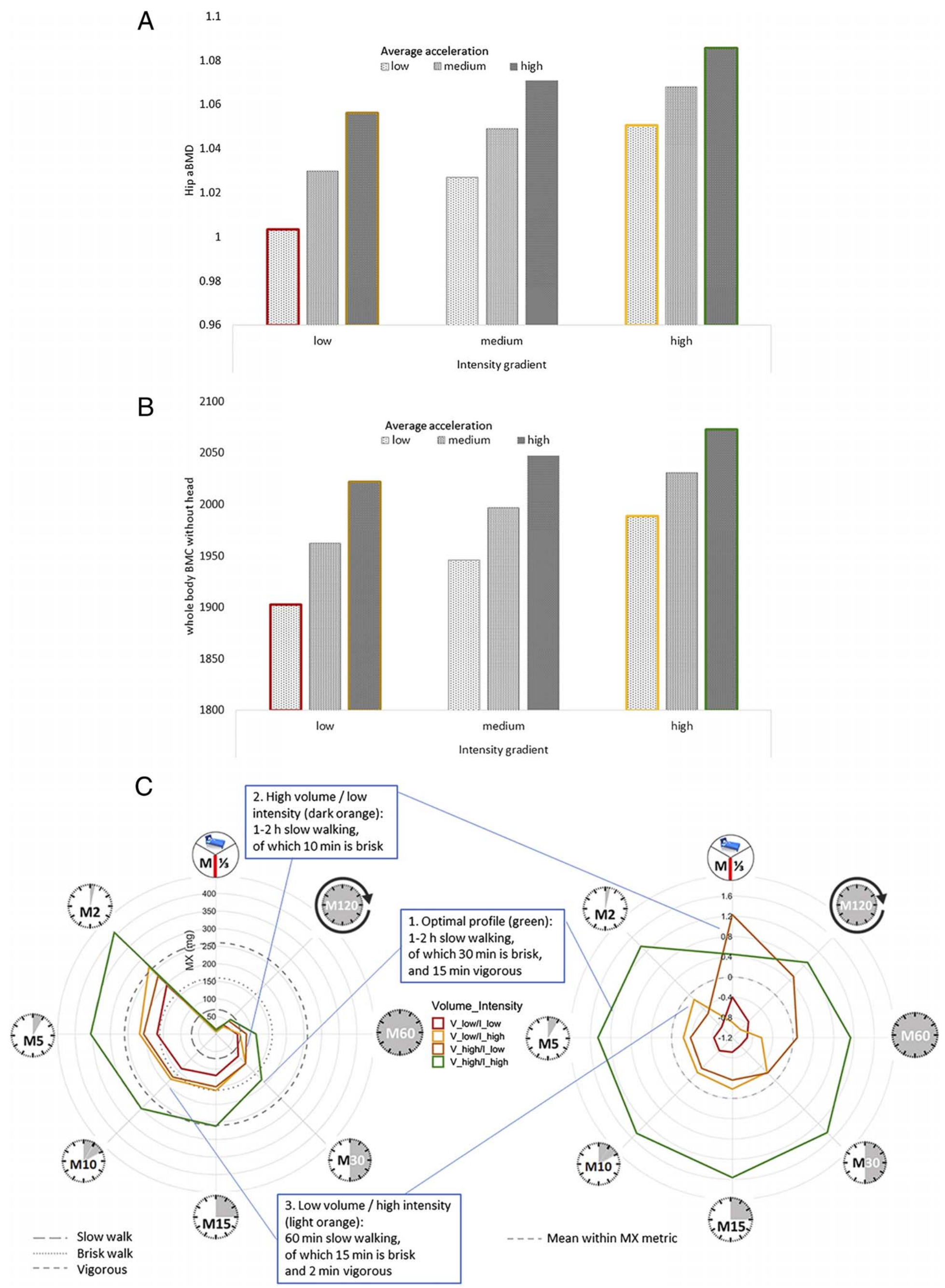

FIGURE 1—Translation of additive effects of volume and intensity distribution on (A) hip aBMD and (B) whole-body BMC without head and (C) associated activity profiles. The shades of green and red/orange in panel c corresponds with the color of the column borders in panels a and b to identify the corresponding average acceleration/intensity gradient combination and associated bone health outcome. V, volume; I, intensity gradient. A and B, The relationship between activity volume and Hip aBMD (A) and total body BMC without head (B) when the intensity gradient was low (1 SD below the mean), medium (at its mean) and high (1 SD above the mean). C, Illustration of the physical activity profile associated with low volume/low intensity, low volume/high intensity, high volume/low intensity, high volume/high intensity for raw MX metrics (left) and standardized MX metrics (right). Each plot shows (clockwise) M$\frac{1}{3}_{DAY}$, M120, M60, M30, M15, M10, M5, and M2. As the MX metrics in the plot on the right are standardized within metric the mean = 0 (*dashed gray line*) and SD = 1.

Figure 2B shows the raw (left panel) and standardized (right panel) MX metrics for low-, mid-, and high-intensity gradient physical activity profiles, but similar average acceleration (midtertile). On average, all profiles accumulated 60 min of physical activity equivalent to at least slow walking and 10 min equivalent to at least brisk walking. However, when the intensity gradient was high, 15 to 30 min of walking was brisk of which the most active 5 to 10 min was vigorous activity, compared with 0 and 2 min of vigorous activity when the intensity gradient was low and medium, respectively (left panel). The comparatively high levels of M$\frac{1}{3}_{DAY}$ intensity gradient was low and medium (right panel) resulted in the similar average acceleration despite little high-intensity activity.

Main effect of volume (hip FN CSA and hip FN Z). Figures 3A and 3B illustrate the main effect for average

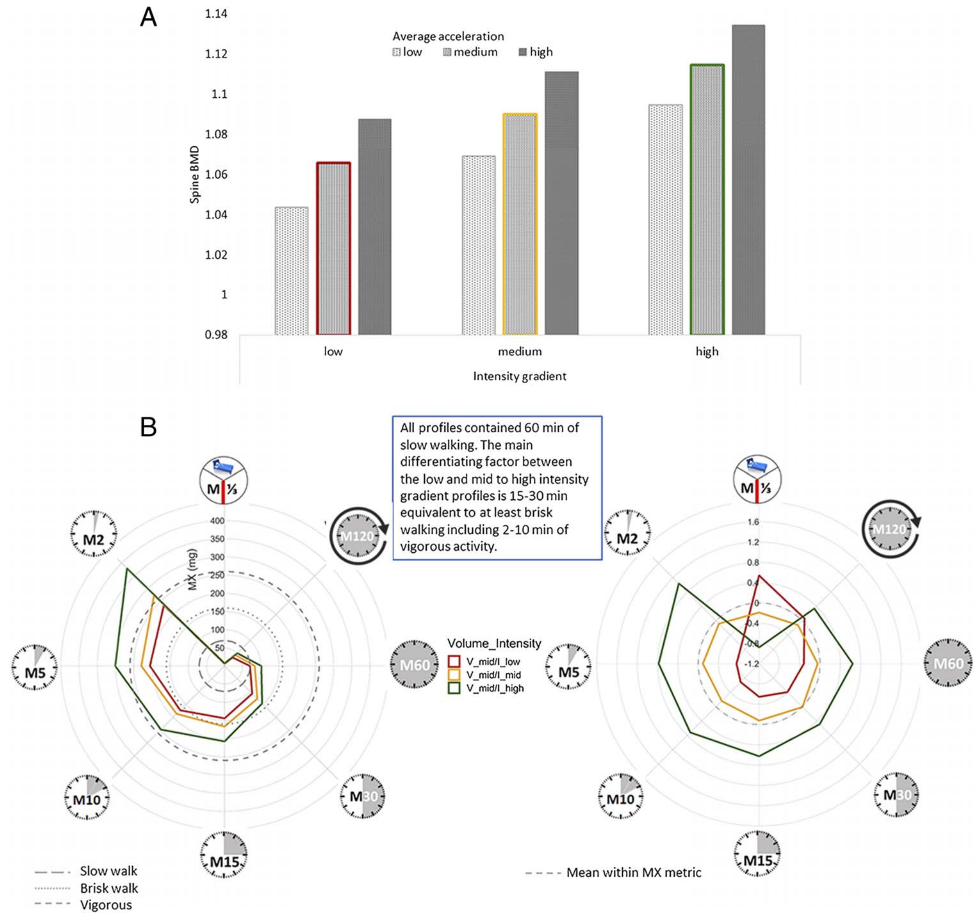

FIGURE 2—Translation of main effect of intensity distribution on (A) spine aBMD in males and (B) associated activity profiles. The shades of green and red/orange in panel B corresponds with the color of the column borders in panel A to identify the corresponding average acceleration/intensity gradient combination and associated Spine aBMD. A, The relationship between activity volume and Spine aBMD in boys when the intensity gradient was low (1 SD below the mean), medium (at its mean) and high (1 SD above the mean). B, Illustration of the physical activity profile (men) associated with low-, medium-, and high-intensity distributions, but similar volume for raw MX metrics (left) and standardized MX metrics (right). Each plot shows (clockwise) $M^{1}\!/_{3DAY}$, M120, M60, M30, M15, M10, M5, and M2. As the MX metrics in the plot on the right are standardized within metric the mean = 0 (dashed gray line) and standard deviation = 1. V, volume; I, intensity gradient.

acceleration on hip FN CSA and FN *Z* When the average acceleration is high (1 SD above the mean, e.g., column outlined in green), the hip FN CSA and FN *Z* are high. Conversely, when the average acceleration is lower (mean or 1 SD below the mean, e.g., columns outlined in orange and red, respectively), the hip FN CSA and FN *Z* are lower. The observations for the average acceleration hold, somewhat irrespective of the intensity gradient; the highlighted columns indicate the effect when the intensity gradient is similar (at the mean). However, there is a borderline significant independent association for the intensity gradient for hip FN CSA ($P = 0.068$), suggesting an additive association of volume and intensity. This explains the slightly higher predicted hip FN CSA for a participant with low-intensity gradient/high average acceleration than for a participant with high-intensity gradient/low average acceleration.

Figure 3C shows the raw (left panel) and standardized (right panel) metrics for low, mid, and high average acceleration physical activity profiles, but similar intensity gradient (midtertile). On average, all profiles accumulated 60 min at an intensity equivalent to least slow walking (left panel), but, vigorous activity was relatively rare. When average acceleration was medium or high this included 15 min of brisk walking (left panel) and there were also relatively high values for $M^{1}\!/_{3DAY}$, M120, M60, and M30 (right panel), suggesting long periods of walking and pottering around. The data suggest that 15 min of brisk walking and high volumes of physical activity (e.g., several hours of walking and pottering around) is associated with higher hip FN CSA and FN *Z*, even with little (<5 min) vigorous activity.

DISCUSSION

Optimal bone health was associated with physical activity profiles that were high in both volume and intensity distribution. Although independent associations of the intensity gradient confirmed the importance of high-intensity physical activity for optimal BMC and aBMD, additive associations of volume and intensity suggest that increasing physical activity of any intensity could also be advantageous for hip aBMD and total body BMC. For spine aBMD vigorous-intensity physical activity was key in men, but no associations were evident in women. For the hip structure analysis outcomes, large volumes

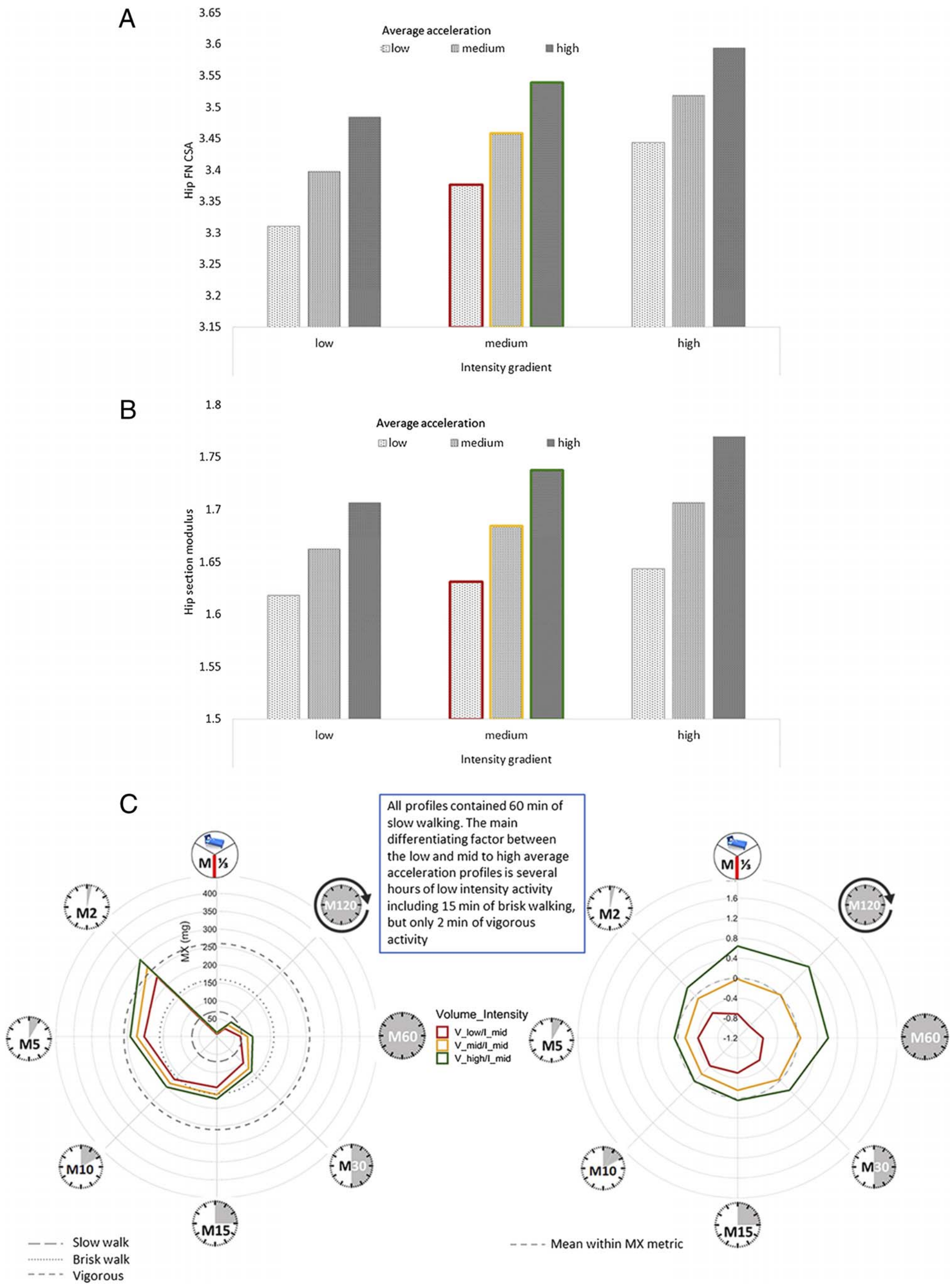

FIGURE 3—Translation of main effect of volume on (A) hip FN CSA and (B) hip section modulus and (C) associated activity profiles. The shades of green and red/orange in panel C corresponds with the color of the column borders in panels A and B to identify the corresponding average acceleration/intensity gradient combination and associated hip structure analysis outcome. A and B, The relationship between activity volume and hip FN CSA (A) and hip section modulus (B) when the intensity gradient was low (1 SD below the mean), medium (at its mean) and high (1 SD above the mean). C, Illustration of the physical activity profile associated with low, medium and high volume, but similar intensity distribution for raw MX metrics (left) and standardized MX metrics (right). Each plot shows (clockwise) $M\frac{1}{3}_{DAY}$, M120, M60, M30, M15, M10, M5, and M2. As the MX metrics in the plot on the right are standardized within metric the mean = 0 (dashed gray line) and SD = 1. V, volume; I, intensity gradient.

of physical activity accumulated at relatively low intensities were important even if vigorous-intensity activity was absent or low. These subtleties would likely be missed by simply analyzing MVPA, vigorous physical activity or total physical activity.

These findings are largely consistent with previous analyses of the IBDS data but allow translation in terms of the whole intensity spectrum. This may facilitate greater insight into the mechanisms underlying associations between physical activity and bone health. For example, Janz et al. (17) reported that children who accumulated more MVPA between the ages of 5 and 17 yr had better bone mass and bone geometry outcomes at age 17 yr. No differences were noted between bone mass and bone geometry in the associations detected with MVPA. However, the MVPA and total volume of physical activity are highly correlated (28), preventing any investigation into the relative importance of volume and intensity. As the intensity gradient and average acceleration metrics are relatively independent of each other (2), we were able to identify differences in the relative importance of volume and intensity of physical activity for midrange bone mass and midrange bone geometry outcomes.

The lack of an association between physical activity and spine aBMD in girls is also consistent with the work of others (29) as well as with earlier findings from the IBDS. Francis et al. (30) reported that although boys' MVPA and vigorous PA at age 5 yr predicted spine and hip aBMD at age 13 yr and/or 15 yr, in girls, the associations were only significant for hip aBMD. Francis et al. speculated that this may relate to the lower physical activity level in girls relative to boys. Consistent with this, we found the volume of physical activity was still higher in boys in physical activity measured across waves 6 to 9 (age, 17–23 yr). This higher volume was achieved through a higher intensity of activity distributed across the majority of MX metrics.

Herein, we illustrate how the data may be translated in terms of easily understood indicative activities (e.g., slow walking, brisk walking, running) or intensities (e.g., MVPA, vigorous physical activity) while not losing sight of the importance of accounting for the entire spectrum of intensity of physical activity across the day (1,9). Contrasting the physical activity profiles associated with optimal, midrange and poor bone outcomes can be used to inform targeted physical activity recommendations in terms of indicative types of activity and/or intensities.

For bone mass, relatively high-intensity physical activity was present in all profiles associated with midrange bone outcomes. Examination of the radar plots suggested approximately 60 min of walking, of which 30 min was brisk and 15 min was vigorous-intensity activity was associated with higher bone mass. Conversely, for hip CSA and bending resistance in cross-section (structural geometry outcomes) examination of the radar plots shows a relative lack of higher intensity activity in the interim profiles associated with midrange bone outcomes. Accumulating several hours of slower walking of which only around 15 min is brisk walking, even with very little vigorous activity appears to be beneficial for hip structural geometry. If these subtle differences in the relative importance of volume and intensity of physical activity for bone mass and structural geometry are evident in other data sets, this may help elucidate mechanisms underlying these aspects of bone health.

Strengths of this study include the longitudinal design of the IBDS, the well phenotyped nature of the sample and repeated accelerometer measures of physical activity. The use of data-driven accelerometer measures facilitated determination of the relative contributions of volume and intensity to each of the bone outcomes. Further, the MX metrics enable interpretation in terms of easily understandable typical activities that can accommodate the physical activity intensity/volume combinations pertinent for a given outcome.

There are some limitations to this study that should be noted. Firstly, the accelerometer wear protocol was waking wear for waves 6–7 and optional 24 h wear for waves 8–9. The IBDS is a longitudinal study and, as such, has the challenge of balancing the need for consistent protocols across time with the desire to take advantage of evolving methods and technology. To facilitate calculation of the intensity gradient from non–24 h data, we imputed data based on the assumption that physical activity during night-time nonwear would have been minimal intensity and controlled for the proportion of the cycle the monitor was worn (and thus the proportion of the data imputed). As results were reasonably robust across sensitivity analyses, we are confident in the findings we report. As 24 h wear of accelerometers is becoming more usual in studies with hip-worn (e.g., [31]) and wrist-worn accelerometers (e.g., [32]), this will become less of an issue moving forward. Second, we had a relatively high proportion of invalid accelerometer data due to the use of metrics which cover the whole physical activity spectrum rather than just the most active parts of the day (2). However, the included participants did not differ from those excluded for the majority of wave 9 outcomes. Eighty-five percent of included participants provided physical activity data for more than one wave. To maximize our sample size, we took the mean activity across waves and controlled for each participant's mean age across included waves. Results were largely consistent when data were analyzed cross-sectionally for individual waves (data not shown), and with previous reports from the IBDS (17,30,33) that included more participants and considered one physical activity intensity at a time as opposed to the intensity distribution. Irrespective, we acknowledge there is a risk of spurious associations. Further, although accelerometry is useful for capturing overall activity, it does not capture all types of physical activity, for example, muscle strengthening exercises which are associated with bone health (33). Finally, the DXA measures at age 23 yr were cross-sectional in nature. It is possible bone mass, density and structure were due to genetics or other factors that were not measured.

In conclusion, use of data-driven accelerometer metrics that cover the whole physical activity profile indicate that the optimal physical activity profile for all bone outcomes is high in both intensity and volume. However, differences in physical activity patterns between people with poor and midrange bone outcomes suggest the intensity of physical activity may be key for bone mass, whereas volume accumulated may be key for hip structural geometry outcomes. Applying analyses that account for physical activity accumulated across the spectrum of intensity could facilitate insight into mechanisms underlying associations with health and the development of tailored prescriptions.

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