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Abstract

Purpose: To investigate whether prospectively reallocating time away from sedentary behaviour into different physical activity intensities is associated with 12-month change to cardiometabolic health in a cohort at high risk of type 2 diabetes (T2DM). **Methods:** Participants with known risk factors for T2DM were recruited from primary care (Leicestershire, UK) as part of the Walking Away from Type 2 Diabetes trial (n=808). Participants were followed-up at 12, 24 and 36 months. Sedentary behaviour (SB), light-intensity physical activity (LPA) and moderate-to-vigorous intensity physical activity (MVPA) were measured objectively by accelerometer. Post-challenge glucose, triglycerides, HDL-cholesterol, systolic blood pressure and waist circumference were analysed individually and combined into a clustered cardiometabolic risk score (CMRS). Associations of changing SB over each consecutive 12-month period were analysed taking account of repeated measures. **Results:** Reallocating 30 minutes from SB to LPA was associated with 0.21 (95% CI 0.03, 0.38) cm reduction in waist circumference, 0.09 (0.04, 0.13) mmol/l reduction in 2-h glucose, 0.02 (0.00, 0.04) mmol/l reduction in triglycerides and 0.02 (0.01, 0.03) reduction in CMRS. Every 30 minutes reallocation from SB to MVPA was associated with 1.23 (0.68, 1.79) cm reduction in waist circumference, 0.23 (0.10, 0.36) mmol/l reduction in 2-h glucose, 0.04 (0.00, 0.009) reduction in triglycerides and 0.07 (0.04, 0.11) reduction in CMRS. Reallocating 30 minutes from LPA into MVPA was also associated with 1.02 (0.43, 1.60) cm reduction in waist circumference, 0.16 (0.02, 0.30) mmol/l reduction in 2-h glucose and 0.05 (0.01, 0.09) reduction in CMRS. **Conclusion:** Over 12 months, reallocating time away from SB into LPA or MVPA was associated with improved cardiometabolic health in a population at risk of T2DM, with the greatest benefits observed for MVPA.

Keywords: Sedentary behaviour; physical activity; isotemporal substitution; cardiometabolic; type 2 diabetes; high risk; accelerometer

Introduction

Over recent years, sedentary behaviour (SB), defined as any sitting, reclining or lying time less than 1.5 METS during waking hours (1), has emerged as an important determinant of chronic disease and all-cause mortality (2), with consistent associations also reported for markers of cardiometabolic health (3). However, whether associations between SB and health are independent of physical activity volume or intensity continues to be debated (4). Such debates are somewhat artificial as by definition these behaviours are co-dependant. During waking hours it is not possible to alter sedentary time without also altering time spent in light-intensity physical activity (LPA) or moderate-to-vigorous physical activity (MVPA).

Isotemporal substitution has been proposed as a statistical approach for dealing with this co-dependence as it models the reallocation from one behaviour to another within a finite boundary such as waking hours (5). As humans in industrialised societies spend the majority of their waking hours sedentary (6), isotemporal substitution has been used to investigate the associations of reallocating time away from this dominant behaviour into others. These studies have provided mounting evidence showing beneficial associations of reallocating sedentary time into light-intensity as well as more intensive forms of physical activity (7-12). However, studies to date have used a single measure of physical activity and sedentary behaviour to model cross-sectional associations with markers of health or a future risk of mortality (7-10), rather than using prospective data where behavioural reallocation has actually occurred. The lack of prospective data has been noted as a limitation in a recent review of the current evidence (13), with data also lacking in older adults or those with a high risk of chronic disease. Whilst some

studies are starting to apply isotemporal or compositional techniques to prospective data, they have predominately focused on occupational interventions (14, 15). Therefore, prospective data is needed from other settings and in populations reflecting those most likely to be referred into preventative lifestyle interventions.

This study investigates the relative importance of reallocating objectively measured SB into LPA or MVPA on associations with changes to metabolic health, using repeated prospective data over a 12 month period. We hypothesise that reallocating time from SB into both LPA and MVPA is associated with improved cardiometabolic health.

Methods

Study population

This study reports prospective observational data from the randomised Walking Away from Type 2 Diabetes trial, the methods of which have been published elsewhere (16, 17). Participants were randomised to receive an information leaflet or the group-based 3-hour Walking Away from Type 2 Diabetes structured education programme followed by annual follow-on support, the aim of which was to increase physical activity through walking (16, 17). Participants were followed up at 12, 24 and 36 month. In the main trial there was no difference between groups in change to SB, LPA or MVPA at any time point (17), therefore groups were pooled for the purposes of this analysis and analysed as a single cohort.

A total of 808 participants at increased risk of type 2 diabetes (T2DM) were recruited through 10 primary care practices in Leicestershire, UK. Individuals with an increased risk of impaired glucose regulation (IGR) (defined as impaired glucose tolerance (IGT) and/or impaired fasting glycaemia (IFG) and/or undiagnosed T2DM) were identified using a modified version of the Leicester Risk Score, which assesses diabetes risk non-invasively using routinely collected data (18). Individuals scoring above the 90th percentile in each practice were invited to take part in the study. This approach has been shown to have reasonable sensitivity and specificity for identifying participants with IGR (18, 19). Individuals were unaware of their diabetes risk status on entering the study. Those who had previously diagnosed T2DM, were currently taking steroids or were unable to take part in walking activity were excluded. Written informed consent was obtained from all eligible participants and the study had full ethical and governance approval from the Nottingham Research Ethics Committee 2 and the Leicestershire, Northamptonshire and Rutland Comprehensive Local Research network in April 2009.

Objective sedentary and physical activity time assessment

Participants were asked to wear a blinded accelerometer (Actigraph GT3X, Pensacola, FL, USA) around their waist, for a minimum of seven consecutive days during waking hours. Data were recorded in 15 second epochs and integrated into 60 second epochs. Time spent in SB (< 100 count/min), in LPA (100 to 1951) and in MVPA (≥ 1952 count/min) were calculated applying the widely used Freedson cut-points (20). The threshold for MVPA was assessed in a sensitivity analysis (see the statistical analysis section below).

Non-wear time was defined as a minimum of 60 minutes of continuous zero counts. At least 600 minutes of wear time per day were considered valid with at least four days of valid data required for inclusion (17). A commercially available data analysis tool (KineSoft version 3.3.76, Kinesoft, Loughborough, UK) was used to process accelerometer data.

Demographic, anthropometric, lifestyle and biochemical measurements

Previous cardiovascular events, ethnicity and smoking status were obtained following an interview-administered questionnaire conducted by a healthcare professional. Body weight (Tanita TBE 611, Tanita, West Drayton, UK), waist circumference (midpoint between the lower costal margin and iliac crest) and height were measured to the nearest 0.1 kg and 0.5 cm, respectively. Average sleep duration was assessed by a single item question "On average, how many hours do you sleep in 24 h".

All participants underwent a standardised oral glucose tolerance test at each time point. Participants were asked to fast from 10pm on the evening before the test and to avoid vigorous-intensity physical activity in the preceding 24 hours. Fasting glucose, 2-hour post 75g glucose challenge (2-h) glucose and fasted lipid profile (triglycerides, HDL- and total cholesterol) were analysed in the same clinical laboratory located within Leicester Royal Infirmary, UK, using stable methodology standardized to external quality assurance reference values. Biochemical analysis was conducted blinded to accelerometer data.

Data inclusion

The Walking Away trial recruited 808 participants. This study included those with at least one change value between any consecutive 12-month time periods for the accelerometer variables (n = 647, 80%).

Calculation of the clustered cardiometabolic risk Z score

In order to assess the overall cardiometabolic risk profile of each individual within the dataset, a clustered cardiometabolic risk score (CMRS) was computed at each time point incorporating indicators of central obesity (waist circumference), dyslipidaemia (triglycerides and HDL-cholesterol), hypertension (systolic blood pressure), glycaemic control (HbA1c) and peripheral insulin resistance (2-h glucose) using a method reported and validated previously (21, 22). All variables in the model were correlated at $r < 0.4$ (see Table, Supplemental Digital Content 1, Baseline correlation matrix showing Pearson correlation coefficients between factors included in the clustered cardiometabolic risk score and those excluded, http://links.lww.com/MSS/B804). Fasting glucose, BMI or diastolic blood pressure were not included due to potential collinearity with variables already in the model (see Table, Supplemental Digital Content 1, Baseline correlation matrix showing Pearson correlation coefficients between factors included in the clustered cardiometabolic risk score and those excluded, http://links.lww.com/MSS/B804). Individual variables were standardised (value − mean]/SD) after inverting HDL-cholesterol and log transforming triglycerides. Standardised scores were then summed and divided by the number of included factors to create CMRS. A higher score represents a higher risk.

Statistical analysis

Isotemporal substitution models were used to quantify the association of reallocating time away from SB into LPA or MVPA over a 12 month period with changes to markers of metabolic health (waist circumference, 2-h glucose, fasting glucose, triglycerides, HDL-cholesterol, and systolic blood pressure) and CMRS. In order to inform health recommendations for physical activity, we also model the associations of replacing LPA with MVPA. Isotemporal substitution specifically takes into account that, in behavioural terms, time is not infinite; spending more time in one kind of activity requires less time spent in other activities during waking hours (5). Previous studies using accelerometers have used cross sectional data where the time spent in different compositions must add up to total accelerometer wear time or time spent awake (7, 8, 11, 12). Here we apply the same approach to prospective data considering that change in SB, LPA and MVPA must be bounded by overall change in wear time.

Generalised estimating equations, using a normal distribution with identity link (change values were normally distributed) and an exchangeable correlation matrix were carried out taking into account repeated 12-month change measures over 3 levels (baseline to 12 months, 12 to 24 months, 24 to 36 months) and for potential clustering by GP practice. This approach utilises and maximises all collected data by allowing each individual to contribute up to 3 observations to the analysis. Models were adjusted for change in accelerometer variables according to the isotemporal substitution approach; change in LPA, change in MVPA and change in wear time were simultaneously added to the model with the resulting regression coefficient for change in LPA and MVPA reflecting the association for reallocation away from SB or LPA. Models were

also adjusted for measurement time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline values of the accelerometer and dependent variable to account for possible regression to the mean. Baseline was defined as the starting level of the change value (e.g. change between baseline and 12 months was adjusted for the value at baseline, change between 12 to 24 months was adjusted for the value at 12 months and change between 24 to 36 months was adjusted for the value at 24 months) as has been described previously with repeated annual data looking at 12 month change (23). Models were checked for collinearity; the correlation between accelerometer variables was lower than 0.40 for all models.

Generalised estimating equations were also used to analyse differences in accelerometer variables across time.

For descriptive purposes, data were categorised into the dominant behavioural reallocation (the change in behaviour that accounted for the largest portion of time) over each 12 month period taking in to account wear time. No overall change was defined when all possible behavioural reallocations were less than 5 minutes in duration. SB → LPA defined the dominant reallocation as SB into LPA. All other possible reallocations were categorised as: SB → MVPA, LPA → MVPA, LPA → SB, MVPA → SB, MVPA → LPA. Generalised estimating equation models, incorporating categories over 3 levels (baseline to 12 months, 12 to 24 months, 24 to 36 months) adjusted for measurement time point, intervention allocation, age, sex, ethnicity, CVD status, and smoking status were used to investigate whether derived categories were associated with CMRS, with the largest category (most observations) used as reference.

Sensitivity analysis

Two sensitivity analyses were conducted. First, we assessed whether associations for reallocating time from SB to LPA were affected if the threshold for MVPA was reduced from 1952 to 1041 counts per minute, as it has been suggested the lower threshold is more appropriate for older populations (24). Second, in order investigate the potential impact of missing data, multiple imputation was used to replace missing accelerometer data. Data were imputed over 5 datasets using the AUTO IMPUTATIONS command in SPSS. Imputation was based on the descriptive covariates reported in this analysis (age, sex, ethnicity, smoking status, previous CVD event) along with intervention arm and time point.

Data were analysed in SPSS (version 24). $P < 0.05$ was considered significant. Data are reported as mean (95% CI) unless stated otherwise.

Results

This study included 647 participants (80% of the total sample) who contributed at least one observation to the analysis (see Table, Supplemental Digital Content 2, Baseline characteristics of those included and excluded from the main analysis, http://links.lww.com/MSS/B805). On average, included participants were 65 years old, with a BMI of 31.1 kg/m^2 and slept for 7.5 hours; 35% were women.

Those included in this study contributed between 1539 (for 2-h glucose) and 1601 (for systolic blood pressure) observations to the analysis for individual risk factors, and 1453 observations for CMRS (Table 1).

The amount of time spent in SB, LPA and MVPA at each time point for those included in the analysis is presented in Figure 1. On average, after adjusting for change in wear time, sedentary time increased by 8.9 (7.1, 10.7) mins/day per year, LPA decreased by 7.0 (5.2, 8.6) mins per day per year and MVPA decreased by 2.0 (1.5, 2.5) mins/day per year. There was no meaningful change in wear time overall (-1.4 mins/day per year; -1.9, 0.6). The same pattern of results with increasing SB were observed in the full dataset when missing accelerometer data were imputed (see Figure, Supplemental Digital Content 3, Time spent sedentary, in light-intensity and moderate-to-vigorous intensity physical activity at each follow-up time point after imputing missing accelerometer data, http://links.lww.com/MSS/B806).

Reallocating time from SB into LPA or MVPA over 12 months was associated with change in waist circumference, 2-h glucose, triglycerides and CMRS (Table 1), with the strongest associations seen for reallocation into MVPA. Every 30 minutes reallocation from SB to LPA was associated with a 0.21 (0.03, 0.38) cm reduction in waist circumference, a 0.09 (0.04, 0.13) mmol/l reduction in 2-h glucose, a 0.02 (0.00, 0.04) mmol/l reduction in triglycerides and a 0.02 (0.01, 0.03) reduction in CMRS. Every 30 minutes reallocation from SB to MVPA was associated with a 1.23 (0.68, 1.79) cm reduction in waist circumference, a 0.23 (0.10, 0.36) mmol/l reduction in 2-h glucose, a 0.04 (0.00, 0.009) reduction in triglycerides and a 0.07 (0.04, 0.11) reduction in CMRS. Reallocating 30 minutes from LPA into MVPA was also associated

with a 1.02 (0.43, 1.60) cm reduction in waist circumference, a 0.16 (0.02, 0.30) mmol/l reduction in 2-h glucose and a 0.05 (0.01, 0.09) reduction in CMRS.

The same pattern of associations were observed for reallocating sedentary time into light-intensity physical activity when a lower threshold for MVPA was applied (see Table, Supplemental Digital Content 4, Isotemporal associations for prospectively reallocating sedentary time into light-intensity physical activity, http://links.lww.com/MSS/B807), or when missing accelerometer data were imputed (see Table, Supplemental Digital Content 5, Isotemporal associations for reallocating sedentary time into light-intensity or moderate-to-vigorous intensity physical activity after imputing missing accelerometer data, http://links.lww.com/MSS/B808).

When categorised into the dominant behavioural relocation over each 12 month period, the largest proportion (44.0%) of observations were for reallocating LPA into SB, with the opposite reallocation (SB into LPA) accounting for 33.9% of observations (Figure 2). Compared to those increasing their sedentary time at the expense of LPA, those that increased their LPA or MVPA at the expense of SB reduced their CMRS (Figure 2).

Discussion

In a population at risk of T2DM, reallocating SB into either LPA or MVPA over a 12 month period was associated with an improved CMRS, driven by reduced waist circumference, 2-h glucose, and triglycerides. There was a dose-response relationship for intensity, such that

reallocating LPA to MVPA was additionally associated with reductions to waist circumference, 2-h glucose and overall CMRS. Reallocating approximately 105 minutes of SB time into LPA would be needed to achieve the same benefit to cardiometabolic health as reallocating 30 minutes of SB into MVPA.

Our findings are consistent with those reported for cross sectional data, which have found beneficial associations with markers of cardiometabolic health reported for reallocating waking time from SB, with the strongest associations seen for reallocation into MVPA or stepping activities (13). Our findings are also consistent with a prospective post-hoc analysis of the occupational Stand Up Victoria trial which demonstrated through compositional data analysis that metabolic health is maximised with low sedentary time and more time spent stepping (25). Several previous studies have also reported prospective associations between change in objective or self-reported sedentary behaviour and metabolic health in statistical models that have not accounted for behavioural co-dependence (21, 26). For example, a 10 year change in self-reported sedentary behaviours was detrimentally associated with clustered metabolic risk, waist circumference and lipid profile (26), with similar results reported over 6 years with objectively measured of sedentary time (21). Our findings add to these previous studies by quantifying the associations for prospectively reallocating time away from sedentary behaviour in those at risk of type 2 diabetes recruited from primary care.

Sedentary behaviour is the dominant waking behavioural allocation within industrialised societies (6). An important finding from this study was the observation that over just 36 months of follow-up, SB increased by almost 9 minutes/day per year, resulting in less time spent in both

LPA and MVPA. To our knowledge, only one previous study has investigated change over time in objectively assessed sedentary behaviour and reported a 26 minute increase in SB over a 6 year period in an adult Swedish population (27). These findings are supported by cross sectional data showing that the proportion of time spent sedentary is greater in older age (28). Our study suggests that this increase in sedentary time at the expense of both LPA and MVPA is associated with worsening metabolic health. Given defects in nutrient sensing, worsening insulin resistance, and poor metabolic health are hallmarks of aging (29), the longitudinal trend for increasing sedentary time could act to accelerate the aging process. Conversely, even reallocating relatively small amounts of SB (in this cohort 30 minutes equated to an average of 6% or less of total sedentary time) into LPA or MVPA could act to reverse this process and improve cardio metabolic health. The finding for the relative importance of LPA provides evidence in support of recent updates to the physical activity guidelines in the United States which suggests for the first time that inactive individuals may benefit from replacing sedentary time with LPA (30). However, it also supports the continued focus on MVPA as the most effective method of promoting cardiometabolic health per unit of time.

Our observational findings are supported by short-term experimental studies which have consistently reported that reducing prolonged sitting time by 30 minutes or more over a course of day, through employing regular light-intensity physical activity breaks, improves markers of cardiometabolic health (31), with stronger effects reported in those with low fitness levels and higher levels of insulin resistance (32, 33). Studies have also shown that when light-intensity and moderate-intensity exercise training programmes are matched for exercise volume in those with T2DM, similar reductions in HbA1c were reported (34), whilst meta-analyses of exercise

training studies have concluded that exercise volume, but not intensity, is a significant determinant of HbA1c reduction (35, 36). Therefore the dose-response association for reallocating SB to LPA or MVPA observed in this study could be driven by the higher volume of physical activity per unit of time. This has important behavioural implications, as increasing MVPA by 30 mins per day represents over a 100% increase for the population included in this study, whereas 30 minutes of LPA would only represented a 10% increase in the average time currently spent in LPA. Therefore, it is possible that increasing physical activity volume through decreasing SB and increasing LPA may be more feasible than increasing MVPA for many individuals at risk of T2DM or other chronic diseases. However, this hypothesis needs to be tested empirically before specific public health recommendations can be made.

This study has several strengths, most notably the prospective design and objectively assessed SB, LPA and MVPA. The study population is both a strength and a limitation as it is reflective of populations referred into diabetes prevention or health promotion programmes, whilst it may not reflect the general population. The optimal method for modelling reallocation of behaviour in physical activity research is debated, with arguments for and against alternatives to isotemporal substitution such as compositional data analysis approaches (37, 38). However, we have previously shown that isotemporal substitution and compositional data analysis approaches provide similar results when applied to physical activity and sedentary behaviour data (39). Limitations include the fact that accelerometers were only worn during waking hours, therefore we were unable to assess the impact of substituting sleep for sedentary behaviour, another strategy that could potentially be used to reduce sedentary behaviour and improve health. However, it has previously been shown in this population that optimal metabolic health is

associated with around 6.5 to 7.5 hours of self-reported sleep duration (40). As the interquartile range of self-reported sleep duration within this study was 7-8 hours, the majority of the population were already achieving or exceeding levels of sleep associated with optimal metabolic health. Substituting sedentary behaviour into sleep may therefore be less relevant to health than substituting into physical activity for the majority of this population. In addition, there was no meaningful change to waking accelerometer wear time during this study, providing support that change in activities outside of the wear period were unlikely to be affecting results. The definition of SB used in this study was also based on a lack of movement rather than posture. Finally, although prospective in nature, the observational design does not allow direct inferences about causality and confounding by unmeasured factors, including diet, remains a possibility.

Conclusion

This study found that reallocating SB into either LPA or MVPA was associated with improved cardiometabolic health in a primary care based population at high risk of T2DM, with the greatest improvements seen for MVPA. Against a background of increasing objectively measured SB over time seen in this and other studies (27), these findings have an important public health relevance, as they suggest that altering this trajectory may lead to improve cardiometabolic health in populations already displaying risk factors for T2DM. However, interventional level research is needed to confirm the findings of this study. In particular, interventions are needed to test the behavioural acceptability and sustainably of reallocating SB into different intensities of physical activity along with the effect on health to further understand optimal approaches to reducing SB behaviour and improving cardiometabolic health.

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Author contributions

TY developed the research idea and drafted the paper; TY, MJD and KK contributed to the design of the Walking Away from Type 2 Diabetes trial; JH and CLE contributed to data collection; TY undertook data analysis with support from FZ; TY, CLE, JH, FZ, KK and MJD all revised the paper for important intellectual content

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Tables

Table 1: Isotemporal associations for prospectively reallocating sedentary time into light-intensity or moderate-to-vigorous intensity physical activity

Models included the following variables: change in light-intensity physical activity, change in moderate-to-vigorous intensity physical activity, change in wear time, follow-up time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline values of the accelerometer and dependant variables

Figures

Figure 1: Time spent sedentary, in light-intensity and moderate-to-vigorous intensity physical activity at each time point

Data as mean (95% CI)

Figure 2: Change in the cardiometabolic risk score across categories of the 12-month dominant behavioural change

Models adjusted for follow-up time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline value

Data as mean change (95% CI). **The % values represent the proportion of the sample within each category**

** = $p < 0.01$ and * = $p < 0.05$ compared to reference (REF) category

Supplementary Digital Content

Supplemental Digital Content 1.docx—Baseline correlation matrix showing Pearson correlation coefficients between factors included in the clustered cardiometabolic risk score (shown in bold) and those excluded

Supplemental Digital Content 2.docx—Baseline characteristics of those included and excluded from the main analysis

Supplemental Digital Content 3.docx—Time spent sedentary, in light-intensity and moderate-to-vigorous intensity physical activity at each follow-up time point after imputing missing accelerometer data

Supplemental Digital Content 4.docx—Isotemporal associations for prospectively reallocating sedentary time into light-intensity physical activity

Supplemental Digital Content 5.docx—Isotemporal associations for reallocating sedentary time into light-intensity or moderate-to-vigorous intensity physical activity after imputing missing accelerometer data

Figure

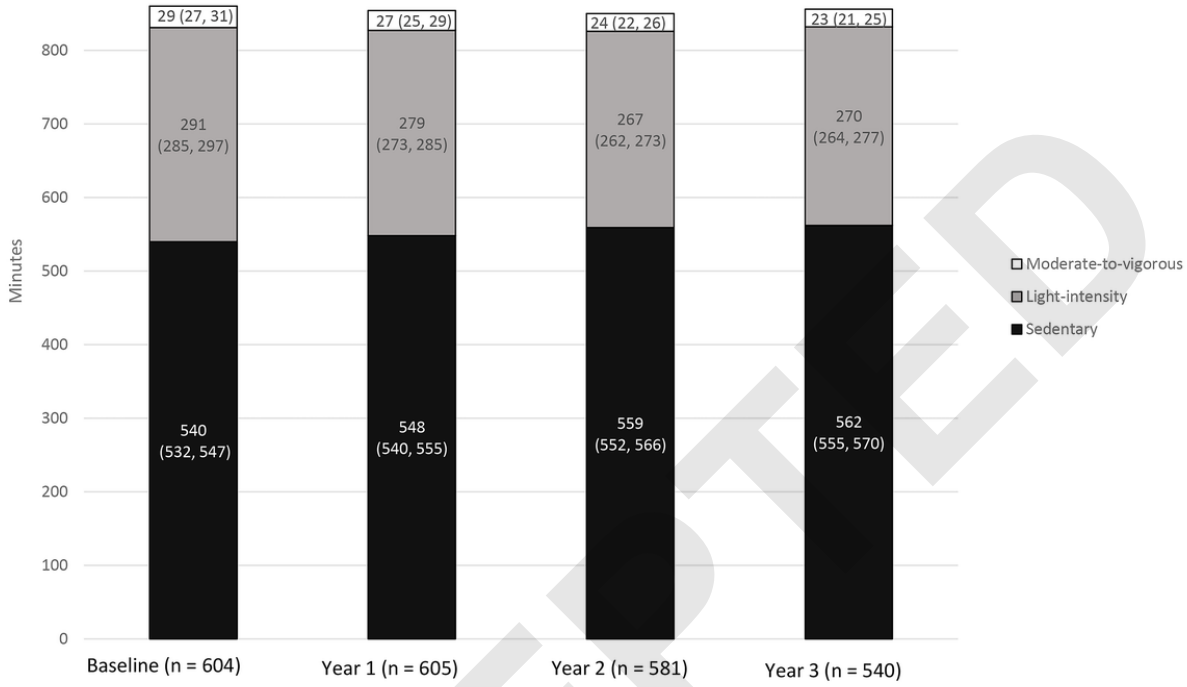


Figure 2

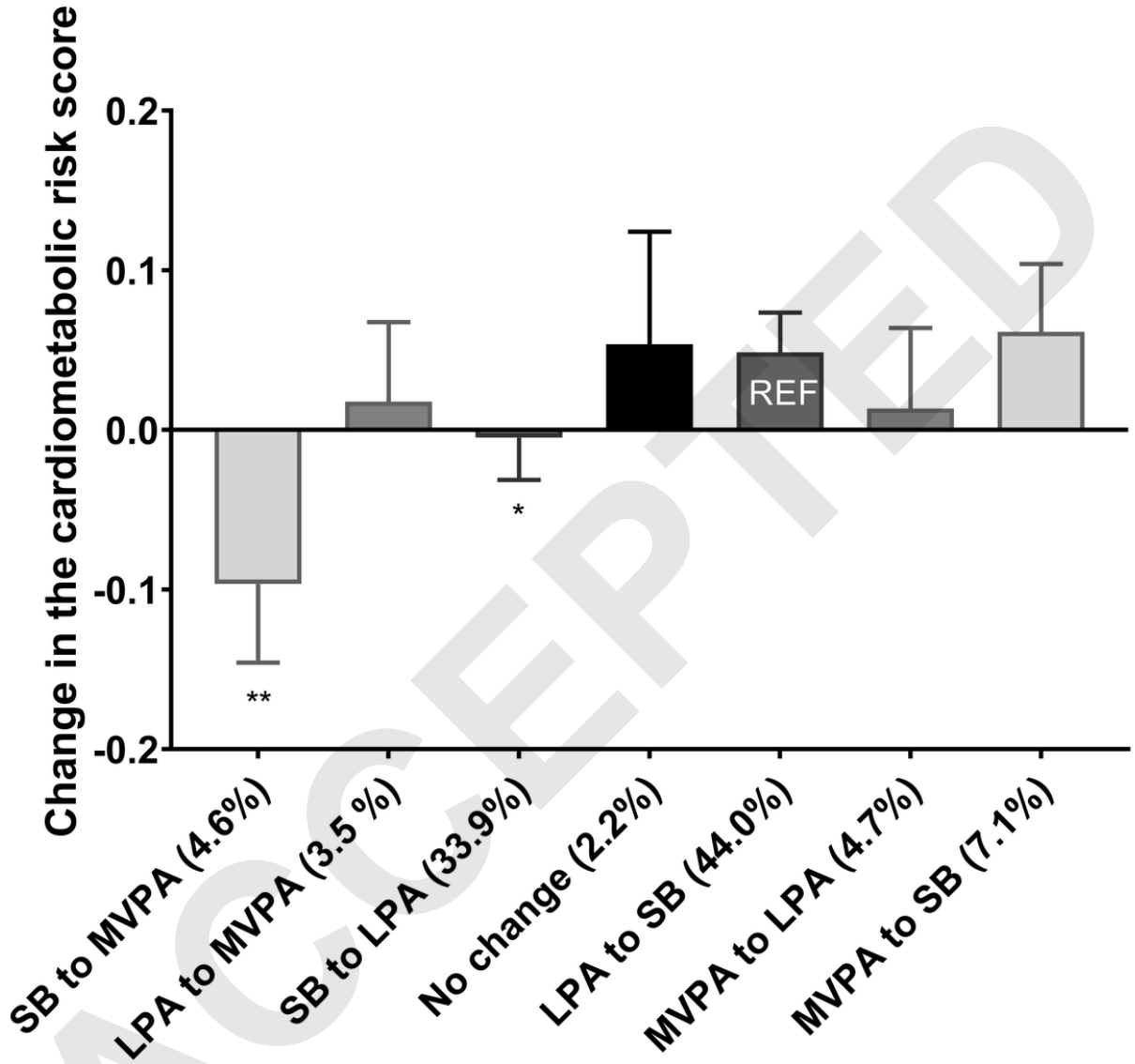


Table 1: Isotemporal associations for prospectively reallocating 30 minutes of sedentary time into light-intensity or moderate-to-vigorous intensity physical activity

	Participants contributing data (n)	Observations (n)	Sedentary time into light-intensity physical activity	Sedentary time into moderate-to-vigorous intensity physical activity	Light-intensity physical activity into moderate-to-vigorous intensity physical activity
Waist circumference (cm)	643	1590	**-0.21 (-0.38, -0.03)**	**-1.23 (-1.79, -0.68)**	**-1.02 (-1.60, -0.43)**
2-h glucose (mmol/l)	638	1539	**-0.09 (-0.13, -0.04)**	**-0.23 (-0.36, -0.10)**	**-0.16 (-0.30, -0.02)**
HbA1c (mmol/l)	639	1571	-0.00 (-0.01, 0.01)	-0.02 (-0.05, 0.00)	-0.02 (-0.05, 0.00)
Triglycerides (mmol/l)	640	1585	**-0.02 (-0.04, -0.00)**	**-0.04 (-0.09, 0.00)**	-0.02 (-0,07, 0.03)
HDL-Cholesterol (mmol/l)	637	1562	0.00 (-0.00, 0.01)	-0.00 (-0.02, 0.02)	-0.00 (-0.02. 0.02)

Systolic blood pressure (mmHg)	642	1601	-0.45 (-0.85, 0.05)	-0.35 (-1.71, 1.01)	0.28 (-1.16, 1.72)
Cardiometabolic risk score[a]	622	1453	**-0.02 (-0.01, -0.03)**	**-0.07 (-0.11, -0.04)**	**-0.05 (-0.09, -0.01)**

Bold values indicate significant results

[a] = higher score represents higher risk

Models included the following variables: change in light-intensity physical activity, change in moderate-to-vigorous intensity physical activity, change in wear time, follow-up time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline values of the accelerometer and dependant variables

Supplementary Digital Content 1

Baseline correlation matrix showing Pearson correlation coefficients between factors included in the clustered cardiometabolic risk score (shown in bold) and those excluded.

	Waist circumference	**2-h glucose**	**HDL-cholesterol**	**Triglycerides**	**HbA1c**	**Systolic blood pressure**	Diastolic blood pressure	BMI	Fasting glucose
Waist circumference	1	.076	-.342	.173	.102	-.084	.143	.768	.171
2-h glucose	.076	1	-.127	.202	.342	.143	.048	.076	.357
HDL-cholesterol	-.342	-.127	1	-.341	-.112	.083	-.008	-.175	-.108
Triglycerides	.173	.202	-.341	1	.105	.119	.120	.112	.101
HbA1c	.102	.342	-.112	.105	1	-.038	.004	.081	.412
Systolic blood pressure	-.084	.143	.083	.119	-.038	1	.467	-.118	.086
Diastolic blood pressure	.143	.048	-.008	.120	.004	.467	1	.250	.084
BMI	.768	.076	-.175	.112	.081	-.118	.250	1	.088
Fasting glucose	.171	.357	-.108	.101	.412	.086	.084	.088	1

Supplementary Digital Content S2

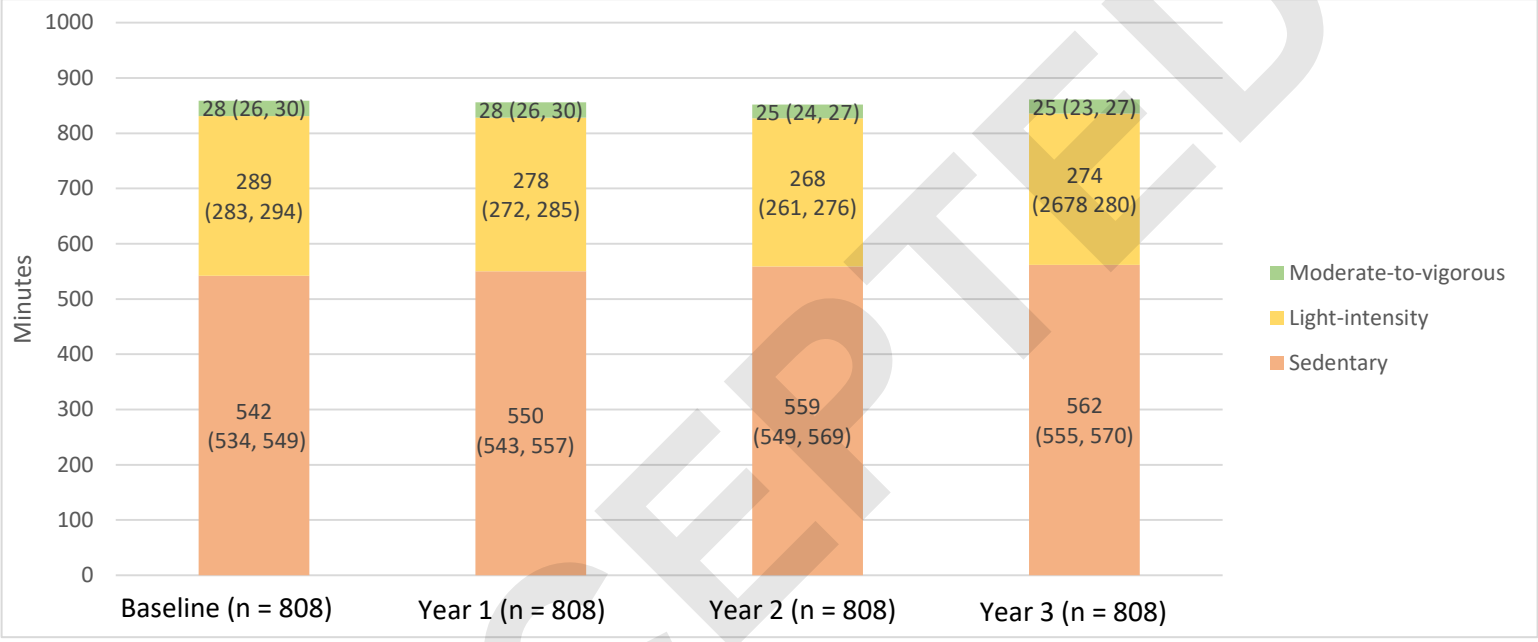
Baseline characteristics of those included and excluded from the main analysis

	Included N = 647	Excluded N = 161
Sex		
Women	228 (35)	66 (41)
Men	419 (65)	95 (59)
Age (years)	65 (60, 70)	63 (54, 68)
Current smoker	49 (8)	29 (18)
Ethnicity		
White European	574 (89)	143 (89)
Other	73 (11)	18 (11)
Previous CVD event	79 (12)	30 (19)
BMI (kg/m^2)	31.1 (28.12, 34.6)	33.7 (30.3, 37.8)
Average sleep duration (hours)	7.5 (7.0, 8.0)	7.0 (6.5, 8.0)
Waist circumference (cm)	100 (93, 108)	103 (94, 144)
Systolic blood pressure (mmHg)	144 (131, 155)	137 (125, 151)
Diastolic blood pressure (mmHg)	87 (80, 93)	86 (80, 93)
HbA1c	5.8 (5.6, 6.1)	5.9 (5.6, 6.1)
2-h glucose (mmol/l)	6.0 (4.9, 7.5)	6.3 (4.8, 8.2)
Fasting glucose (mmol/l)	5.2 (4.8, 5.6)	5.2 (4.8, 5.7)
Total Cholesterol (mmol/l)	5.1 (4.4, 5.9)	5.0 (4.2, 5.8)
HDL Cholesterol (mmol/l)	1.4 (1.2, 1.6)	1.2 (1.1, 1.5)
Triglycerides (mmol/l)	1.3 (1.0, 1.7)	1.4 (1.0, 1.9)

Data as number (%) or median (IQR)

Supplementary Digital Content 3

Time spent sedentary, in light-intensity and moderate-to-vigorous intensity physical activity at each follow-up time point after imputing missing accelerometer data



Supplementary Digital Content 4

Isotemporal associations for prospectively reallocating sedentary time into light-intensity physical activity, when moderate intensity physical activity is defined at a lower threshold of 1041 counts per minute compared to the threshold of 1952 counts per minute used in the main manuscript

	Sedentary time into light-intensity physical activity defined as 100 to 1040 counts per minute	Sedentary time into low light-intensity physical activity defined as 100 to 1951counts per minute
Waist circumference (cm)	-0.18 (-0.45, 0.09)	-0.21 (-0.38, -0.03)
2-h glucose (mmol/l)	-0.08 (-0.15, -0.01)	-0.09 (-0.13, -0.04)
HbA1c (mmol/l)	-0.01 (-0.02, 0.01)	-0.00 (-0.01, 0.01)
Triglycerides (mmol/l)	-0.03 (-0.07, -0.01)	-0.02 (-0.04, -0.00)
HDL-Cholesterol (mmol/l)	0.00 (-0.01, 0.02)	0.00 (-0.00, 0.01)
Systolic blood pressure (mmHg)	-0.33 (-0.90, 0.22)	-0.45 (-0.85, 0.05)
Cardiometabolic risk score[a]	-0.02 (-0.04, -0.00)	-0.02 (-0.03, -0.01)

[a] = higher score represents higher risk

Models included the following variables: change in light-intensity physical activity, change in moderate-to-vigorous intensity physical activity, change in wear time, follow-up time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline values of the accelerometer and dependant variables

Supplementary Digital Content 5

Isotemporal associations for reallocating sedentary time into light-intensity or moderate-to-vigorous intensity physical activity after imputing missing accelerometer data

	Participants contributing data (n)	Observations (n)	Sedentary time into Light-intensity physical activity	Sedentary into moderate to vigorous intensity physical activity	Light-intensity physical activity into moderate-to-vigorous intensity physical activity
Waist circumference (cm)	707	1872	**-0.17 (-0.34, -0.01)**	**-0.89 (-1.44, -0.34)**	**-1.02 (-1.60, -0.43)**
2-h glucose (mmol/l)	707	1820	**-0.08 (-0.14, -0.02)**	**-0.20 (-0.35, -0.05)**	**-0.16 (-0.30, -0.02)**
HbA1c (mmol/l)	714	1892	-0.00 (-0.01, 0.01)	-0.02 (-0.04, 0.01)	-0.02 (-0.04, 0.01)
Triglycerides (mmol/l)	711	1883	**-0.02 (-0.04, -0.00)**	-0.02 (-0.08, 0.02)	-0.02 (-0.07, 0.03)
HDL-Cholesterol (mmol/l)	707	1855	0.00 (-0.01, 0.01)	-0.00 (-0.02, 0.02)	-0.00 (-0.02, 0.02)
Systolic blood pressure (mmHg)	709	1898	-0.37 (-0.76, 0.02)	-0.27 (-1.59, 1.06)	0.28 (-1.16, 1.72)
Cardiometabolic risk score	689	1735	**-0.02 (-0.04, -0.00)**	**-0.06 (-0.11, -0.02)**	-0.04 (-0.09, 0.00)

Models included the following variables: change in light-intensity physical activity, change in moderate-to-vigorous intensity physical activity, change in wear time, follow-up time point, intervention allocation, age, sex, ethnicity, CVD status, smoking status and baseline values of the accelerometer and dependant variable