# ARTICLE

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# Low movement, deep-learned sitting patterns, and sedentary behavior in the International Study of Childhood Obesity, Lifestyle and the Environment (ISCOLE)

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**BACKGROUND/OBJECTIVES:** Sedentary behavior (SB) has both movement and postural components, but most SB research has only assessed low movement, especially in children. The purpose of this study was to compare estimates and health associations of SB when derived from a standard accelerometer cut-point, a novel sitting detection technique (CNN Hip Accelerometer Posture for Children; CHAP-Child), and both combined.

**METHODS:** Data were from the International Study of Childhood Obesity, Lifestyle, and the Environment (ISCOLE). Participants were 6103 children (mean  $\pm$  SD age 10.4  $\pm$  0.56 years) from 12 countries who wore an ActiGraph GT3X+ accelerometer on the right hip for approximately one week. We calculated SB time, mean SB bout duration, and SB breaks using a cut-point (SB<sub>movement</sub>), CHAP-Child (SB<sub>posture</sub>), and both methods combined (SB<sub>combined</sub>). Mixed effects regression was used to test associations of SB variables with pediatric obesity variables (waist circumference, body fat percentage, and body mass index z-score). **RESULTS:** After adjusting for MVPA, SB<sub>posture</sub> showed several significant obesity associations favoring lower mean SB bout duration (b = 0.251-0.449; all p < 0.001) and higher SB breaks (b = -0.005--0.052; all p < 0.001). Lower total SB was unexpectedly related to greater obesity (b = -0.077--0.649; p from <0.001-0.02). For mean SB bout duration and SB breaks, more associations were observed for SB<sub>posture</sub> (n = 5) than for SB<sub>movement</sub> (n = 3) or SB<sub>combined</sub> (n = 1), and tended to have larger magnitude as well. **CONCLUSIONS:** Using traditional measures of low movement as a surrogate for SB may lead to underestimated or undetected adverse associations between SB and obesity. CHAP-Child allows assessment of sitting posture using hip-worn accelerometers. Ongoing work is needed to understand how low movement and posture are related to one another, as well as their potential health implications.

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# INTRODUCTION

Sedentary behavior (SB) is a risk factor for numerous health conditions, including cardiovascular and cardiometabolic disease [1, 2]. However, there is a history of debate surrounding how SB should be defined [3, 4], especially for children [5, 6]. In 2017, the Sedentary Behavior Research Network concluded its Terminology Consensus Project, defining SB as "any waking behavior characterized by an energy expenditure of  $\leq 1.5$  metabolic equivalents (METs), while in a seated, reclining or lying posture" [7, 8]. Thus, SB is now recognized as having two components, one related to movement and metabolism while the other is related to posture [9]. Wearable devices can potentially measure both components, but posture is uniquely challenging to capture. This is especially true for hip-worn accelerometers, which are widely used in SB

research [10]. Accordingly, most accelerometer-based research has defined SB using cut-points that capture movement rather than posture [11, 12].

Recently, a deep-learned model called CHAP-Child (CNN Hip Accelerometer Posture for children) was developed for assessing posture in children using raw acceleration data from hip-worn ActiGraph monitors [13] (ActiGraph LLC, Pensacola, FL, USA). Crossvalidation results showed >85% mean balanced accuracy when comparing CHAP-Child against an established thigh-worn inclinometry device called activPAL [13] (PAL Technologies Ltd., Glasgow, Scotland). Thus, CHAP-Child has strong potential to complement existing hip-accelerometer cut-point approaches by enabling concurrent estimation of sitting behavior. Although both components of SB can already be concurrently assessed using activPAL,

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CHAP-Child remains highly relevant because ActiGraph devices are among the most widely used in research [14]. Thus, CHAP-Child may open new insights when applied to historical data. The need for such research is especially great given the scarcity of posturefocused device data from prior studies in children [15].

The purpose of the present study was to explore the potential of CHAP-Child by applying it in a global epidemiology context. Specifically, we used data from the International Study of Childhood Obesity, Lifestyle, and the Environment (ISCOLE) [16] to compare patterns and health associations of SB when measured using a traditional cut-point [17], CHAP-Child [13], or a combination of both. In doing so, we demonstrated the integration of movement and posture data, while also exploring their interrelationships and potential implications for pediatric obesity.

# METHODS

### Participants and protocol

The ISCOLE was a multicenter study conducted in 12 countries. It was designed to explore global correlates of pediatric obesity at multiple levels [16]. Participants were 9- to 11-year-old children who were recruited from approximately 20 schools per country. They were asked to wear an ActiGraph GT3X+ accelerometer on the right hip continuously (24 h per day) for  $\geq$ 7 days and have their waist circumference, body fat percentage, and anthropometrics measured. Body fat percentage was assessed using bioelectrical impedance analysis (Tanita SC-240; Tanita Corporation of America, Arlington Heights, IL). Body mass index z-score (BMI-z) was determined using growth charts from the World Health Organization [18], following instructions available from https://cdn.who.int/media/docs/default-source/child-growth/growth-reference-5-19-years/

computation.pdf?sfvrsn=c2ff6a95\_4. The overall study was approved by the Pennington Biomedical Research Center Institutional Review Board, and additional approvals were obtained for each site from their respective ethics committees. All participants provided written informed assent prior to beginning the study, and parents provided written informed consent.

#### Data processing

The existing study database was queried to obtain participant data (demographics, anthropometrics, and obesity measures). ActiGraph data were processed for SB in three ways, namely using cut-point (movement-based), CHAP-Child (posture-based), and combined (movement and posture) methods. For simplicity, we denote estimates from these methods as SB<sub>movement</sub> SB<sub>posture</sub>, and SB<sub>combined</sub>, respectively.

Cut-point method (SB<sub>movement</sub>). The SB<sub>movement</sub> method was applied using standard cut-point techniques that are reflected in a majority of SB research [11]. Specifically, raw ActiGraph data were converted to 60-s epochs (.agd format) using ActiLife software, and vertical axis activity counts were analyzed (counts per min; cpm). Counts are a cumulative measure of acceleration in an epoch [19]. The "low frequency extension" option was selected during the ActiLife conversion, which improves backward compatibility with devices that were used in the original cutpoint validation [20]. Each epoch was classified as SB<sub>movement</sub> if activity counts were  $\leq 100$  cpm during awake wear time (see Section 1 of the supplementary information for definition of awake wear time). The latter cut-point was developed for adolescent girls in a study by Treuth et al. [17] and later popularized for general use by Matthews et al. [11].

*CHAP-child* (*SB<sub>posture</sub>*). Raw ActiGraph data (.gt3x format) were exported to .csv files using ActiLife software. These files were processed using CHAP-Child. To accelerate the process, computations were made on 24 nodes of the Children's Mercy High Performance Computing Cluster. Our project website (https://adalabucsd.github.io/DeepPostures/) provides more information about implementing CHAP-Child and parallelizing the file processing. Output files were in 10-s epochs, with each epoch labeled as sitting or non-sitting. SB<sub>posture</sub> was defined as any sitting epoch that occurred during awake wear time (identified by cross-referencing the cutpoint data described previously).

Combined method ( $SB_{combined}$ ). Our general approach was to define  $SB_{combined}$  as any epoch that was classified as both  $SB_{movement}$  and  $SB_{posture}$ . However, extra steps were necessary to reconcile the different

time resolutions of those measures (60-s and 10-s epochs, respectively). Rather than using a standard one-to-many merge, in which every 60-s epoch of SB<sub>movement</sub> would be used to label the corresponding six 10-s epochs of SB<sub>posture</sub>, we opted to use a sliding window approach. Specifically, raw ActiGraph data were converted to 10-s epochs, and each epoch was summed with the five after it to obtain a cpm value. Timestamps were assigned at the middle of each window. This resulted in cpm values calculated every 10 s, with each value reflecting activity counts in the surrounding  $\pm 30$  s. The cut-point was then applied to obtain an estimate of SB<sub>movement</sub> for each window. Lastly, the estimates were timestamp-matched to the estimates of SB<sub>posture</sub>, enabling determination of SB<sub>combined</sub> for each 10-s epoch. Although this approach was complex, it was essential for ensuring temporal alignment of both data streams, while also avoiding documented limitations of "cut-point scaling" (i.e., reduction of the cut-point from 100 cpm to 16 counts per 10 s) [21].

Cleaning and aggregating. After obtaining epoch-level estimates of SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>, additional operations were performed to clean and aggregate the data. Data were excluded from all participants with <4 days of valid data, where a valid day was defined as having  $\geq 10$  h of awake wear time [22]. Data were also screened for implausible values, with participants removed if their data indicated >90% of time spent in SB<sub>movement</sub>, SB<sub>posture</sub>, or SB<sub>combined</sub>. The 90% threshold represented 2.5 SD's above the pooled mean across all 3 methods. Lastly, participants with missing obesity or covariate data were excluded.

Data aggregation was performed exclusively on awake-wear data from valid days. The awake-wear periods were identical for each method (SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>), promoting comparability of the outputs. For each method, the following SB variables were calculated: total SB time (hr/day), mean SB bout duration (min; total SB time/number of SB bouts), and SB breaks (n/day; count of the total interruptions between SB bouts). For the latter two, SB bouts were defined as consecutive epochs of SB, with no allowance for interruptions.

#### Descriptive and statistical analyses

For descriptive analysis, we focused on comparing patterns of SB accumulation when measured by the different methods (SB<sub>movement</sub>, SB<sub>posture</sub>, or SB<sub>combined</sub>). We used density plots to compare the distributions for each method when measuring total SB time, mean SB bout duration, and SB breaks. We also used two-dimensional density heat maps to compare joint distributions with moderate-to-vigorous physical activity (MVPA). The age-adjusted method of Freedson et al. [23] was used to determine MVPA. Basic descriptive statistics were reported for each SB variable and measurement method, along with Pearson correlation matrices to characterize their degree of relatedness.

For statistical analysis, we fitted mixed effects models to examine relationships between the SB variables and pediatric obesity variables. Each model regressed one of the three obesity variables (waist circumference, body fat percentage, and BMI-z) against one of the three SB variables (total SB time, mean SB bout duration, and SB breaks) measured by one of the three methods (SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>). Fixed-effect covariates in the baseline model (Model 1) included country, age, sex, and awake wear time. Random effects for school were included to capture variation in the model intercept and the slope of the SB variables. Additional testing (Model 2) was performed when adding a fixed effect for MVPA (min/day) to identify if associations were independent of physical activity. Coefficients were calculated in both units of measure (b) and SD-scale ( $\beta$ ), the latter obtained after standardizing all continuous variables (except the obesity variable) to have a mean of 0.0 and SD of 1.0. P-values were adjusted using the false discovery rate correction to account for multiple comparisons [24].

Together (descriptive and statistical), the analyses were designed to provide both technical and practical perspectives on the impact of defining and measuring SB in different ways.

# RESULTS

The original database included 7372 participants. Of those, accelerometer data were available for 6757. Data were lost for an additional 654 participants due to the following: Insufficient valid wear days (n = 229); estimates of >90% time in SB (n = 15); and missing obesity or covariate data (n = 410). Thus, the analytical sample size was 6103. Table 1 shows participant

Table 1. Participant characteristics.

	Female ( <i>N</i> = 3320)	Male ( <i>N</i> = 2783)	Overall ( <i>N</i> = 6103)
Age (yr)	$10.4 \pm 0.56$	$10.4 \pm 0.56$	$10.4 \pm 0.56$
Maturity Offset	$-1.41 \pm 0.67$	$-2.95 \pm 0.57$	$-2.11 \pm 0.99$
Height (cm)	141.9 ± 7.7	141.4 ± 7.3	141.7 ± 7.6
Weight (kg)	$37.5 \pm 9.5$	36.9 ± 9.1	37.2 ± 9.3
Site			
Australia	265 (8.0%)	227 (8.2%)	492 (8.1%)
Brazil	212 (6.4%)	207 (7.4%)	419 (6.9%)
Canada	298 (9.0%)	215 (7.7%)	513 (8.4%)
China	52 (1.6%)	79 (2.8%)	131 (2.1%)
Colombia	457 (14.0%)	438 (16.0%)	895 (15.0%)
Finland	252 (7.6%)	228 (8.2%)	480 (7.9%)
India	309 (9.3%)	265 (9.5%)	574 (9.4%)
Kenya	279 (8.4%)	242 (8.7%)	521 (8.5%)
Portugal	365 (11.0%)	281 (10.0%)	646 (11.0%)
South Africa	263 (7.9%)	171 (6.1%)	434 (7.1%)
United Kingdom	255 (7.7%)	196 (7.0%)	451 (7.4%)
United States	313 (9.4%)	234 (8.4%)	547 (9.0%)
Weight Status			
Underweight	322 (9.7%)	204 (7.3%)	526 (8.6%)
Healthy Weight	2172 (65.0%)	1965 (71.0%)	4137 (68.0%)
Overweight	637 (19.0%)	448 (16.0%)	1085 (18.0%)
Obese	189 (5.7%)	166 (6.0%)	355 (5.8%)
Waist Circumference (cm)	63.8 ± 8.7	64.2 ± 8.9	64.0 ± 8.8
Body Fat (%)	$22.6\pm7.6$	18.7 ± 7.1	$20.8\pm7.6$
BMI Z-Score	$0.40 \pm 1.20$	$0.49 \pm 1.27$	$0.44 \pm 1.24$

Values are mean  $\pm$  SD for continuous variables and n (%) for categorical variables.

BMI percentiles calculated from World Health Organization growth charts [18].

BMI body mass index.

information. Sampling was fairly even by sex (54% female) and country (6.9–9.4% per country except for China, Portugal, and Columbia, depending on the amount of raw data files available for each). Hereafter, summary statistics are given as mean  $\pm$  SD.

#### Descriptive analysis

Supplementary Table S1 (see Section 2 of the supplementary information) shows aggregate summary statistics for accelerometer-derived variables. Correlations are shown in Supplementary Tables S2 and S3 (see Section 3 of the supplementary information). SB<sub>movement</sub> and SB<sub>combined</sub> typically showed stronger correlation with one another than either method showed with SB<sub>posture</sub>. Correlations with MVPA were mostly negative, but the magnitude differed depending on the SB variable. For total SB, correlations with MVPA were <-0.52 when measured by  $SB_{movement}$  and  $SB_{combined}\text{,}$  versus -0.34 for  $SB_{posture}\text{.}$  In contrast, correlations for mean SB bout duration were >-0.39 versus -0.55, respectively. Correlations between SB breaks and MVPA were marginal for  $SB_{movement}$  (-0.15) and  $SB_{combined}$  (-0.03) yet positive for SB<sub>posture</sub> (0.45).

Figure 1 shows density plots of each variable's distribution. For total SB, distributions were similar for SB<sub>movement</sub> and SB<sub>combined</sub>,

Figure 2 shows joint distributions between SB variables and MVPA. When looking at total SB and mean SB bout duration, the densities had similar shape across SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>. However, for SB breaks, the density contour was radial when measured by SB<sub>movement</sub> and SB<sub>combined</sub>, whereas it was more elliptical for SB<sub>posture</sub>, such that density of SB breaks tended to increase with greater density of MVPA. Together, these trends showed a fairly consistent relationship of MVPA with SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>, with nuanced differences when looking at SB breaks.

#### Associations with obesity markers

*Waist circumference.* In Model 1, there were significant associations (p < 0.001) for all SB variables, except for SB breaks when measured by SB<sub>movement</sub> and SB<sub>combined</sub> (p = 0.69 - 0.76) (Table 2). All coefficients were in the expected direction (positive for total SB time and mean SB bout duration; negative for SB breaks), except for SB breaks when measured using SB<sub>combined</sub>. The highest-magnitude SD-scale coefficients were seen for SB<sub>posture</sub> and were 1.1–26.7 times higher than for SB<sub>movement</sub> or SB<sub>posture</sub>.

When adding MVPA as a covariate (Model 2), all coefficients reversed direction for total SB, indicating more SB time was significantly associated with lower waist circumference (Table 2). SD-scale coefficients for SB<sub>posture</sub> were attenuated compared to Model 1, yet remained significant for all three SB variables ( $p \le 0.02$ ). Coefficients for SB<sub>movement</sub> and SB<sub>combined</sub> were sometimes attenuated and other times amplified, with inconsistent patterns of significance (p from <0.001–0.69). The highest-magnitude SD-scale coefficients were again seen for SB<sub>posture</sub> (1.3–10.9 times higher than for SB<sub>movement</sub> or SB<sub>posture</sub>) when looking at mean bout duration and SB breaks, but not for total SB.

Results for body fat percentage. Coefficients for Model 1 followed a similar pattern to what was seen for waist circumference, with significant associations (p < 0.001) for all SB variables except SB breaks when measured by SB<sub>movement</sub> and SB<sub>combined</sub> (p = 0.26 - 0.47) (Table 3). Coefficients were again in the expected directions for Model 1, while the total SB coefficients reversed direction in Model 2.

In Model 2, SB<sub>posture</sub> was the only method to retain a significant coefficient for mean SB bout duration (p = 0.004), while all three methods had significant coefficients for SB breaks (p < 0.02) (Table 3). Compared to Model 1, coefficients were generally smaller in magnitude, with exceptions for total SB (when measured by SB<sub>posture</sub>) and SB breaks (when measured by SB<sub>movement</sub> and SB<sub>combined</sub>). SD-scale coefficients for SB<sub>posture</sub> tended to be 1.2–11.2 times higher than for SB<sub>movement</sub> or SB<sub>combined</sub>, but there were exceptions (marginally lower coefficients compared to one or both of the other methods) for total SB in Model 1 and SB breaks in Model 2.

Results for BMI-z. In Model 1, all associations for SB<sub>posture</sub> were significant (p < 0.001) and in the expected direction. Neither SB<sub>movement</sub> nor SB<sub>combined</sub> had significant associations for SB breaks (p = 0.26 - 0.95), and there was also no significant association for mean SB bout duration when measured by SB<sub>combined</sub> (p = 0.06) (Table 4). The remaining coefficients were significant (p < 0.02) and in the expected direction. SD-scale coefficients for SB<sub>posture</sub> had 1.3–5.9 times higher magnitude than for SB<sub>movement</sub> or SB<sub>combined</sub>, with one exception (158 times higher than SB<sub>movement</sub> when looking at SB breaks).

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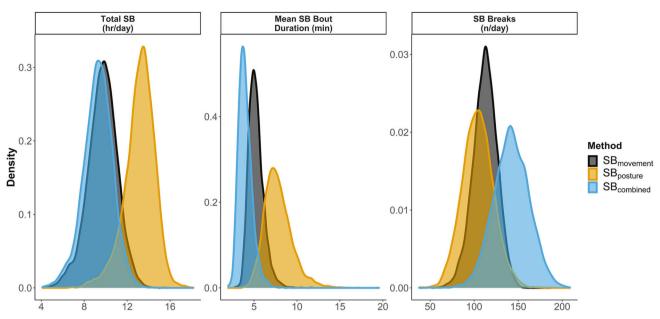


Fig. 1 Density plots comparing the distributions of sedentary behavior (SB) variables when assessed by the SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub> methods. Variables shown are total SB (left), mean SB bout duration (middle), and SB breaks (right).

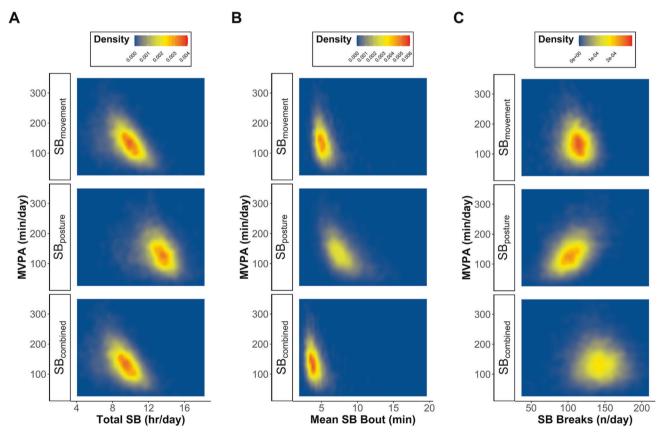


Fig. 2 Two-dimensional density plots depicting joint distributions of sedentary behavior (SB) variables with moderate-to-vigorous physical activity (MVPA). Variables shown are total SB (A), mean SB bout duration (B), and SB breaks (C). Row panels depict the distributions for the SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub> methods (top, middle, and bottom rows, respectively).

For Model 2, all coefficients for total SB time again became significantly negative (p < 0.01) (Table 4). The only other coefficients to remain significant were for SB breaks when measured by SB<sub>movement</sub> and SB<sub>posture</sub> (p < 0.01). The SD-scale

coefficients for SB<sub>posture</sub> had 1.1–11.6 times higher magnitude than the coefficients for SB<sub>movement</sub> or SB<sub>combined</sub> when looking at mean SB bout duration and SB breaks, but not total SB.

4

Table 2. Association	s between accelerometer-derived	sedentary behavior	variables and wais	t circumference (cm).
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	SB <sub>movement</sub>	SB <sub>posture</sub>	<b>SB</b> <sub>combined</sub>
Model 1			
SB Time (hr/day)	b: 0.664 (0.443, 0.885) <sup>a</sup>	b: 0.830 (0.552, 1.108) <sup>a</sup>	b: 0.726 (0.505, 0.946) <sup>a</sup>
	β: 0.916 (0.612, 1.219) <sup>a</sup>	β: 1.162 (0.773, 1.551) <sup>a</sup>	β: 0.990 (0.687, 1.292) <sup>a</sup>
Mean SB bout (min)	b: 0.742 (0.440, 1.044) <sup>a</sup>	b: 0.874 (0.708, 1.040) <sup>a</sup>	b: 0.694 (0.366, 1.023) <sup>a</sup>
	β: 0.650 (0.383, 0.917) <sup>a</sup>	β: 1.397 (1.131, 1.663) <sup>a</sup>	β: 0.553 (0.291, 0.815) <sup>a</sup>
SB Breaks (n/day)	b: -0.005 (-0.029, 0.018)	b: -0.087 (-0.102, -0.072) <sup>a</sup>	b: 0.003 (-0.012, 0.018)
	β: -0.072 (-0.398, 0.255)	$\beta$ : -1.522 (-1.781, -1.263) <sup>a</sup>	β: 0.057 (-0.248, 0.361)
Model 2			
SB Time (hr/day)	b: -0.760 (-1.067, -0.454) <sup>a</sup>	b: -0.428 (-0.773, -0.082) <sup>a</sup>	b: -0.531 (-0.830, -0.232) <sup>a</sup>
	$\beta$ : -1.046 (-1.471, -0.620) <sup>a</sup>	$\beta$ : -0.598 (-1.082, -0.115) <sup>a</sup>	$\beta$ : -0.724 (-1.134, -0.314) <sup>a</sup>
Mean SB bout (min)	b: 0.076 (-0.233, 0.385)	b: 0.449 (0.250, 0.648) <sup>a</sup>	b: -0.077 (-0.415, 0.261)
	β: 0.067 (-0.206, 0.339)	β: 0.717 (0.398, 1.036) <sup>a</sup>	β: -0.066 (-0.335, 0.204)
SB Breaks (n/day)	b: -0.049 (-0.074, -0.025) <sup>a</sup>	b: -0.052 (-0.069, -0.034) <sup>a</sup>	b: -0.007 (-0.022, 0.008)
	$\beta$ : -0.681 (-1.012, -0.350) <sup>a</sup>	$\beta$ : -0.903 (-1.205, -0.601) <sup>a</sup>	β: -0.135 (-0.435, 0.166)

Coefficients are presented as either b (all model variables are in units of measure) or  $\beta$  (all model variables are mean-centered and SD-scaled, except waist circumference). Values are formatted as follows: coefficient (unadjusted 95% confidence interval).

SB sedentary behavior.

<sup>a</sup>Coefficient significantly different from 0 (p < 0.05).

Model 1: Adjusting for site, age, sex, and accelerometer wear time.

Model 2: Same as Model 1 with additional inclusion of moderate-to-vigorous physical activity.

Table 3. Associations between accelerometer-derived sedentary behavior variables and body fat (%).

	SB <sub>movement</sub>	SB <sub>posture</sub>	<b>SB</b> <sub>combined</sub>
Model 1			
SB Time (hr/day)	b: 0.648 (0.476, 0.820) <sup>a</sup>	b: 0.576 (0.350, 0.802) <sup>a</sup>	b: 0.667 (0.491, 0.844) <sup>a</sup>
	β: 0.888 (0.654, 1.121) <sup>a</sup>	β: 0.805 (0.489, 1.121) <sup>a</sup>	β: 0.900 (0.666, 1.133) <sup>a</sup>
Mean SB bout (min)	b: 0.722 (0.480, 0.964) <sup>a</sup>	b: 0.686 (0.552, 0.819) <sup>a</sup>	b: 0.743 (0.477, 1.009) <sup>a</sup>
	β: 0.638 (0.424, 0.851) <sup>a</sup>	β: 1.096 (0.882, 1.310) <sup>a</sup>	$\beta$ : 0.590 (0.379, 0.802) <sup>a</sup>
SB Breaks (n/day)	b: -0.008 (-0.027, 0.011)	b: -0.071 (-0.084, -0.059) <sup>a</sup>	b: -0.008 (-0.021, 0.004)
	β: -0.112 (-0.380, 0.157)	$\beta$ : -1.250 (-1.465, -1.035) <sup>a</sup>	β: -0.162 (-0.418, 0.0945)
Model 2			
SB Time (hr/day)	b: -0.545 (-0.796, -0.294) <sup>a</sup>	b: -0.649 (-0.932, -0.367) <sup>a</sup>	b: -0.431 (-0.675, -0.186) <sup>a</sup>
	$\beta$ : -0.751 (-1.097, -0.405) <sup>a</sup>	$\beta$ : -0.909 (-1.304, -0.513) <sup>a</sup>	$\beta$ : -0.587 (-0.920, -0.254) <sup>a</sup>
Mean SB bout (min)	b: 0.131 (-0.120, 0.383)	b: 0.251 (0.090, 0.412) <sup>a</sup>	b: 0.068 (-0.210, 0.347)
	β: 0.115 (-0.107, 0.337)	β: 0.402 (0.146, 0.658) <sup>a</sup>	β: 0.054 (-0.167, 0.275)
SB Breaks (n/day)	b: -0.047 (-0.067, -0.028) <sup>a</sup>	b: -0.037 (-0.052, -0.023) <sup>a</sup>	b: -0.016 (-0.029, -0.004) <sup>a</sup>
	$\beta$ : -0.653 (-0.926, -0.380) <sup>a</sup>	$\beta$ : -0.652 (-0.902, -0.402) <sup>a</sup>	$\beta$ : -0.326 (-0.580, -0.073) <sup>a</sup>

Coefficients are presented as either *b* (all model variables are in units of measure) or  $\beta$  (all model variables are mean-centered and SD-scaled, except body fat). Values are formatted as follows: coefficient (unadjusted 95% confidence interval). *SB* sedentary behavior.

<sup>a</sup>Coefficient significantly different from 0 (adjusted p < 0.05).

Model 1: Adjusting for site, age, sex, ethnicity/race, maturity offset, and accelerometer wear time.

Model 2: Same as Model 1 with additional inclusion of moderate-to-vigorous physical activity.

#### DISCUSSION

The present findings support the importance of assessing posture and pattern-focused variables (mean bout duration and SB breaks) in pediatric SB research. A key finding was that  $SB_{posture}$  tended to be more strongly associated with obesity variables than what was seen for  $SB_{movement}$  or  $SB_{combined}$ . The associations for  $SB_{posture}$ also had a stronger tendency to retain statistical significance when adjusting for MVPA. Findings were especially notable for patternfocused variables, where changes of 1.0–2.8 min (mean SB bout) and 8.2–17.5 breaks/day (SB breaks) were comparable with a 1.0 hr/day change in total SB, in terms of the associated change in obesity variables. Considering that most pediatric SB research has used movement-based measures of total SB, the present study's overall findings suggest a need for more posture- and patternfocused research.

SB is formally defined as having two components, one relating to movement and metabolism while the other relates to posture [7]. This creates a need to measure both components in SB research, which has historically been challenging. By following the methods outlined in the present study, it is now possible to measure both components via a single hip-worn ActiGraph device. However, the weak associations for SB<sub>combined</sub> may suggest there

Table 4.	Associations be	etween acceler	ometer-derived	sedentary	behavior	variables and	body m	nass index z-sco	re (BMI-z, unitless).
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	SB <sub>movement</sub>	SB <sub>posture</sub>	<b>SB</b> <sub>combined</sub>
Model 1			
SB Time (hr/day)	b: 0.052 (0.023, 0.081) <sup>a</sup>	b: 0.078 (0.040, 0.116) <sup>a</sup>	b: 0.061 (0.031, 0.091) <sup>a</sup>
	β: 0.070 (0.030, 0.109) <sup>a</sup>	β: 0.109 (0.056, 0.162) <sup>a</sup>	β: 0.082 (0.042, 0.121) <sup>a</sup>
Mean SB bout (min)	b: 0.053 (0.014, 0.092) <sup>a</sup>	b: 0.085 (0.063, 0.107) <sup>a</sup>	b: 0.044 (0.000, 0.088)
	β: 0.046 (0.012, 0.080) <sup>a</sup>	β: 0.136 (0.101, 0.170) <sup>a</sup>	β: 0.035 (0.000, 0.070)
SB Breaks (n/day)	b: 0.000 (-0.003, 0.003)	b: -0.009 (-0.011, -0.007) <sup>a</sup>	b: 0.001 (-0.001, 0.003)
	β: 0.001 (-0.043, 0.046)	$\beta$ : -0.158 (-0.193, -0.123) <sup>a</sup>	β: 0.027 (-0.014, 0.069)
Model 2			
SB Time (hr/day)	b: -0.140 (-0.183, -0.097) <sup>a</sup>	b: -0.077 (-0.125, -0.029) <sup>a</sup>	b: -0.106 (-0.147, -0.064) <sup>a</sup>
	$\beta$ : -0.193 (-0.252, -0.134) <sup>a</sup>	$\beta$ : -0.108 (-0.175, -0.041) <sup>a</sup>	$\beta$ : -0.144 (-0.200, -0.087) <sup>a</sup>
Mean SB bout (min)	b: -0.025 (-0.066, 0.016)	b: 0.028 (0.001, 0.055)	b: -0.048 (-0.095, -0.002)
	β: -0.025 (-0.061, 0.011)	β: 0.045 (0.002, 0.087)	β: -0.039 (-0.076, -0.002)
SB Breaks (n/day)	b: -0.005 (-0.008, -0.002) <sup>a</sup>	b: -0.005 (-0.007, -0.002) <sup>a</sup>	b: 0.000 (-0.002, 0.002)
	$\beta$ : -0.069 (-0.113, -0.024) <sup>a</sup>	$\beta$ : -0.081 (-0.122, -0.039) <sup>a</sup>	β: 0.007 (-0.035, 0.048)

Coefficients are presented as either *b* (all model variables are in units of measure) or  $\beta$  (all model variables are mean-centered and SD-scaled, except BMI-z). Values are formatted as follows: coefficient (unadjusted 95% confidence interval).

SB sedentary behavior.

<sup>a</sup>Coefficient significantly different from 0 (p < 0.05).

Model 1: Adjusting for site, age, sex, ethnicity/race, maturity offset, and accelerometer wear time.

Model 2: Same as Model 1 with additional inclusion of moderate-to-vigorous physical activity.

is limited value in combining measures of movement and posture, at least in pediatric obesity research. Instead, the present findings may suggest the postural component of SB has greater importance for pediatric obesity than the movement component. Implications for other health conditions should be investigated in future studies.

Our results for total SB were consistent with prior research in the ISCOLE, as presented by Katzmarzyk et al. [25]. In particular, they observed the same pattern we saw for all three methods (SB<sub>movement</sub>, SB<sub>posture</sub>, and SB<sub>combined</sub>), with greater total SB being associated with lower obesity when adjusting for MVPA. These findings underscore the complex interrelationship of total SB and MVPA, lending further support to the notion that total SB does not have MVPA-independent health associations in pediatric obesity [26–28]. There may also be implications for 24-h research and compositional analyses examining interactions between sleep, SB, MVPA, and light-intensity activity. In the ISCOLE, prior work along this line has shown adverse associations when reallocating MVPA time to other behaviors, especially SB [29, 30].

Although MVPA strongly influenced our findings for total SB, its influence was not as strong for the pattern-focused SB variables (mean SB bout duration and SB breaks). These variables are crucial to consider since some research in adults has shown potential benefits of shortening SB bouts and increasing SB breaks [31-37]. A suggested mechanism of benefit is that brief muscle contractions during a SB break may improve blood flow and promote glucose uptake and homeostasis [38]. However, pattern-focused analyses in youth have produced equivocal evidence [39]. The present results showed adverse associations between prolonged and uninterrupted SB patterns and obesity markers. Notably, these associations were most consistent for SB<sub>posture</sub>, with fewer associations observed for SB<sub>movement</sub> and only one for SB<sub>combined</sub>. Some previous research has produced similar findings, with adverse associations for the SB pattern variables but not total SB [40]. This suggests a need for interventions that specifically focus on breaking up periods of SB throughout the day [40].

From a measurement perspective, the present findings should be considered alongside the ongoing trend toward wrist-worn rather than hip-worn monitors in epidemiological studies. The current CHAP-Child model is specific to hip-worn devices and opens important doors for retrospective analyses in large datasets such as ISCOLE. However, there is a clear need for an adapted model that applies to data from wrist-worn monitors as well. Currently, it is unclear whether deep-learned algorithms for wrist-worn monitors can achieve a similar level of validity to what was originally shown for the current CHAP-Child model [13]. However, the present findings for SB<sub>posture</sub> underscore the importance of exploring this in future research.

It should also be noted that SB<sub>movement</sub> is a cut-point based method while SB<sub>posture</sub> is machine learning-based (specifically, deep learning). The advent of machine learning has been well documented in accelerometer-based calibration studies, but limited user-friendliness remains a major limitation [41]. This may explain why there has been limited response to explicit recommendations for cut-points to be abandoned [42]. For CHAP-Child and its predecessors [43, 44], web-based support is available to promote usability and uptake, including opportunities for researchers to attempt using the methods and provide feedback on improving its usability (see https://adalabucsd.github.io/DeepPostures/). While these are ongoing efforts, they may help to make CHAP-Child more usable in future research.

#### Strengths and limitations

A key strength of this study was its innovative methodology centered on the use of CHAP-Child to compare  $SB_{movement}$ ,  $SB_{posturer}$ , and  $SB_{combined}$  (obtained from a single hip-worn device). Our methods can now be replicated and applied to a wealth of existing data, which may provide new health insights without the need to collect new data. Another strength of the study was epidemiological application in a large and multinational pediatric sample.

Despite the above strengths, there were also limitations. One limitation was the complexity of the methods, which may pose a barrier to use for the time being. This was partially exemplified in our analyses, as the required data (.gt3x format) were not available in some cases. As noted previously, ongoing efforts are in place to make CHAP-Child and related methods [43, 44] easier to use.

Additional limitations of the ISCOLE study have been discussed elsewhere [25], including the cross-sectional nature of the dataset

and the overall limitations of accelerometry. In particular, the ISCOLE study was not designed to establish causality in the analyses. Notably, the present analysis overcame one limitation indicated by Katzmarzyk et al. [25], namely the inability of accelerometer data to capture posture. Ongoing work is needed to continue refining accelerometer-based methods and overcome other limitations that face pediatric research.

#### Conclusions

Posture and pattern-focused SB variables are critical to assess in pediatric SB research. CHAP-Child is a promising method for such assessments, allowing posture and movement to be assessed using a single hip-worn device. This is a major step forward in SB assessment, especially since ActiGraph is a leading brand in device-based research [14]. Ongoing research is needed to more fully characterize the interrelationships between SB variables and MVPA, as well as interrelationships between movement and posture.

#### CODE AVAILABILITY

Code from the analysis is available on request.

#### REFERENCES

- Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. Diabetes. 2007;56:2655–67.
- Young DR, Hivert MF, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, et al. Sedentary behavior and cardiovascular morbidity and mortality: a science advisory from the American Heart Association. Circulation. 2016;134. https:// www.ahajournals.org/doi/10.1161/CIR.00000000000440.
- Pate RR, O'neill JR, Lobelo F. The evolving definition of sedentary. Exerc Sport Sci Rev. 2008;36:173–8.
- Gibbs BB, Hergenroeder AL, Katzmarzyk PT, Lee IM, Jakicic JM. Definition, measurement, and health risks associated with sedentary behavior. Med Sci Sports Exerc. 2015;47:1295–300.
- Reilly JJ, Janssen X, Cliff DP, Okely AD. Appropriateness of the definition of 'sedentary' in young children: whole-room calorimetry study. J Sci Med Sport. 2015;18:565–8.
- Saint-Maurice PF, Kim Y, Welk GJ, Gaesser GA. Kids are not little adults: what MET threshold captures sedentary behavior in children? Eur J Appl Physiol. 2016;116:29–38.
- Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, et al. Sedentary Behavior Research Network (SBRN) – Terminology Consensus Project process and outcome. Int J Behav Nutr Phys Act. 2017;14(Jun):75 https:// doi.org/10.1186/s12966-017-0525-8.
- Sedentary Behaviour Research Network. Letter to the Editor: Standardized use of the terms "sedentary" and "sedentary behaviours". Appl Physiol Nutr Metab. 2012;37:540–2.
- 9. Crouter SE, Hibbing PR, LaMunion SR. Use of objective measures to estimate sedentary time in youth. J Meas Phys Behav. 2018;1:136–42.
- Janssen X, Cliff DP. Issues related to measuring and interpreting objectively measured sedentary behavior data. Meas Phys Educ Exerc Sci. 2015;19:116–24.
- Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, et al. Amount of time spent in sedentary behaviors in the United States, 2003–2004. Am J Epidemiol. 2008;167:875–81.
- Kozey-Keadle S, Libertine A, Lyden K, Staudenmayer J, Freedson PS. Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc. 2011;43:1561–7.
- Carlson JA, Ridgers ND, Nakandala S, Zablocki R, Tuz-Zahra F, Bellettiere J, et al. CHAP-child: an open source method for estimating sit-to-stand transitions and sedentary bout patterns from hip accelerometers among children. Int J Behav Nutr Phys Act. 2022;19(Aug):109 https://doi.org/10.1186/s12966-022-01349-2.
- Wijndaele K, Westgate K, Stephens SK, Blair SN, Bull FC, Chastin SFM, et al. Utilization and harmonization of adult accelerometry data: review and expert consensus. Med Sci Sports Exerc. 2015;47:2129–39.
- Cliff DP, Hesketh KD, Vella SA, Hinkley T, Tsiros MD, Ridgers ND, et al. Objectively measured sedentary behaviour and health and development in children and adolescents: systematic review and meta-analysis. Obes Rev. 2016;17:330–44.
- Katzmarzyk PT, Barreira TV, Broyles ST, Champagne CM, Chaput JP, Fogelholm M, et al. The International Study of Childhood Obesity, Lifestyle and the Environment (ISCOLE): design and methods. BMC Public Health. 2013;13(Sep):900 https://doi.org/10.1186/1471-2458-13-900.

- Treuth MS, Schmitz K, Catellier DJ, McMurray RG, Murray DM, Almeida MJ, et al. Defining accelerometer thresholds for activity intensities in adolescent girls. Med Sci Sports Exerc. 2004;36:1259–66.
- de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ. 2007;85:660–7.
- 19. Chen KY, Bassett DR. The technology of accelerometry-based activity monitors: Current and future. Med Sci Sports Exerc. 2005;37:S490–500.
- Cain KL, Conway TL, Adams MA, Husak LE, Sallis JF. Comparison of older and newer generations of ActiGraph accelerometers with the normal filter and the low frequency extension. Int J Behav Nutr Phys Act. 2013;10:51 https://doi.org/ 10.1186/1479-5868-10-51.
- Hibbing PR, Bassett DR, Crouter SE. Modifying accelerometer cut-points affects criterion validity in simulated free-living for adolescents and adults. Res Q Exerc Sport. 2020;91:514–24.
- Troiano RP, Berrigan D, Dodd KW, MåSse LC, Tilert T, Mcdowell M. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc. 2008;40:181–8.
- Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. Med Sci Sports Exerc. 2005;37:S523–30.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc B Stat Methodol. 1995;57:289–300.
- Katzmarzyk PT, Barreira TV, Broyles ST, Champagne CM, Chaput JP, Fogelholm M, et al. Physical activity, sedentary time, and obesity in an international sample of children. Med Sci Sports Exerc. 2015;47:2062–9.
- Tremblay MS, LeBlanc AG, Kho ME, Saunders TJ, Larouche R, Colley RC, et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth. Int J Behav Nutr Phys Act. 2011;8:1 https://doi.org/10.1186/ 1479-5868-8-98.
- Carson V, Hunter S, Kuzik N, Gray CE, Poitras VJ, Chaput JP, et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth: an update. Appl Physiol Nutr Metab. 2016;41:S240–65.
- Biddle SJH, García Bengoechea E, Wiesner G. Sedentary behaviour and adiposity in youth: a systematic review of reviews and analysis of causality. Int J Behav Nutr Phys Act. 2017;14(Mar):43 https://doi.org/10.1186/s12966-017-0497-8.
- Dumuid D, Stanford TE, Pedišić Ž, Maher C, Lewis LK, Martín-Fernández JA, et al. Adiposity and the isotemporal substitution of physical activity, sedentary time and sleep among school-aged children: a compositional data analysis approach. BMC Public Health. 2018;18(Dec):311 https://doi.org/10.1186/s12889-018-5207-1.
- 30. Dumuid D, Pedišić Ž, Stanford TE, Martín-Fernández JA, Hron K, Maher CA, et al. The compositional isotemporal substitution model: a method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. Stat Methods Med Res. 2019;28:846–57.
- Saunders TJ, Larouche R, Colley RC, Tremblay MS. Acute sedentary behaviour and markers of cardiometabolic risk: a systematic review of intervention studies. J Nutr Metab. 2012;2012:1–12. https://doi.org/10.1155/2012/712435.
- Saunders TJ, Atkinson HF, Burr J, MacEwen B, Skeaff CM, Peddie MC. The acute metabolic and vascular impact of interrupting prolonged sitting: A systematic review and meta-analysis. Sports Med. 2018;48:2347–66.
- Saunders TJ, McIsaac T, Douillette K, Gaulton N, Hunter S, Rhodes RE, et al. Sedentary behaviour and health in adults: an overview of systematic reviews. Appl Physiol Nutr Metab. 2020;45:S197–217.
- Owen N, Healy GN, Dempsey PC, Salmon J, Timperio A, Clark BK, et al. Sedentary behavior and public health: integrating the evidence and identifying potential solutions. Annu Rev Public Health. 2020;41:265–87.
- 35. Wheeler MJ, Green DJ, Cerin E, Ellis KA, Heinonen I, Lewis J, et al. Combined effects of continuous exercise and intermittent active interruptions to prolonged sitting on postprandial glucose, insulin, and triglycerides in adults with obesity: a randomized crossover trial. Int J Behav Nutr Phys Act. 2020;17(Dec):152 https:// doi.org/10.1186/s12966-020-01057-9.
- Homer AR, Taylor FC, Dempsey PC, Wheeler MJ, Sethi P, Townsend MK, et al. Frequency of interruptions to sitting time: Benefits for postprandial metabolism in type 2 diabetes. Diabetes Care. 2021;44:1254–63.
- Higgins S, Pomeroy A, Bates LC, Paterson C, Barone Gibbs B, Pontzer H, et al. Sedentary behavior and cardiovascular disease risk: an evolutionary perspective. Front Physiol. 2022;13(Jul):962791 https://doi.org/10.3389/fphys.2022.962791.
- Bergouignan A, Latouche C, Heywood S, Grace MS, Reddy-Luthmoodoo M, Natoli AK, et al. Frequent interruptions of sedentary time modulates contraction- and insulin-stimulated glucose uptake pathways in muscle: ancillary analysis from randomized clinical trials. Sci Rep. 2016;6(Aug):32044 https://doi.org/10.1038/ srep32044.
- Verswijveren SJJM, Lamb KE, Bell LA, Timperio A, Salmon J, Ridgers ND. Associations between activity patterns and cardio-metabolic risk factors in children and adolescents: a systematic review. PLOS One. 2018;13(Aug):e0201947 https:// doi.org/10.1371/journal.pone.0201947.

- 8
- Bejarano CM, Gallo LC, Castañeda SF, Garcia ML, Sotres-Alvarez D, Perreira KM, et al. Patterns of sedentary time in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) youth. J Phys Act Health. 2021;18:61–9.
- Pfeiffer KA, Clevenger KA, Kaplan A, Van Camp CA, Strath SJ, Montoye AHK. Accessibility and use of novel methods for predicting physical activity and energy expenditure using accelerometry: a scoping review. Physiol Meas. 2022. https:// doi.org/10.1088/1361-6579/ac89ca.
- Strath SJ, Pfeiffer KA, Whitt-Glover MC. Accelerometer use with children, older adults, and adults with functional limitations. Med Sci Sports Exerc. 2012;44:S77–85.
- Greenwood-Hickman MA, Nakandala S, Jankowska MM, Rosenberg D, Tuz-Zahra F, Bellettiere J, et al. The CNN Hip Accelerometer Posture (CHAP) method for classifying sitting patterns from hip accelerometers: a validation study. Med Sci Sports Exerc. 2021;53:2445–54.
- 44. Bellettiere J, Nakandala S, Tuz-Zahra F, Winkler EAH, Hibbing PR, Healy GN, et al. CHAP-adult: a reliable and valid algorithm to classify sitting and measure sitting patterns using data from hip-worn accelerometers in adults aged 35+. J Meas Phys Behav. 2022;5:215–23.

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## **AUTHOR CONTRIBUTIONS**

Designed and implemented parent study: PK. Acquired funding for present study: LN, JC, AL, MJ, AK. Developed the methods: JC, SN, JB, JZ, AK, LN, MAGH. Processed data:

CS, PH, PK. Devised analysis: PH, JC, LN, MJ. Drafted manuscript: PH, JC, LN. Reviewed, revised, and approved manuscript: All authors.

### **COMPETING INTERESTS**

This study was funded by NIH R01DK114945. The parent study (ISCOLE) was funded by The Coca-Cola Company. With the exception of requiring that the study be global in nature, the parent study funder had no role in the design and conduct of the study. The authors declare no conflicts of interest.

# **ADDITIONAL INFORMATION**

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