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CLINICAL RESEARCH
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Device-measured physical activity and cardiometabolic health: the Prospective Physical Activity, Sitting, and Sleep (ProPASS) consortium

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Abstract

Background and Aims Physical inactivity, sedentary behaviour (SB), and inadequate sleep are key behavioural risk factors of cardiometabolic diseases. Each behaviour is mainly considered in isolation, despite clear behavioural and biological interdependencies. The aim of this study was to investigate associations of five-part movement compositions with adiposity and cardiometabolic biomarkers.

Methods Cross-sectional data from six studies ($n = 15\,253$ participants; five countries) from the Prospective Physical Activity, Sitting and Sleep consortium were analysed. Device-measured time spent in sleep, SB, standing, light-intensity physical activity (LIPA), and moderate-vigorous physical activity (MVPA) made up the composition. Outcomes included body mass index (BMI), waist circumference, HDL cholesterol, total:HDL cholesterol ratio, triglycerides, and glycated haemoglobin (HbA1c). Compositional linear regression examined associations between compositions and outcomes, including modelling time reallocation between behaviours.

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Results The average daily composition of the sample (age: 53.7 ± 9.7 years; 54.7% female) was 7.7 h sleeping, 10.4 h sedentary, 3.1 h standing, 1.5 h LIPA, and 1.3 h MVPA. A greater MVPA proportion and smaller SB proportion were associated with better outcomes. Reallocating time from SB, standing, LIPA, or sleep into MVPA resulted in better scores across all outcomes. For example, replacing 30 min of SB, sleep, standing, or LIPA with MVPA was associated with −0.63 (95% confidence interval −0.48, −0.79), −0.43 (−0.25, −0.59), −0.40 (−0.25, −0.56), and −0.15 (0.05, −0.34) kg/m^2 lower BMI, respectively. Greater relative standing time was beneficial, whereas sleep had a detrimental association when replacing LIPA/MVPA and positive association when replacing SB. The minimal displacement of any behaviour into MVPA for improved cardiometabolic health ranged from 3.8 (HbA1c) to 12.7 (triglycerides) min/day.

Conclusions Compositional data analyses revealed a distinct hierarchy of behaviours. Moderate-vigorous physical activity demonstrated the strongest, most time-efficient protective associations with cardiometabolic outcomes. Theoretical benefits from reallocating SB into sleep, standing, or LIPA required substantial changes in daily activity.

Structured Graphical Abstract

Key Question

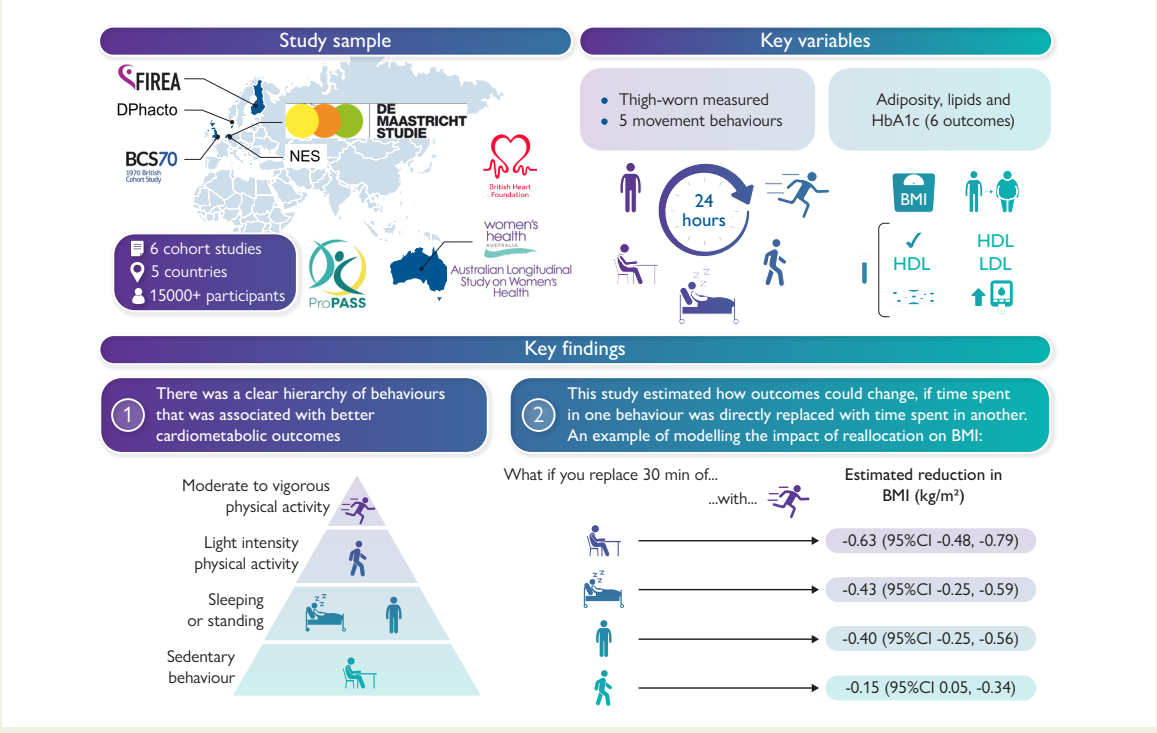
How is movement behaviour (sleep, sedentary behaviour, standing, various intensity levels of activity) across the 24-hour period associated with cardiometabolic outcomes?

Key Finding

Cross-sectional device-measured data from six studies showed a clear hierarchy of favourable movement behaviours across the 24-hour period. Redistribution of time from sedentary behaviour to moderate-vigorous physical activity was most strongly associated with healthier cardiometabolic outcomes.

Take Home Message

Compositional data analyses reveal a distinct hierarchy of behaviours. Theoretical benefits from reallocating physical behaviours requires substantial changes in daily activity.



Hierarchy of favourable movement behaviours across the 24 h day suggests more time spent in moderate-vigorous physical activity and less time spent sedentary are most strongly associated with healthier cardiometabolic outcomes. BMI, body mass index; HbA1c, glycated haemoglobin.

Keywords Cohort consortium • Cardiometabolic outcomes • Physical activity • Sedentary behaviour • Sleep • Standing • Compositional data analysis

Introduction

Cardiometabolic diseases—including cardiovascular disease (CVD), obesity, and diabetes mellitus—are the leading cause of mortality worldwide.[1,2] The global burden of these diseases has risen over the past three decades, with annual CVD-related deaths increasing from 12.1 to 18.6 million, while diabetes-related deaths have doubled to 1.25 million.[3–6] Concerningly, these trends are forecasted to continue.[7–9] Positive engagement in health behaviours, such as physical activity, reducing sedentary behaviour (SB), and ensuring sufficient quality and quantity of sleep, can help prevent cardiometabolic disease[1,10] yet are largely underutilized.

Regular moderate-vigorous physical activity (MVPA) has established cardiometabolic benefits via direct inflammatory, metabolic, or cardiovascular mechanisms.[11,12] However, the effects of light-intensity physical activity (LIPA) are less clear.[13] This may be due to poor ascertainment of LIPA using self-reported questionnaires[14] or threshold-based approaches of hip or wrist-based accelerometery, which fail to distinguish between standing and subtle ambulatory activities.[15] There is a strong argument against classifying passive standing as LIPA, given the very low energy expenditure involved.[16] Finally, there is consistent evidence of associations between SB and increased cardiometabolic disease risk,[17] while there is mixed evidence on the adverse effects of both short and long sleep durations.[18,19]

Time spent in these daily movement behaviours (sleep, SB, standing, LIPA, MVPA) form a 24 h composition, with any change in one behaviour resulting in a corresponding increase or decrease in another. Until recently, controlled exercise trials and observational studies have mainly examined each behaviour in isolation.[13,20] Assumptions that these behaviours are independent and that the 24 h day is infinite (e.g. effect estimates represent per 1 h increase in behaviour) can lead to potentially imprecise estimates that cannot be translated to real-world interventions or guidelines. Treating these data as a complete 24 h day using compositional data analysis can overcome this limitation.[21] Previous evidence of movement compositions has suggested that more time in MVPA and less time in SB are associated with favourable health outcomes.[22–24] However, these studies have largely relied upon small sample sizes, considered compositions with awake time only or incorporated self-reported sleep measures, and were unable to differentiate between sedentary and standing activity (i.e. due to wrist or hip worn accelerometers).

The majority of current public health guidelines (i.e. WHO, USA, UK) focus solely on physical activity and SB.[25,26] There is a clear need for better empirical evidence to support '24-hour' guidelines[27] and encompass recommendations on daily sleep, SB, and activity intensity volume. The Prospective Physical Activity, Sitting, and Sleep (ProPASS) consortium resource[28] overcomes major limitations of previous literature[22–24] by using harmonized individual-level data from six studies with thigh-worn accelerometery and a unified approach to derive 24 h movement behaviours. Our aim was to examine the associations between compositions of 24 h movement behaviours (defined as time spent in sleep, SB, standing, LIPA, MVPA) and six cardiometabolic outcomes. Using the mean sample behavioural profile, we estimated the impact of reallocating time from one behaviour to another.

Methods

Sample

ProPASS is an international research collaboration platform consisting of 15+ observational cohort studies with thigh-worn accelerometry.[28] For this initial project, we included cross-sectional data from six participating studies: The Maastricht Study (TMS; The Netherlands, $n = 7515$),[29] the 1970 British Birth Cohort Study (BCS70; UK, $n = 5229$),[30] the Australian Longitudinal Study on Women's Health (ALSWH; Australia, $n = 941$),[31] the Danish PHysical ACTivity cohort with Objective measurements cohort (DPhacto; Denmark, $n = 771$),[32] the Nijmegen Exercise Study (NES; The Netherlands, $n = 537$),[33] and the Finnish Retirement and Aging Study (FIREA; Finland, $n = 253$).[34] Ethical approval and informed consent were provided at the cohort level and included consent for future data analysis; an overview of each study is provided in Supplementary data online, *Table S1* with complete study details available elsewhere.[28–34] Data were physically pooled at the University of Sydney after signing all necessary data transfer agreements that adhered to cohort-specific requirements; this included harmonization of covariates and outcomes, as well as cleaning and processing of raw accelerometer data.

Movement behaviours

All cohorts collected movement behaviour data using a 7-day, 24 h/day thigh-worn accelerometer protocol; four studies used ActivPAL3/4 devices (BCS70, TMS, ALSWH, NES), one used Axivity devices (FIREA), and one used ActiGraph devices (DPhacto). Raw accelerometer data were centrally processed using previously validated software, ActiPASS v 1.32. ActiPASS identifies behaviours in 2 s windows with a 50% overlap, resulting in a resolution of 1 s epochs, and implements algorithms for non-wear, sleep detection, posture, and activity intensity (intensity derived from cadence[35–37]). Compared with other device-based classification measures, ActiPASS has demonstrated excellent accuracy across wake time movement behaviours (>90%) and sleep (84%) and has been validated for use across different thigh-worn accelerometer brands.[15,38–41] Five movement behaviours were classified: sleep, SB (sitting or lying episodes outside of sleep intervals), standing, LIPA (ambulatory movement without purposeful walking, walking with cadence <100 steps/min), and MVPA (running, cycling, inclined stepping, walking with cadence ≥100 steps/min).[15,38–42] Participants with at least one valid wear day (≥20 h of wear/day), ≥1 period of walking detection, and >0 min of sleep were included in analyses. Time spent in each behaviour was calculated as average minutes/day.

Cardiometabolic outcomes

Two markers of adiposity were assessed by trained nurses or researchers during home or clinic-based visits: body mass index (BMI, kg/m^2; calculated from height and weight) and *waist circumference* (cm). Cardiometabolic blood biomarkers were measured in five studies (not available in DPhacto) and included: HDL cholesterol (mmol/L), *total:HDL cholesterol ratio*, *triglycerides* (mmol/L), and *glycated haemoglobin* (HbA1c, mmol/mol; measured in ALSWH, BCS70, and TMS only). Measurement and assay methodology were similar across study, with consistently low coefficients of variation. Full details of outcome ascertainment by study, including assay details, are provided in Supplementary data online, *Tables S2* and *S3*.

Covariates

Covariates were selected *a priori* based on data availability and known associations with movement behaviours and cardiovascular outcomes.[22–24] The following covariates were collected in all cohorts: *age* (years), *sex* (male, female), *smoking status* (non-smoker, current smoker), *alcohol consumption* (tertiles based on self-reported weekly consumption), *self-rated health* (five-point Likert scale), *lipid-modifying, hypertensive or glucose-lowering medications* (yes, no), *history of CVD* (yes, no), and fasting blood sample status (fasted, non-fasted; blood biomarker outcomes only). Additionally, a subset of cohorts collected data on *mobility limitations* ($n = 4$ cohorts; continuous score from 0 to 100 of the SF-36 10-item physical function subscale, where 0 indicates poor mobility and 100 indicates no mobility problems), *occupational class* ($n = 5$ cohorts; not working, low, intermediate, high occupational class), and *education* ($n = 4$ cohorts; none or lower than high school, high school qualifications/typically attained at age 16 years, further education qualifications/typically attained at age 16–18 years, university degree, and higher/typically 18+ years). Full details of ascertainment and subsequent

harmonization of covariates in each cohort are provided in Supplementary data online, *Table S2*.

Statistical analyses

We define a composition as the average daily time spent in each of SB, sleep, standing, LIPA, and MVPA behaviours. First, average daily times are normalized such that the sum of all behaviours is equivalent to 1440 min (24 h) to account for any non-wear or unrecognized time. The 24 h time composition is then expressed as a set of four isometric log-ratio (*ilr*) coordinates capturing information and variability of the relative time spent in each of the five behaviours. Briefly, the first coordinate describes the behaviour of interest relative to time spent in the other four behaviours, the second coordinate describes the second behaviour relative to time spent in the other three, the third coordinate describes the third behaviour relative to time spent in the other two, and the fourth and final coordinate describes the fourth behaviour relative to time spent in the fifth. Inclusion of all four coordinates in a single regression model allows the relation between all behaviours to be captured. We pivoted the data to create five sets of coordinates, which allows the investigation of the first coordinate (i.e. a single movement behaviour relative to time spent in all other behaviours).[43] Therefore, we used the following set of *ilr* coordinates to capture time spent in all five behaviours: (i) SB compared with sleep, standing, LIPA, and MVPA; (ii) sleep compared with standing, LIPA, and MVPA; (iii) standing compared with LIPA and MVPA; and (iv) LIPA compared with MVPA. Further detail into this approach is available elsewhere.[21,43]

We conducted a one-stage individual participant meta-analysis using linear regressions to examine associations of each behaviour relative to the others with each outcome, repeating the below models for each set of pivoted coordinates. Coefficients indicate the change in outcome (e.g. kg/m^2 or mmol/L) for each one-unit *ilr* increase. We tested for sex interactions before building models in two stages: (i) adjusted for sex, age, and cohort and (ii) adjusted for sex, age, cohort, smoking, alcohol, self-reported health, medications, CVD history, and fasting status (blood biomarker outcomes only). Due to cohort-specific missing data, sex–age–cohort-adjusted models were examined in both the maximal available sample and those with complete covariate data. Maximal available sample refers to those with data on the movement composition and the outcome, whereas complete cases refer to those with data on the movement composition, outcome, and all covariates. We repeated the models with additional adjustments for education, mobility limitations, and occupational class in cohorts with data on all three additional covariates (ALSWH, BCS70, and TMS). To provide results ready for translation to behavioural interventions, we conducted isotemporal substitution to model how reallocation of time from one behaviour to another—based on the mean 24 h behavioural profile—impacted each outcome[44,45] in sex–age–cohort-adjusted models. Clinically meaningful reductions were defined as a 5% reduction based on the referent BMI for the mean sample composition;[46] minimal significant reductions were defined as a change in outcome using lower 95% confidence interval (CI) limits.

We conducted several additional analyses stratifying by sex (females and males) and by MVPA level (low: <MVPA median; ≥MVPA median). As a sensitivity analysis, we repeated both sex and adjusted models in a subset of individuals with 3 valid days of at least 23+ h/day, including 1 weekend day. Finally, we examined differences in movement behaviours and outcomes between those with complete covariate data and those missing data on one or more covariates. All analyses were performed in RStudio using the *tidyverse*, *compositions*, *robCompositions*, and *zCompositions* packages.

Results

Sample description

Of 15 271 participants with valid accelerometer data on all 5 behaviours, 15 253 (99.9%) had data on at least one outcome. *Table 1* provides descriptive characteristics of the sample for all movement behaviours, outcomes, and covariates. Briefly, 54.7% ($n = 8341$) of the sample were female, with a mean age of 53.7 years ± 9.7 (range: 18–87). The majority of the sample were non-smokers (85.4%), self-rated their health as good or better (87.2%), were not taking lipid-modifying, hypertensive or glucose-lowering medications (70.1%), and had no history of CVD (90.2%). Average daily wear time across the wear period was 22.8 h ± 1.8. The mean composition of the full sample, defined as the average time spent in each behaviour normalized to a 24 h day, was 7.7 h sleeping, 10.4 h sedentary, 3.1 h standing, 1.5 h in LIPA, and 1.3 h in MVPA. Supplementary data online, *Figure S1A* demonstrates absolute differences in time spent in each movement behaviour by cohort, while Supplementary data online, *Figure S1B* provides percent differences compared with the overall mean sample composition. Inter-cohort differences were largest for standing, LIPA, and MVPA, with comparable time spent in sleeping and SB. The maximal available sample in sex–age–cohort-adjusted models ranged from 11 270 (triglycerides; $n =$ 9450 complete cases) to 15 204 (BMI; $n = 12\,166$ complete cases).

Association between movement behaviours and adiposity

A greater proportion of time spent sedentary was associated with higher BMI (see Supplementary data online, *Table S4*); conversely—and in order of size of association—more time engaging in MVPA, LIPA, standing, or sleep was associated with lower BMI. Associations were robust to adjustment for all covariates (Models 2 and 3, Supplementary data online, *Tables S4* and *S5*). Reallocation of time from any behaviour into MVPA, while holding the others constant, had the largest theoretical reduction in BMI (*Figure 1*). For example, reallocating 30 min of SB, sleep, standing, or LIPA into MVPA was associated with −0.63 (95% CI: −0.48, −0.79), −0.43 (95% CI: −0.25, −0.59), −0.40 (95% CI: −0.25, −0.56), or −0.15 (95% CI: 0.05, −0.34) kg/m^2 lower BMI, respectively. Conversely, reallocating time from LIPA or MVPA into sleep, standing, or SB was associated with higher BMI (*Figure 1A* and *B*). The minimal daily behavioural change required to observe significant theoretical reductions in BMI was displacement of 7.2 min of SB into MVPA.

Associations were similar for waist circumference across MVPA, standing, sleep, and SB (*Figure 2*). Reallocating 30 min of SB, sleep, or standing into MVPA was associated with lower waist circumferences of −2.44 (95% CI: −1.97, −2.78), 1.75 (95% CI: −1.38, −2.22), and −1.34 (95% CI: −0.98, −1.78) cm, respectively. Although displacement of LIPA into MVPA remained favourable for waist circumference [30 min: −2.49 (−1.95, −2.94) cm], there was a negative association with waist circumference if time spent in LIPA replaced time spent sleeping or standing (*Figure 2D*). However, associations were attenuated after adjustment for covariates (Models 2 and 3, Supplementary data online, *Tables S4* and *S5*). The minimal behavioural change required to observe statistically significant theoretical reductions in waist circumference was displacement of 5.0 min/day of LIPA into MVPA. A 5% reduction in BMI (−1.33 kg/m^2) would be yielded if 64.8 (95% CI: 52.8, 76.8) minutes or 1.78 (95% CI: 1.37, 2.38) hours of SB were reallocated into MVPA or LIPA, respectively.

Association between movement behaviours and lipids

A smaller proportion of time in SB and a greater proportion in MVPA was associated with higher HDL cholesterol, lower total:HDL cholesterol ratio, and lower triglyceride levels (see Supplementary data online, *Table S3*; *Figures 3*–*5A*–*E*). For example, reallocation models suggested that improvements were observed after as few as 6.0, 8.9, and

Table 1 Descriptive characteristics in maximal available sample ($n = 15\,253$)

Outcomes, mean ± SD	Full sample ($n = 15\,253$)	Females ($n = 8341$; 54.7%)	Males ($n = 6912$; 45.3%)
BMI (kg/m^2)	27.0 ± 4.9	26.7 ± 5.4	27.4 ± 4.3
Waist circumference (cm)	94.1 ± 13.9	89.2 ± 13.2	100.2 ± 12.1
HDL cholesterol (mmol/L)	1.57 ± 0.46	1.7 ± 0.5	1.4 ± 0.4
HDL: total cholesterol ratio	3.64 ± 1.23	3.3 ± 1.0	4.0 ± 1.3
HbA1c (mmol/mol)	38.0 ± 8.7	36.7 ± 7.3	39.4 ± 9.8
Triglycerides (mmol/L)	1.48 ± 1.04	1.3 ± 0.8	1.7 ± 1.2
Movement behaviour composition[a] (h/day; % of day)			
Sleep	7.7 (31.9%)	7.9 (32.8%)	7.4 (30.9%)
Sedentary behaviour	10.4 (43.2%)	9.9 (42.3%)	10.9 (45.4%)
Standing	3.1 (13.0%)	3.3 (13.9%)	2.9 (11.9%)
LIPA	1.5 (6.4%)	1.5 (6.3%)	1.6 (6.5%)
MVPA	1.3 (5.5%)	1.4 (5.7%)	1.3 (5.3%)
Main analyses covariates [mean ± SD or *n* (%)]			
Age (years)	53.7 ± 9.7	52.7 ± 9.1	55.1 ± 10.2
Cohort			
TMS	7515 (49.3)	3790 (45.4)	3725 (53.9)
BCS70	5236 (34.3)	2797 (33.5)	2439 (35.3)
ALSWH	941 (6.1)	941 (11.3)	0 (0)
DPhacto	777 (5.1)	359 (4.3)	412 (6.0)
NES	537 (3.5)	244 (2.9)	293 (4.2)
FIREA	253 (1.7)	210 (2.5)	43 (0.6)
Smoking status			
Non-smoker	12 953 (85.4)	7205 (86.8)	5748 (83.7)
Current smoker	2211 (14.6)	1093 (13.2)	1118 (16.3)
Alcohol consumption			
Tertile 1 (low)	4463 (33.8)	3058 (42.6)	1405 (23.3)
Tertile 2	4514 (34.2)	2529 (35.2)	1985 (32.9)
Tertile 3 (high)	4231 (32.0)	1591 (22.2)	2640 (43.8)
Self-reported health[b]			
Excellent	1849 (12.3)	1102 (13.4)	747 (11.0)
Very good	4905 (32.7)	2701 (32.9)	2204 (32.4)
Good	6329 (42.2)	3337 (40.6)	2992 (44.1)
Fair	1634 (10.9)	908 (11.1)	726 (10.7)
Poor	287 (1.9)	164 (2.0)	123 (1.8)
Medication (lipid-modifying, hypertensive, or glucose-lowering)	4333 (29.9)	1859 23.3)	2474 (38.1)
History of CVD	1486 (9.8)	615 7.4)	871 (12.7)

Continued

Table 1 *Continued*

Outcomes, mean ± SD	Full sample ($n = 15\,253$)	Females ($n = 8341$; 54.7%)	Males ($n = 6912$; 45.3%)
Supplementary analyses covariates[c] [mean ± SD or *n* (%)]			
Physical function (SF-36)	87.2 ± 18.8	86.5 ± 18.9	88.0 ± 18.6
Occupational class			
Not working	3850 (29.3)	2014 (28.1)	1836 (30.6)
Low	2152 (16.4)	1023 (14.3)	1129 (18.8)
Intermediate	3645 (27.7)	1927 (26.9)	1718 (28.7)
High	3502 (26.6)	2192 (30.6)	1310 (21.9)
Education			
None or less than high school	1666 (11.9)	764 (9.9)	902 (14.2)
High school (~16 years)	3908 (27.8)	2209 (28.7)	1699 (26.7)
Further education (~16–18 years)	5399 (38.4)	2955 (38.4)	2444 (38.4)
University degree or higher	3080 (21.9)	1760 (22.9)	1320 (20.7)

ALSWH, Australian Longitudinal Study of Women's Health; BMI, body mass index; BCS70, 1970 British Cohort Study; CVD, cardiovascular disease; DPhacto, Danish PHysical ACTivity cohort with Objective measurements; FIREA, Finnish Retirement and Aging Study; HDL, high density lipoprotein; LIPA, light-intensity physical activity; MVPA, moderate-vigorous intensity physical activity; NES, Nijmegen Exercise Study; SD, standard deviation; SF-36, Short-Form 36; TMS, The Maastricht Study.
[a]Re-scaled to a 24 h day to create the composition.
[b]Response terminology differs slightly by cohort, given translation of original question (see Supplementary data online, *Table S1*).
[c]Covariates available in restricted cohorts only (see Supplementary data online, *Table S1*).

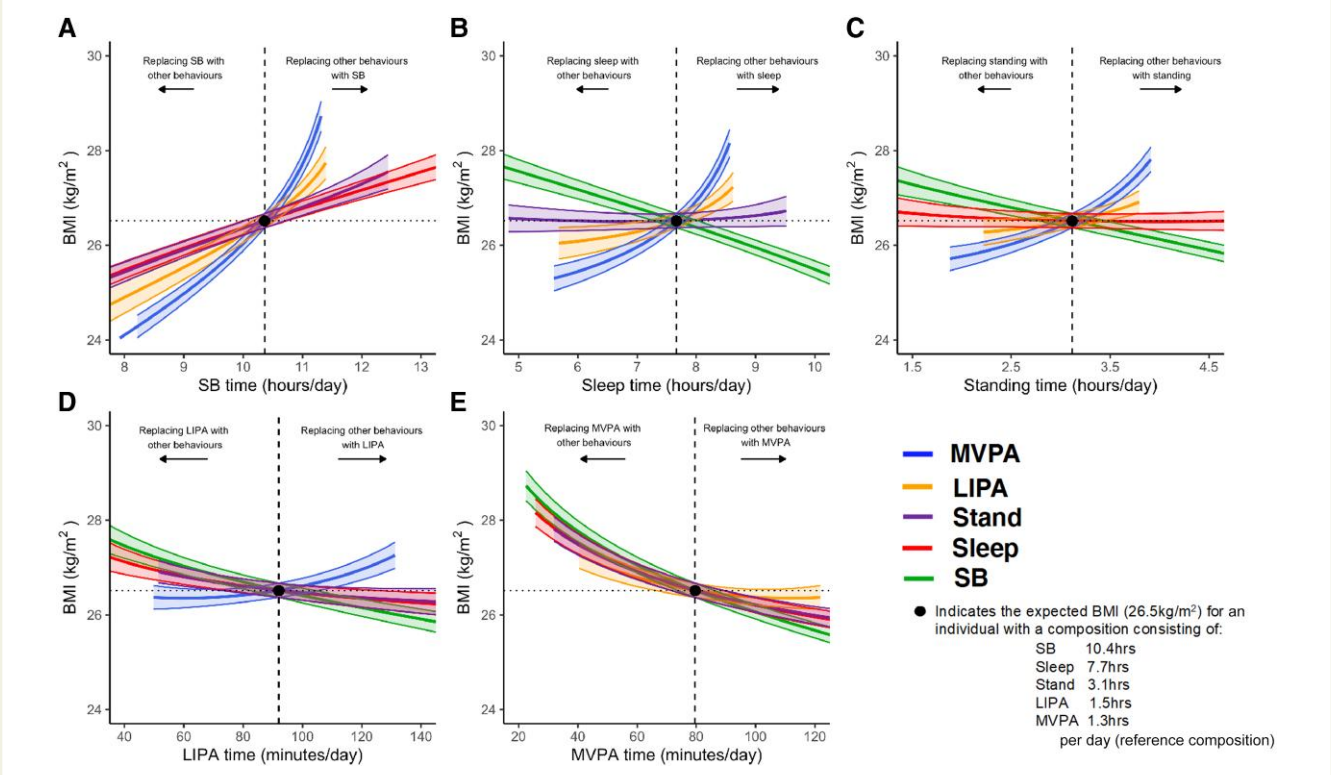


Figure 1 Substitution models ($n = 15\,204$) for body mass index for (*A*) sedentary behaviour; (*B*) sleep; (*C*) standing; (*D*) light intensity physical activity; (*E*) moderate-to-vigorous intensity physical activity. Data to the left of the reference line indicate the predicted change in body mass index if a given behaviour (e.g. sedentary behaviour in *A*) is replaced by each of the other four behaviours. Data to the right of the reference line indicate the predicted change in body mass index if a given behaviour (e.g. sedentary behaviour in *A*) replaces each of the other four behaviours. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

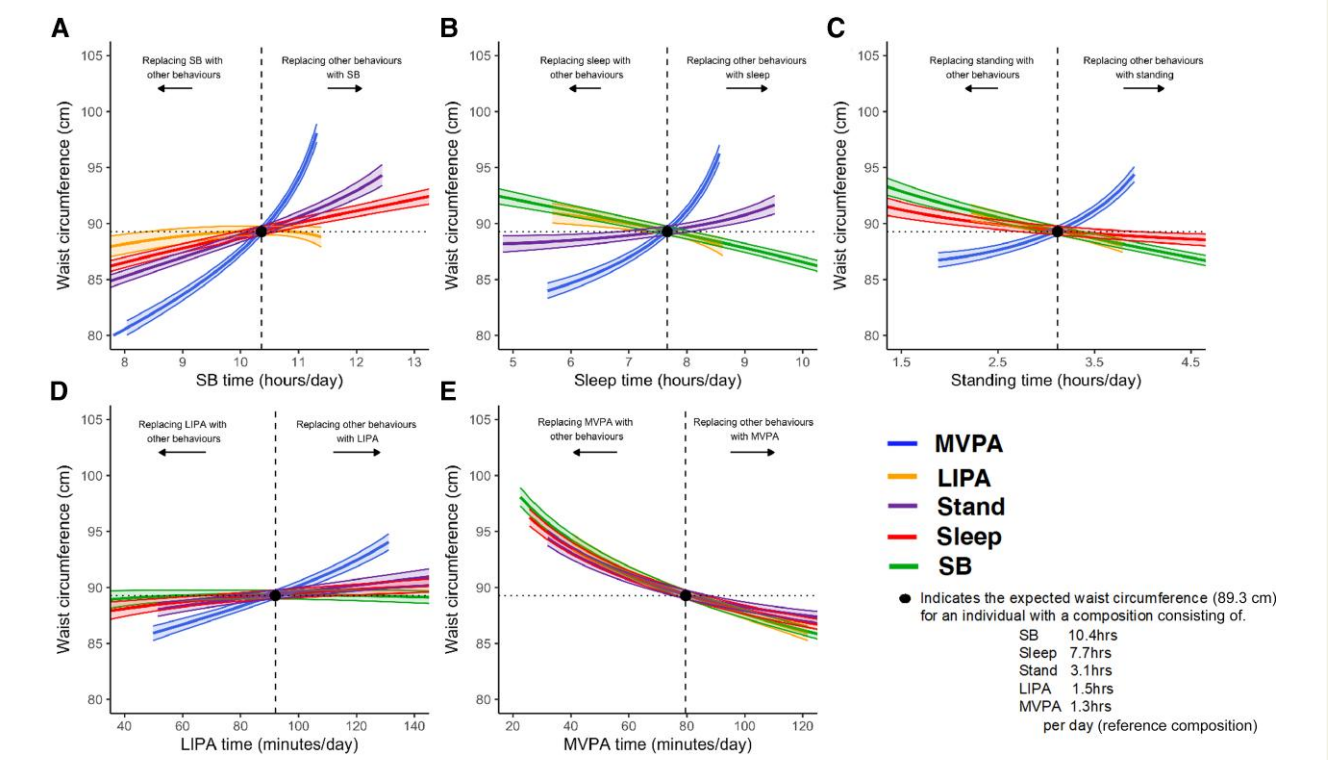


Figure 2 Substitution models ($n = 14\,541$) for *waist circumference* outcome for (*A*) sedentary behaviour; (*B*) sleep; (*C*) standing; (*D*) light intensity physical activity; (*E*) moderate to vigorous intensity physical activity. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

12.7 min of SB were replaced by MVPA (*Figures 3–5E*), respectively. Associations remained after adjustment for covariates (Models 2 and 3, Supplementary data online, *Tables S3* and *S4*).

Beyond the beneficial impact of reallocating time from LIPA to MVPA, there was little evidence that LIPA displacement was associated with HDL or total:HDL cholesterol ratio (*Figures 3–5D*; Supplementary data online, *Tables S3* and *S4*). Conversely, positive associations between a greater proportion of time spent standing and favourable lipid outcomes remained across all outcomes and models. Standing was detrimental when displacing MVPA time but advantageous when replacing 1+ hour sleep or 1.75+ hour of SB (*Figures 3–5C*). Reallocating time between LIPA and standing—in either direction—was negligible for HDL and total:HDL cholesterol ratio, while theoretical reductions in triglycerides level were observed after 39 min of LIPA was displaced into standing.

Finally, more time spent sleeping relative to other behaviours was associated with poorer lipid outcomes; however, this differed by displaced behaviour (*Figures 3–5B*). When sleep displaced MVPA or standing time (*Figures 4–6B*), there were deleterious associations with all outcomes. For example, replacing 30 min of MVPA with sleep was associated with a −0.10 mmol/L (−0.08, −0.12), +0.17 (0.12, 0.21), and +0.13 mmol/L (0.08, 0.17) difference in HDL, total:HDL cholesterol ratio, and triglycerides. Reallocation between sleep, SB, and LIPA was negligible, with a meaningful change in HDL only emerging after ∼1.5 h of displacement from SB to sleep (*Figure 3B*).

Association between movement behaviours and HbA1c

A greater proportion of time spent in MVPA, standing, or sleeping and a smaller proportion of time spent in SB were associated with lower HbA1c. Associations remained after adjustment for covariates (see Supplementary data online, *Tables S3* and *S4*). Relative to other time reallocations, displacement of any other behaviour into MVPA was associated with the most favourable estimates for HbA1c levels (*Figure 6*). When MVPA replaced 30 min spent in SB, sleep, standing, or LIPA, we observed lower HbA1c of 1.33 (1.06, 1.61), 1.12 (0.80, 1.40), 1.04 (0.72, 1.36), and 2.00 (1.63, 2.37) mmol/mol, respectively (*Figure 6E*).

Light-intensity physical activity was the most deleterious behaviour for HbA1c; e.g. a 30 min displacement of MVPA, standing, sleep, or SB into LIPA was associated with 2.33 (1.89, 2.77), 0.70 (0.31, 1.11), 0.63 (0.29, 1.00), and 0.42 (0.11, 0.78) mmol/mol higher HbA1c, respectively (*Figure 6D*). Note these displacement changes were observed in the age–sex–cohort models, but associations were attenuated after adjustment for covariates, most notably with the addition of physical limitations (Models 2and 3, Supplementary data online, *Tables S3* and *S4*). While more time in SB was associated with higher HbA1c levels, with no impact of displacement between standing and sleeping (*Figure 6A–C*). The minimal daily behavioural change needed to observe a significant change in HbA1c was 3.8 min of MVPA displacing LIPA. A summary of all behavioural displacements across each outcome is provided in Supplementary data online, *Table S6*.

Sex-stratified analyses

Males spent more time sedentary (10.2 ± 1.9 vs. 9.3 ± 1.8 h/day), less time sleeping (6.9 ± 1.5 vs. 7.4 ± 1.3 h/day), and less time engaging in LIPA (4.5 ± 1.4 vs. 4.9 ± 1.5) and MVPA (1.2 ± 0.5 vs. 1.3 ± 0.5 h/day) than females (*Table 1*). Given poorer risk factors in males (i.e. lower HDL and higher BMI, waist circumference, HDL:total cholesterol ratio, HbA1c, and triglycerides) and greater time spent in unhealthy

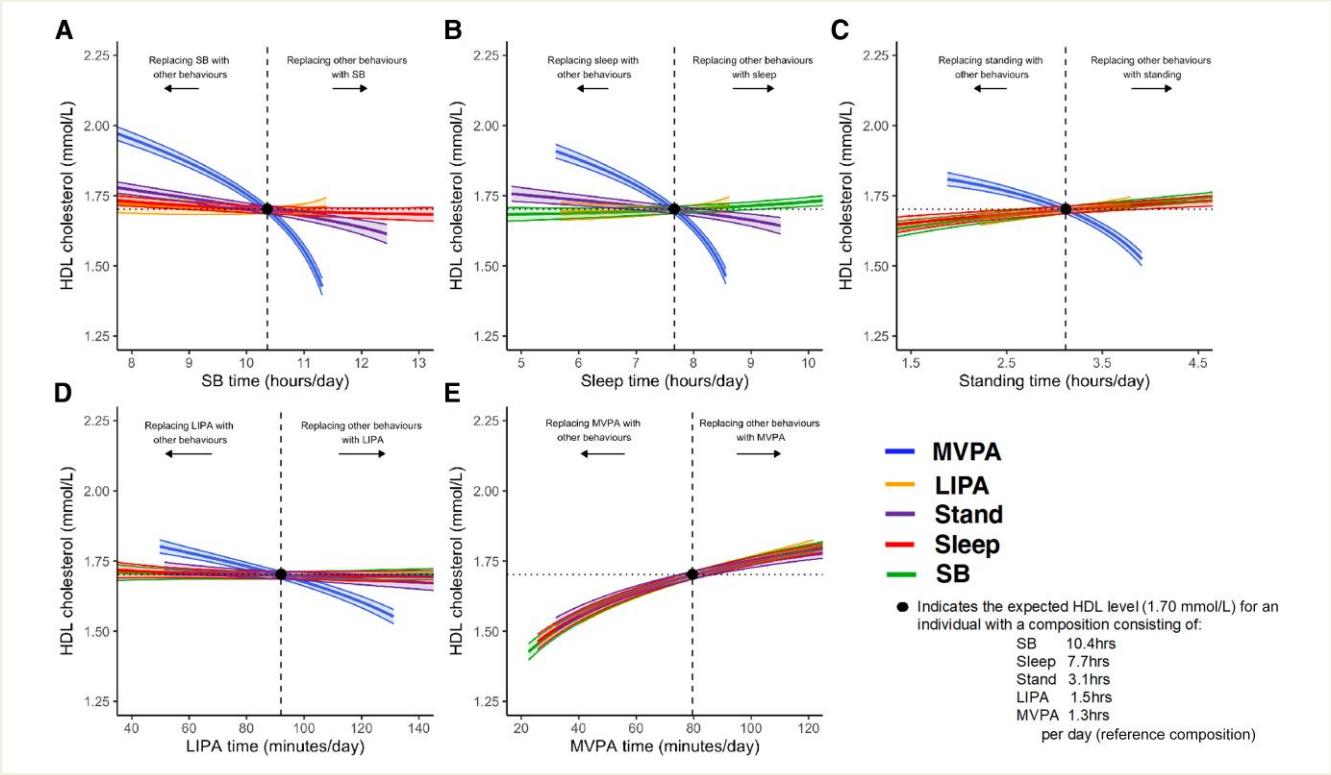


Figure 3 Substitution models ($n = 13\,060$) for *HDL cholesterol* outcome for (*A*) sedentary behaviour; (*B*) sleep; (*C*) standing; (*D*) light intensity physical activity; (*E*) moderate to vigorous intensity physical activity. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

movement behaviours as well as potential sex differences in physiological responses to exercise,[47] we subsequently stratified by sex. Associations did not change, although there were larger associations between the movement compositions and outcomes in females (see Supplementary data online, *Table S7* and *Figures S2 and S3*). For example, associations between more time spent in LIPA or standing relative to other behaviours were attenuated for some outcomes in males, whereas reallocation models indicated steeper associations in females.

Moderate-vigorous physical activity–stratified analyses

Similarly, associations largely did not change when stratified by MVPA (low MVPA: <76.2 min/day; high MVPA: ≥76.2 min/day; see Supplementary data online, *Table S8* and *Figures S4 and S5*), although associations between time spent in sleeping—relative to other behaviours—and poorer lipid outcomes weakened in stratified groups (see Supplementary data online, *Table S8*). Reallocation models indicated steeper associations in those with low MVPA, compared with those with high MVPA (see Supplementary data online, *Figures S4 and S5*). For example, in those with low MVPA, a 5% reduction in BMI (−1.38 kg/m^2) would be yielded if 1.22 (95% CI: 0.93, 1.64) or 1.29 (95% CI: 0.97, 1.67) hours of SB were reallocated into MVPA and LIPA, respectively. Conversely in those with high MVPA, a 5% reduction in BMI (−1.28 kg/m^2) was outside of the modelled reallocation range for SB, MVPA, and LIPA (e.g. >1.5 h).

Sensitivity analyses

When analyses were repeated in a subset of individuals with greater adherence to wear protocol (i.e. ≥3 valid wear days including ≥1 weekend day; maximal sample size ranging from $n = 10\,998$ for triglycerides to $n = 14\,668$ for BMI), results did not change (see Supplementary data online, *Table S9*). Compared with the complete cases sample (up to $n = 12\,193$), those missing one or more covariate ($n = 3047$) had lower HDL cholesterol (1.48 ± 0.42 vs. 1.57 ± 0.47 mmol/L), lower HDL:total cholesterol ratio (3.61 ± 1.22 vs. 3.79 ± 1.28), higher triglycerides (1.53 ± 1.12 vs. 1.47 ± 1.02 mmol/L), and higher HbA1c (38.6 ± 9.8 vs. 37.9 ± 8.6 mmol/mol) levels. However, adiposity measures were comparable, and there was no different in movement behaviour compositions (see Supplementary data online, *Table S10*).

Discussion

In this large individual participant data analysis of over 15 000 participants, we examined cross-sectional associations between device-measured 24 h movement behaviours and cardiometabolic health outcomes. Our findings revealed a clear hierarchy of favourable movement behaviours across the 24 h day; MVPA was most strongly associated with healthier cardiometabolic outcomes. Using the mean 24 h behavioural composition as a starting point (7.7 h sleeping, 10.4 h SB, 3.1 h standing, 1.5 h LIPA, and 1.3 h MVPA), we observed theoretical benefits across all outcomes when as little as 4–12 min/day were reallocated into MVPA. Conversely, a greater proportion of time spent sedentary

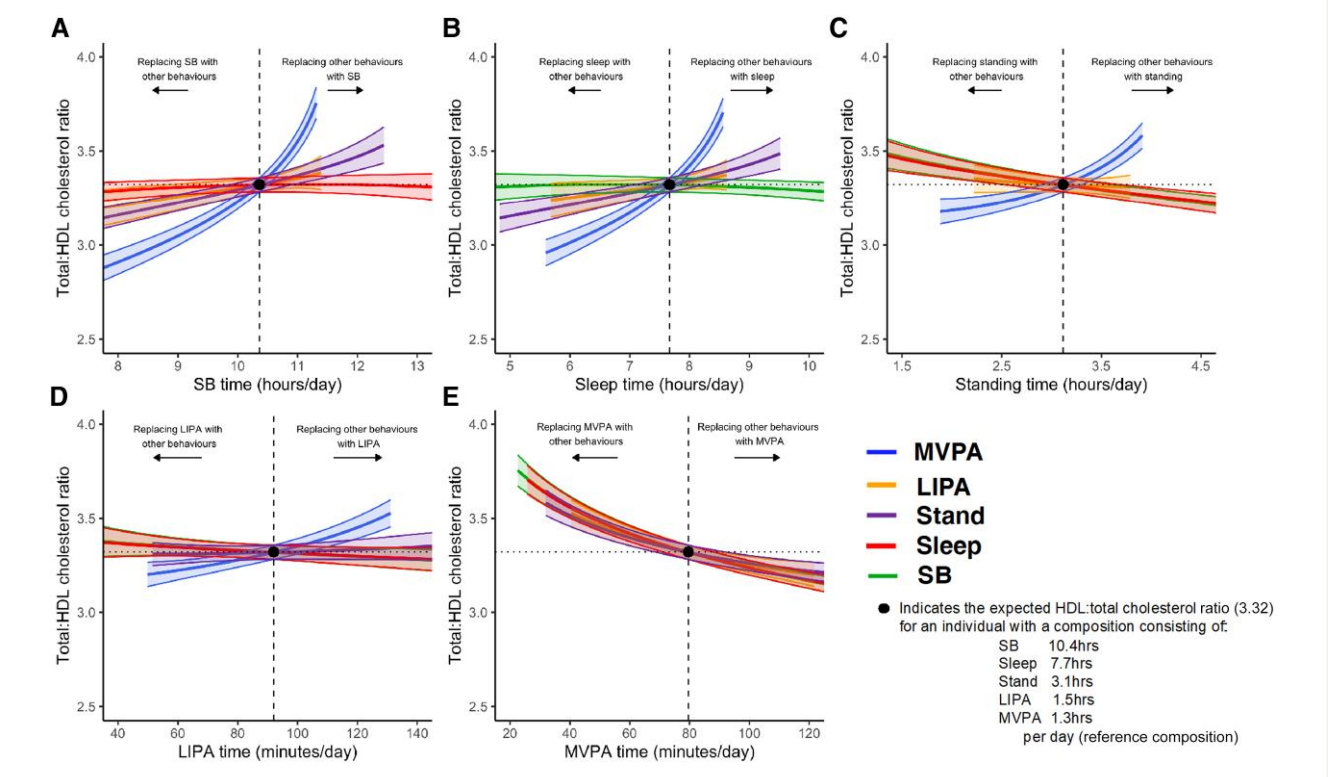


Figure 4 Substitution models ($n = 13\,059$) for *total:HDL cholesterol ratio* outcome for (*A*) sedentary behaviour; (*B*) sleep; (*C*) standing; (*D*) light intensity physical activity; (*E*) moderate to vigorous intensity physical activity. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

was detrimentally associated with all outcomes (*Structured Graphical Abstract*). More time spent in standing was favourably associated with outcomes, although there were inconsistent—and often null—associations for LIPA. Associations between sleep and biomarkers were complex, with an unfavourable association when sleep replaced any time spent active (MVPA, LIPA, and standing) and modest theoretical benefits when it replaced SB.

Hypothesized mechanisms

The inflammatory, metabolic, or vascular mechanisms through which MVPA contributes to improved cardiovascular health are well established.[11,12] Our findings further suggest that even small changes in MVPA are associated with statistically significant and clinically meaningful cardiometabolic benefits. This builds on recent evidence reporting that small amounts of daily vigorous physical activity (accumulated in <2 min bouts) are associated with lower mortality, cancer, and CVD risk.[48,49] The acute benefits of standing on postprandial glucose response may partially explain the small but significant associations observed above.[50,51] High muscle contractions involved in extended standing periods may also influence lipoprotein lipase activity, a key enzyme in glucose and lipid metabolism, and contribute to decreased inflammatory pathways.[50,51] There were some positive associations of displacing SB or sleep into LIPA for BMI, but we largely observed null associations when examining other cardiometabolic biomarkers, which has been observed in other studies of device-measured LIPA and incident CVD.[52–54]

Given the inclusion of fast walking in MVPA, there may have been some higher level LIPA classified as MVPA. In additional, higher levels of MVPA within the study sample is likely to be due to the inclusion short bursts of daily activity (e.g. taking the stairs, running for the bus) that is not typically captured in questionnaire-based physical activity assessment and may also be due to the younger and narrower age range as well as the overall health status of the cohort. Finally, there may be a ceiling effect of physical activity driven by high levels of MVPA in our active and healthy sample; specifically, if an individual with high levels of MVPA is engaging in additional LIPA above and beyond this, there may be little association with subsequent risk factors.

Mechanisms underlying association between insufficient sleep or too much SB and poor cardiometabolic health often focus on indirect factors that lead to weight gain or decreased energy expenditure.[55] However, chronic sleep deprivation has also been linked to the modification of gene expression and lipoproteins involved in inflammatory and cholesterol pathways.[56,57] Our findings suggest that any theoretical cardiometabolic benefits from increased sleep—beyond the reference composition of 7.7 h—are secondary to the direct physiological benefits of physical activity. However, it is unclear how the effects of displacing sleep and physical activity would differ in individuals with high levels of sleep deprivation. We hypothesize that individuals with insufficient sleep (i.e. <6 h) may benefit from prioritizing sleep over physical activity; the need for a more personalized approach to 24 h behaviour is further discussed below.

Comparison to existing evidence

Our study provides novel insights by distinguishing standing from ambulatory LIPA and identifying the minimal theoretical displacements between behaviours required to observe statistical associations with

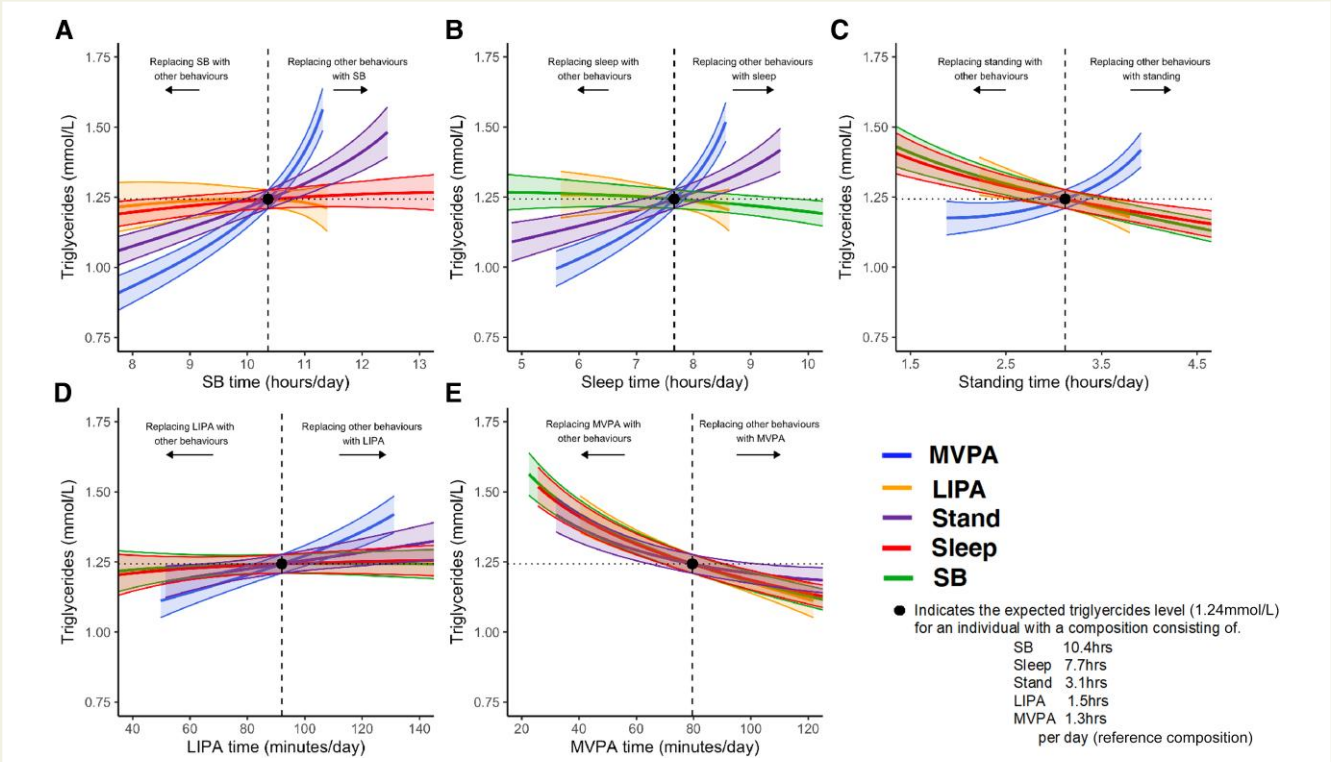


Figure 5 Substitution models ($n = 12\,240$) for *triglycerides* outcome for (*A*) sedentary behaviour; (*B*) sleep; (*C*) standing; (*D*) light intensity physical activity; (*E*) moderate to vigorous intensity physical activity. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

cardiometabolic health outcomes. To our knowledge, this is the first study to suggest that more time spent in standing may be more beneficial than LIPA for cardiometabolic outcomes. This must be interpreted with caution, given the likely inclusion of moderate fast-paced walking in MVPA rather than LIPA and the lack of context on the active or passive nature of the standing behaviour (e.g. stationary resistance training, standing desk, waiting for a bus). Further research must investigate how context and the cognitive and musculoskeletal demands of standing and LIPA activities impact cardiometabolic health. Previous compositional studies have identified the benefits of MVPA and the detrimental consequences of SB for various health outcomes[22–24]; however, these studies reported inconsistent evidence regarding the role of sleep or LIPA activity on cardiometabolic outcomes, which may have been due to inadequate ascertainment of sleep using self-reported data.[22]

Implications

Our findings have substantial implications from both research and clinical perspectives. First, they underscore the importance of MVPA across different adiposity and cardiometabolic biomarker outcomes. Our modelled reallocation suggests that population-level benefits can theoretically be observed after relatively short displacements of time (e.g. replacing other behaviour with 4–12 min of MVPA). However, it is crucial to examine if these effect sizes can be replicated in longitudinal observational or interventional studies that use posture-based accelerometer data. Recently, there have been increased public recommendations on the 'sit less, move more' approach that highlights benefits of any level of physical activity, including LIPA, for reduced mortality risk and improved cardiovascular health.[58–60] However, given more subtle cardiovascular adaptations resulting from LIPA compared with MVPA,[61] the benefits of lighter activities may be more meaningful for mental health or musculoskeletal outcomes[62,63] rather than cardiometabolic outcomes. The findings here reaffirm the importance of the intensity of the activity that is replacing SB; our models suggest that replacing 30 min of SB with MVPA rather than LIPA result in substantially better cardiometabolic outcomes. It was notable that replacing SB with standing had positive associations across all outcomes, a finding that highlights potential intervention opportunities aimed at minimizing sitting or targeting groups who have challenges engaging in MVPA (i.e. those in poorer health, those with few occupational opportunities). Nevertheless, it is crucial finding a balance between increasing time spent in higher intensity activities and decreasing time spent sedentary. For example, data from the National Health and Nutrition Examinations Survey suggest comparable mortality risk between meeting US physical activity guidelines or by an additional 2.5 min of MVPA to 'offset' every 1 h of SB.[23] Therefore, optimal cardiometabolic outcomes can be achieved most efficiently if MVPA is specifically targeted.

Findings must be interpreted at the population level as the starting point for all reallocation plots is the mean sample composition, which has relatively high levels of sleep (7.7 h/day), standing (3.1 h/day), and MVPA (1.3 h/day). Displacement into and away from MVPA did not demonstrate symmetrical associations with outcomes (*Figures 1–6*), and as introduced above, outcomes resulting from behavioural changes are likely to diverge depending on the initial starting profile. For example, previous investigation of dose-response associations between

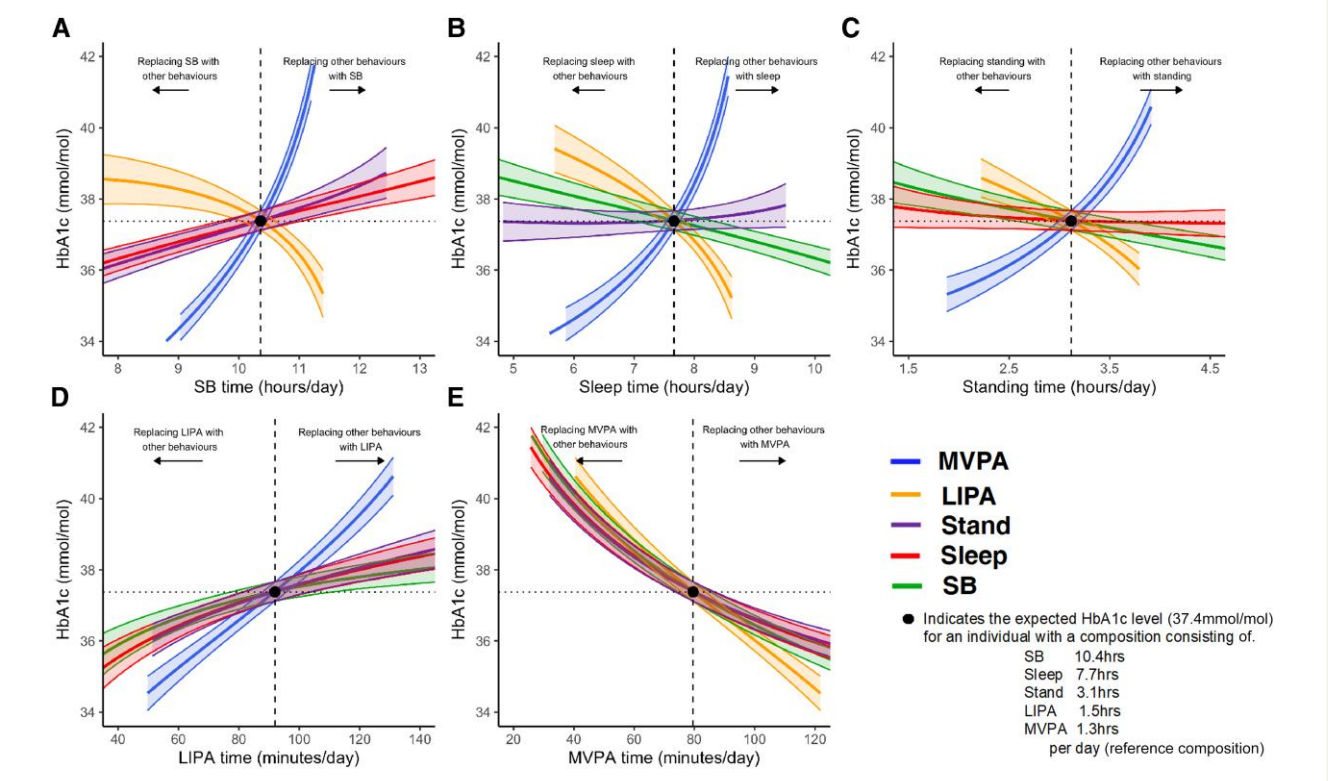


Figure 6 Substitution models ($n = 11\,270$) for *HbA1c* outcome for (*A*) sedentary behaviour; (*B*) sleep; (*C*) light intensity physical activity; (*D*) moderate to vigorous intensity physical activity. Model adjusted for sex (ref: female), age (ref: 53.7 years; mean-centred), and cohort (ref: Maastricht Study)

MVPA and cardiovascular outcomes has demonstrated steep risk reductions at low levels of MVPA, with benefits plateauing at higher MVPA volumes.[49,60,64] This was consistent with MVPA-stratified results, where reallocation plots indicated greater theoretical benefits in those with lower levels of MVPA at baseline. This highlights an increasing need to identify personalized recommendations—or the 'sweet spot'[65]—based on an individual's current 24 h movement behaviours.

Modelling displacement of time between five key daily behaviours can inform design of more realistic lifestyle-based interventions and enable personalized behavioural changes. For example, interventions focusing on displacement between sleep, SB, standing, and LIPA would likely require >1 h of daily behavioural change to impact desired outcomes. This may have limited real-world plausibility compared with the potential impacts of displacing an additional ~5 min in any other behaviour into MVPA. Notably, there are promising occupation-based interventions demonstrating the feasibility of reducing SB at this magnitude (e.g. standing desks or encourage active commuting via cycle to work schemes),[66–68] yet interventions targeting non-working aged individuals or those in non-desk based roles have demonstrated much smaller effects on overall sedentary time.[66,67]

Strengths and limitations

Strengths of this study include the inclusion of 15 000+ participants from six cohorts and five countries to increase generalizability of our findings; the use of a thigh-mounted accelerometer wear position to sensitively capture postural changes; uniform ActiPASS processing of raw accelerometer data files; separation of standing from ambulatory LIPA; ascertainment of blood-based cardiometabolic biomarkers; and the complex compositional data analysis approach that simultaneously considered how time spent in different movement behaviours influences cardiometabolic outcomes.

There are some limitations that must be acknowledged. First, the data are cross-sectional, and therefore causality between movement behaviours and outcomes cannot be inferred. Recent mendelian randomization of device-measured activity in UK Biobank suggests causal associations between MVPA and adiposity, with bidirectional associations between SB and adiposity.[69] It is clear that there are complex bidirectional and dynamic associations between movement behaviours and cardiometabolic outcomes; therefore, longitudinal follow-up data (preferably with repeat measures) is crucial to further investigate these associations. Despite clear advances in the ActiPASS-based detection of activity intensity and SB, sleep time may have been overestimated as time spent in bed rather than biological sleep; nevertheless, previous work has suggested strong agreement between our sleep algorithm and polysomnography.[41] Moderate-vigorous physical activity levels were very high in this cohort. This may be due to both specific cohort characteristics (e.g. high exercise sample in NES, manual occupation in DPhacto, etc.) or high levels of moderate activity classified as MVPA.

Overall characteristics of the sample and the relatively high levels of MVPA indicate that this is a healthy sample. Furthermore, previous evidence suggests that individuals without valid accelerometer data may have poorer health, lower socio-economic position, and lower physical activity levels than those who wore the device.[70] However, previous evidence has suggested that poor sample representativeness does not necessarily impact the estimates of physical activity with cardiovascular outcomes.[71] The MVPA-stratified results suggests we may have

underestimated the benefits of reallocation of behaviour, which appear to be greater at lower levels of MVPA. There may be some residual confounding; due to differences in measurement protocols between studies, some harmonized covariates had lower granularity than the original data collected (e.g. smoking, alcohol, medication use), whilst there were some differences in measurement and analysis of outcomes (see Supplementary data online, *Table S3*). Nevertheless, methodologies were extremely similar, which allowed the data to be pooled across six cohorts and >15 000 participants. We selected established covariates with known associations with movement behaviours and cardiovascular outcomes;[22–24] however, we recognize that there remains some potential for overadjustment; therefore, adjusted estimates may underreport true effect sizes. To avoid overadjustment, we did not adjust the blood biomarker models for adiposity measures, given that adiposity is likely to be on the causal pathway.[72]

Conclusions

This study provides novel evidence of the hierarchy of movement behaviours and their impact on cardiometabolic health markers. Findings emphasize a key public health message that positive cardiometabolic health outcomes can be most efficiently and feasibly achieved with small increases in MVPA. Standing—and for some outcomes LIPA—had positive associations with outcomes, although this was only observed after displacement of substantial amounts of time. Sedentary behaviour was the sole behaviour with clear adverse associations with outcomes, regardless of duration. Compositional data analysis sheds novel insights on the complex interplay of 24 h behaviours for cardiometabolic health outcomes. Taken together, our results suggest that prioritizing a balance of more time in MVPA and less time in SB is the most efficient and effective way to improve and/or maintain good cardiometabolic health.

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The data on which this research is based were drawn from six observational studies in the Netherlands, UK, Australia, Denmark, and Finland. We are grateful to all participants who provided the survey data.

Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

Data Availability

Access to data is not available directly from the authors of this manuscript. Access to cohort data may be available by contacting individual cohort and following their specific governance and access requirements.

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Ethical Approval

Ethical approval was provided by each individual study during data collection and permitted use of data for secondary analysis (e.g. consortium).

Pre-registered Clinical Trial Number

Not applicable.

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