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Objectively measured physical activity and sedentary time are associated with cardio-metabolic risk factors in adults with pre-diabetes: The PREVIEW study

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Abstract

Objective

The aim of the present cross-sectional study was to examine the association between physical activity (PA), sedentary time (ST) and cardio-metabolic risk in adults with pre-diabetes.

Design and Methods

Participants (n=2,326; 25-70 years, 67% female) from eight countries with a body mass index (BMI) >25 $kg \cdot m^{-2}$, impaired fasting glucose (IFG; 5.6–6.9 $mmol \cdot l^{-1}$) and/or impaired glucose tolerance (IGT; 7.8–11.0 $mmol \cdot l^{-1}$ at 2 hr) participated. Seven-day accelerometry objectively-assessed PA levels and sedentary time.

Results

Multiple linear regression revealed that moderate-to-vigorous physical activity (MVPA) was negatively associated with homeostatic model assessment of insulin resistance (HOMA-IR) (standardized β = -0.078 [-0.128,-0.027]), waist circumference (WC); β=-0.177 [-0.122,-0.134]), fasting insulin (β=-0.115 [-0.158,-0.072]), 2-hour glucose (β=-0.069 [-0.112,-0.025]), triglycerides (β=-0.091 [-0.138, -0.044]) and C-reactive protein (CRP; β=-0.086 [-0.127,-0.045]). Sedentary time was positively associated with HOMA-IR (β=0.175 [0.114,0.236]), WC (β=0.215 [0.026,0.131]), fasting insulin (β=0.155 [0.092,0.219]), triglycerides (β=0.106 [0.052,0.16]), CRP (β=0.106 [0.39,0.172]), systolic blood pressure (BP) β=0.078 [0.026,0.131]) and diastolic BP (β=0.106 [0.39,-0.172]). Associations reported between total PA ($counts \cdot minute^{-1}$) and all risk factors were comparable or stronger than MVPA; HOMA-IR (β=-0.151 [-0.194,-0.107]), WC (β=-0.179 [-0.224,-0.134]), fasting insulin (β=-0.139 [-0.183,-0.096]), 2-hour glucose (β=-0.088 [-0.131,-0.045]), triglycerides (β=-0.117 [-0.162,-0.071]) and CRP (β=-0.104 [-0.146,-0.062]).

Conclusions

In adults with pre-diabetes, objectively measured PA and ST were associated with cardio-metabolic risk markers. Total PA was at least as strongly associated with cardio-metabolic risk markers as MVPA, which may imply that the accumulation of total PA over the day is as important as achieving the intensity of MVPA.

Introduction

The global prevalence of diabetes among adults has almost quadrupled since 1980 to 422 million cases in 2014 and continued growth is expected (1). This dramatic rise in prevalence is largely due to the increase in type 2 diabetes which accounts for the majority of all diagnosed cases in adults (1). Changes in lifestyle factors such as sedentary behaviour, insufficient PA, dietary choices and excess weight are important contributors in the development of type 2 diabetes (2). Physical activity plays an important role, independent of weight, in the prevention of type 2 diabetes through its effect on insulin resistance (3). Physical activity leads to the translocation of GLUT-4 transporters to the plasma membrane increasing glucose uptake into skeletal muscle (4). Sedentary time has also been associated with insulin resistance and fasting triglyceride levels, independent of PA and obesity (5). Sedentary time is thought to affect carbohydrate metabolism by decreasing muscle GLUT-4 concentrations while also reducing lipoprotein lipase (LPL) activity and triglycerides clearance (6,7).

Light activity is also associated with cardio-metabolic health and together with sedentary time, occupies the majority of waking hours (8). Indeed, light-intensity activity substantially

contributes to overall daily energy expenditure and may also mean spending less time in sedentary behaviours.

Many studies reporting associations between PA, ST and cardio-metabolic risk factors are limited by the self-reported measures of PA and ST (9,10) which are susceptible to reporting and recall bias. In the limited number that have used objective measures of PA, investigations of international samples measured concurrently with the same protocol are lacking, little consistency exists with regards to the devices, wear time criteria, intensity cut points or epoch lengths used, thereby limiting the ability to make comparisons between these studies. Furthermore, despite those with pre-diabetes being at the highest risk of developing type-2 diabetes and representing the population at which many lifestyle interventions are targeted, few studies have described the relationship between PA and insulin resistance in this population.

Typically, epidemiological research assessing the effect of PA and ST on cardio metabolic risk factors has been conducted in the general population (8,11,12). The few studies conducted in high risk populations have included participants based on a risk score questionnaire (5), family history of type 2 diabetes (9,13) or participants diagnosed with diabetes and pre-diabetes have been combined (14). Consequently, physical characteristic and metabolic parameters of study participants varied substantially. As a result, it is unclear to what extent reported associations could be inferred to individuals with pre-diabetes.

Therefore, the purpose of this study was to quantify the relationship between objectively measured PA and ST with cardio metabolic health and risk of diabetes.

Methods

Participants and setting

A detailed account of the PREVention of diabetes through lifestyle Intervention and population studies in Europe and around the World (PREVIEW) project has been published elsewhere

(15). Participants were recruited into the PREVIEW project between June 2013 and February 2015. The PREVIEW study is a large multi-national diabetes prevention intervention being conducted at eight study sites: University of Copenhagen (Denmark), University of Helsinki (Finland), University of Maastricht (The Netherlands), University of Nottingham (UK), University of Navarra (Spain), Medical University of Sofia (Bulgaria), University of Sydney (Australia) and University of Auckland (New Zealand).

Participants were selected through an internet-based pre-screening tool or telephone interview using the Finnish Diabetes Risk Score (16). A total of 15,611 individuals were contacted for pre-screening. Potential participants were sent a written description of the trial, given verbal information at the study site and signed informed consent prior to a laboratory screening. The laboratory screening was attended by 5,472 participants and included assessment of body mass, stature, resting blood pressure (BP), and a 2-hour OGTT (17). Glucose concentrations were analysed at each study site (HemoCue™, Angelholm, Sweden; Reflotron™, Roche diagnostics, Switzerland; or EML105 Radiometer, Copenhagen) to identify people with pre-existing diabetes.

At the end of this process, 2,326 participants met the following inclusion criteria and found eligible to take part in the study: age 25 – 70 years; BMI >25 kg/m^2; pre-diabetes confirmed at OGTT. Pre-diabetes was defined in line with WHO/IDF and ADA criteria (17) as either (i) IFG, with venous plasma glucose concentration of 5.6 – 6.9 $mmol \cdot l^{-1}$ and/or (ii) IGT, with venous plasma glucose concentration of 7.8 – 11.0 $mmol \cdot l^{-1}$ at 2 hours and fasting plasma glucose <7.0 $mmol \cdot l^{-1}$. Participants were free of pre-existing type 2 diabetes, and any illness and/or medication with potential effect on compliance or the outcomes of the study.

Measurements and procedures

Physical activity

Participants wore an ActiSleep+ (ActiGraph LLC, Pensacola, FL) accelerometer attached to an elastic waist belt worn over the right mid-axillary line. The ActiSleep+ was worn 24 $h \cdot day^{-1}$ for seven consecutive days, removing only for water-based activities. The principal output from the ActiSleep+ is an activity count, which represents raw accelerations that have been rescaled and filtered. Activity counts were collected at 100Hz and aggregated to 60-second epochs (18). Sleep time was determined using a fully-automated algorithm developed for use in 24-hour waist-worn accelerometer protocols. The algorithm produces estimates of nocturnal sleep period that are compared to an expert visual inspection of accelerometer trace (19). After the removal of nocturnal sleep episodes, participants were included in the analyses if they wore the monitor for ≥10 hours on ≥4 days (18) including 1 weekend day (20). Mean activity count during valid wear time ($counts \cdot minute^{-1}$; CPM) has been shown to correlate well with total activity energy expenditure measured by the doubly labelled water technique (21) and was used as an indicator of total PA volume (18, 28). Troiano cut points (18) were used to determine time ($minutes \cdot day^{-1}$) spent at different intensity categories (Sedentary <100, moderate <2,020 and vigorous <5,999 counts per minute). Moderate and vigorous activity were summed to obtain moderate to vigorous physical activity (MVPA).

Cardio-metabolic risk factors

In all study centres, standardized procedures were followed and measurements were performed by trained personnel. Self-administered questionnaires, accelerometer data and fasting blood samples, were collected at baseline. Blood was drawn from the vein in the antecubital fossa after fasting (>10 hours). Blood samples were initially stored locally at -80ºC, then transported and analysed centrally at the National Institution for Health and Welfare (THL) in Helsinki,

Finland where they were analysed for insulin, HbA_{1c}, glucose, high sensitivity C-reactive protein (hs-CRP), total cholesterol, triglycerides, HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C) concentrations. Insulin resistance was calculated using the homeostasis model assessment for insulin resistance, HOMA-IR using the equation: HOMA-IR= Fasting insulin ($mU \cdot l^{-1}$) x Fasting glucose ($mmol \cdot l^{-1}$) / 22.5. HOMA-IR has been validated against the gold standard hyperinsulinemic-euglycemic clamp technique (23). Total adiposity was assessed by dual energy X-ray absorptiometry (DEXA) in four (Copenhagen, Nottingham, Sydney and Auckland), bioelectrical impedance in 3 (Helsinki, Sofia, and Navarra) and with Bodpod (Maastricht) in one site. Self-administered questionnaires assessed general and socio-economic variables, including ethnicity, educational status, household income.

Statistical analysis

Descriptive statistics (mean ± SD) were calculated for continuous variables and frequencies (%) for categorical variables.

Two-fifths of the participants had a missing value on at least one variable, HOMA-IR was missing in 7.8% of all cases, while 17% of values were missing for the accelerometer values (CPM, MVPA, and sedentary time). Multiple imputation with fully conditional specification model (Markov chain Monte Carlo) was used to impute missing values. All variables were included in the imputation and all variables with skewed distribution were log_{10} or square root transformed prior to imputation (24). Ten multiple imputed data sets were generated and pooled estimates were reported. Due to their positively skewed distribution, HDL-C, triglycerides hs-CRP, and waist circumference were logarithmically transformed (log_{10}) while HOMA-IR was square root transformed.

Separate multiple linear regression models were performed to test the independent association between MVPA, CPM and ST with cardio-metabolic health markers (HOMA-IR, fasting insulin, FPG, 2h glucose, HbA_{1c}, waist circumference, triglycerides, total C, HDL-C and LDL-C-) and CRP while adjusting for potential confounders.

Model 1 was adjusted for age, sex, ethnicity (Caucasian, Asian, Black, Arabic, Hispanic or other), smoking (daily, less than weekly, no smoker), accelerometer wear time, intervention centre, sleep duration, body fat%, education level (no formal education, primary/junior school, secondary school, secondary vocational education, higher vocational education or university education) and household income (less than £9360, £9360 - £12,479.99, £12,480 - £15,599.99, £15,600 - £18,719.99, £18,720 -£22,879.99, £22,880 - £27,559.99, £27,560 - £32,759.99, £32,760 – £41,079.99, £41,080 – £53,559.99, £53,560 or more per year). Model 2 was additionally adjusted for ST while MVPA was the main exposure variables or for MVPA when ST was the main exposure variable.

Sex, age (<45.9, 46-54.9, >55 years), BMI and intervention centre differences in the associations between MVPA, sedentary time, or CPM and each cardio-metabolic risk factor were tested for by adding interaction terms to the model.

A variance inflation factor < 4 confirmed that multicollinearity was not a concern (25). Square root and log-transformations were directly compared across cardio-metabolic markers, and results of linear regression analysis presented as standardised beta coefficients. Data were analysed using the Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA) and alpha was set to $p < .05$.

Results

Table 1 displays the descriptive physical and biochemical characteristics of the 2,326 participants (32% male, age 52.2 ± 11.5 years). Waking accelerometer wear time was 928.40 ± 83.37 and 933.10 ± 83.85 minutes/day for men and women respectively. Mean ST was 617.54 ± 98.06 for men and 579.46 ± 91.76 min/day for women. Mean MVPA was 31.58 ± 20.62 min/day for men and 26.18 ± 17.03 min/day for women. Only 50% of participants met the recommended guidelines of 30 minutes of MVPA per day (26).

Tables 2, 3 and 4 show the standardized regression coefficients of CPM, MVPA and ST with the cardio metabolic risk factors.

Counts per minute

Table 2, shows the standardized regression coefficients of CPM, with the cardio metabolic risk factors. After adjusting for age, sex, ethnicity, smoking, accelerometer wear time, intervention centre, sleep duration, body fat%, education level and household income, CPM had significant inverse associations with HOMA-IR, waist circumference, fasting insulin, 2-hour glucose, triglycerides and CRP and a positive association with HDL-cholesterol.

MVPA

Table 3, shows the standardized regression coefficients for MVPA with the cardio metabolic risk factors. In model 1, adjusted for age, sex, ethnicity, smoking, accelerometer wear time, intervention centre, sleep duration, body fat%, education level and household income, MVPA was significantly and negatively associated with HOMA-IR, waist circumference, fasting insulin, 2h glucose, triglycerides and CRP) and positively associated with HDL-cholesterol. After adjusting for ST in model 2, the association with HDL-cholesterol was lost. Associations with other biochemical factors were slightly attenuated but all remained significant.

Sedentary time

Table 4, shows the standardized regression coefficients for ST with the cardio metabolic risk factors. In model 1, adjusted for age, sex, ethnicity, smoking, accelerometer wear time, intervention centre, sleep duration, body fat%, education level and household income, ST was positively associated with waist circumference, systolic BP, diastolic BP, mean arterial pressure, fasting insulin, 2 h glucose, HOMA-IR, triglycerides and CRP, and negatively associated HDL. After adjusting for MVPA in model 2, associations with 2-hour plasma glucose were no longer significant.

Fasting plasma glucose, total cholesterol and LDL-cholesterol were not associated with any of our exposure variables.

Two-way interactions indicate that associations between MVPA and fasting insulin were greater in the older age group (table 3). We did not observe any significant sex, centre, or BMI interactions between measures of PA or ST and any cardio metabolic risk factors.

Conclusions

This study investigated the associations between objectively measured PA and ST and metabolic variables in a worldwide sample of overweight and obese adults (BMI >25 kg/m^2) with pre-diabetes confirmed through an OGTT (27). To our knowledge this is the first international investigation of associations between objectively measured PA and ST with cardio-metabolic risk factors in a population that exclusively meet the criteria for pre-diabetes (IFG 5.6-6.9 or IGT 7.8-11 ($mmol \cdot l^{-1}$). Previous studies conducted in high risk populations have included participants based on a risk score questionnaire (5), family history of type 2 diabetes (9,13) or participants with diabetes and pre-diabetes have been combined (14). Consequently, physical characteristics and metabolic parameters reported in these studies varied substantially from the present study. In our population of participants with pre-diabetes,

MVPA was negatively associated with HOMA-IR, waist circumference, fasting insulin, 2h glucose, triglycerides and CRP after accounting for potential confounders, sleep duration and sedentary time. Our study also demonstrated that total PA volume (counts·minute^{-1}) was at least as strongly associated with the aforementioned risk factors as MVPA.

Before controlling for sedentary time in model 2, total PA volume also accounts for greater variance in cardio-metabolic risk factors than MVPA. Hence, it appears that in this population although both are significant, the accumulation of total PA over a day is a stronger indicator of insulin resistance and some related cardio metabolic risk factors than MVPA.

Previous studies in populations with a family history of diabetes and newly diagnosed diabetes, have shown that total energy expenditure spent on PA (14), counts·minute^{-1} (13) and MVPA (9) were negatively associated with waist circumference, fasting serum triglycerides, systolic BP, fasting plasma glucose, fasting plasma insulin, HOMA-IR and a clustered metabolic risk score. In agreement with our findings, Ekelund *et al* (13), reported that total counts·day^{-1} was more strongly associated with clustered risk and individual cardio metabolic risk factors than MVPA. In the general population, Balkau and colleagues (22) reported associations between MVPA and total PA with insulin resistance using the gold standard clamp technique for determining insulin sensitivity. However, after adjusting for total PA, associations with MVPA were lost (22). These findings, in keeping with the present study would support the hypothesis that the accumulation of total PA volume accounts for greater variance in insulin resistance and some related cardio metabolic risk factors than MVPA.

The present study also demonstrated that after controlling for confounders, ST is positively associated with waist circumference, systolic BP, diastolic BP, fasting insulin, HOMA-IR, triglycerides, CRP, and HDL-cholesterol independent of time spent in MVPA.

In agreement with our findings, Henson et al (5) reported positive associations between ST, 2 hour plasma glucose, triglycerides and HDL-cholesterol, independent total PA in a population

at risk of type 2 diabetes (5). Similarly, positive associations between ST, waist circumference, insulin, HOMA-IR and HDL-cholesterol were reported in an older sample with newly diagnosed type-2 diabetes (28). There is a lack of consensus on the role of ST in pathology of cardio metabolic risk factors. Some authors have reported that once total energy expenditure is taken into account the association between ST and cardio-metabolic health are lost. These findings suggest that ST reduces total energy expenditure by displacing other activities that are more energy costly (22,29). Other investigators have found that the mechanism linking ST to glucose metabolism and metabolic health differ from those of PA and may be related to static posture and unloading of large skeletal muscle groups when seated (7,30). Sedentary time is thought to affect glucose homeostasis and lipid metabolism by reducing muscle GLUT-4 content and insulin-stimulated glucose uptake (6) while also reducing LPL activity leading to impaired triglyceride and HDL cholesterol metabolism (7).

Further light activity is associated with marked improvements in cardio-metabolic health (8) while interventions have shown that replacing ST with postural changes such as standing or light ambulatory activity can improve glycaemic control to a greater extent than structured exercise of the same energy cost (31). In the present analysis, sedentary time was associated with HDL cholesterol, however, associations between MVPA and HDL cholesterol were lost after controlling for ST. Similarly, ST was positively associated with systolic and diastolic blood pressure independent of MVPA while no association was found between CPM or MVPA with either blood pressure variable. Associations between PA, ST and blood pressure variables reported by observational studies have been inconsistent (8,12,14). However, experimental studies in overweight/obese populations have suggested that a reduction of sedentary time and the interruption of prolonged sedentary bouts with light or moderate activity are associated with improved systolic and diastolic blood pressure (32).

While physical activity guidelines continue to focus on participation in MVPA (26), our data demonstrated that in a population with pre-diabetes, total volume of PA was as strongly associated with cardio-metabolic health as MVPA. The implications of this finding may be important considering the levels of PA in this population. Light activity may be more readily adopted by individuals with pre-diabetes particularly if they are physically inactive, overweight/obese, or reluctant to engage in structured exercise (31).

The lack of associations observed for all exposure variables with fasting glucose is consistent with previous research (5,8). This finding reflects the fact that the PA predominantly affects peripheral insulin sensitivity, which is responsible for lowering blood glucose levels after an OGTT when most of the glucose is taken up by skeletal muscle (33).

The strengths of this study are the implementation of a 24h accelerometer wear time protocol that resulted in a greater mean waking wear time (15.5 hours) than many studies of a similar nature (5,18,28). Longer monitoring duration provides greater reliability of average activity estimates. This approach also allowed an objective assessment of sleep time using an algorithm to detect sleep onset and wake time from a 24h waist worn accelerometer trace (19). This allowed the study team to control for the confounding effects of sleep on cardio metabolic risk factors (34).

Type 2 diabetes is high on public health agendas with attention on the prevention or delay of diabetes onset and the management of cardio metabolic risk factors (35,36). National and international guidelines focus on first identifying high-risk individuals and second controlling modifiable risk factors such as body weight, diet, ST and PA, through targeted interventions (37,38). This study provides new evidence of associations between PA and ST with cardio metabolic markers in a population to which the results are most applicable.

Whilst this study has numerous strengths it is also important to acknowledge its limitations. First, the cross-sectional design does not allow insight into the direction of causality between each exposure variable and markers of cardio metabolic health and, although we controlled for many potential confounding factors, we did not account for dietary intake or alcohol consumption which may have influenced our results. Secondly, although accelerometers offer more robust assessments of PA than self-report (39), they are not without limitation. Hip worn accelerometers capture most movement during locomotion, but cannot account for upper body movement, movement that occurs during activities such as cycling or weight lifting (40) or distinguish between light intensity activities such as sitting and standing. Furthermore, the accelerometer is removed during water-based activities and contact sports. Therefore, PA may be underestimated. Given the fixed nature of accelerometer-derived variables (sleep, light activity ST and MVPA) as proportions of wake time, time spent in behaviours within the day are inherently collinear; every increase in time spent in one behaviour unavoidably causes a decrease in the time spent in one or a combination of the other behaviours. Thus, it is not possible to include all subcomponents of the day (sleep, sedentary, light activity, MVPA) in a regression model without violating collinearity assumptions. Consequently, in the present study it is not possible to say with certainty that the positive associations observed between cardio-metabolic risk factors and ST are truly independent and not, in fact, negative associations with light activity. Finally, participants in this study were volunteers to a lifestyle intervention from the 8 study sites worldwide, approximately 50% of the study sample were between 55-70 years. Whilst this may limit the applicability of the current findings to the older age-range, it is this group who are at greater risk of type 2 diabetes and are perhaps more likely to participate in such interventions given their greater availability of time to those still in employment.

In conclusion, this study provides new evidence that in a large diverse population of adults with pre-diabetes, objective measures of PA and ST are associated with markers of cardio metabolic health. Furthermore, associations with total PA volume are at least as strong as MVPA. Taken together, these findings suggest that replacing ST with light activity may provide practical approach to improve cardio-metabolic health in a population with low engagement in MVPA.

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Authors contributions and conflict of interest statements

N. Swindell: Conducted analysis and wrote the manuscript. I have read and understood Diabetes Care policy on declaration of interests and declare that I have no competing interests.

K. Mackintosh: Involved in the conception, physical activity analyses and editing of the manuscript. No conflict of interest to declare.

M. McNarry: Involved in conception, analyses and editing of the manuscript. No conflict of interest to declare.

J. W. Stephens: Assisted in the preparation of the manuscript and study design. No conflict of interest to declare.

D. Sluik: Advised on analysis and preparation of the manuscript. No conflict of interest to declare.

M. Fogelholm: Principle investigator of the Helsinki site, conception of the study and editing of the manuscript. No conflict of interest to declare

M. Drummen: Investigator of the Maastricht University site, editing of the manuscript.

I. MacDonald: Principle investigator of the Nottingham site, conception of the study, editing of the manuscript. Interests include: International Life Sciences Institute (ILSI) Europe Member of Dietary Carbohydrates Task Force, member of expert group on 'Efficacy Markers of Diabetes Risk'; and expert group on 'Carbohydrate-Based Recommendations as a Basis for Dietary Guidelines: A Scientific Review' In all cases travel and subsistence are paid but no attendance fees. Nature Publishing Group (Springer Nature) - Editor International Journal of Obesity, honorarium received. Nestle Research Centre Consultancy for Nutrition in the Life Cycle research travel and accommodation reimbursed. Honorarium paid to the University of Nottingham. Nestle Research Centre - Health Evidence Advisory Board travel and

accommodation reimbursed. Honorarium paid to the University of Nottingham. Mars Incorporated-Waltham Centre for Pet Nutrition Peer-review of pet nutrition research projects honorarium received (Amount received per annum over £5,000: no); Mars UK/Europe - Member of Nutrition Advisory Board, and Health and Wellbeing Committee travel and subsistence costs reimbursed. Honorarium paid to the University of Nottingham. Ikea Member of Science and Health Committee travel and subsistence costs reimbursed. Honorarium paid to the University of Nottingham.

J. Martinez: Principle investigator of the Navarra site, editing of the manuscript. No conflict of interest to declare.

A. Raben: Project coordinator of the PREVIEW project, conception of the study and editing of the manuscript. No conflict of interest to declare.

S. Poppit: Principle investigator of the Auckland site, editing of the manuscript. Holds the Fonterra Chair in Human Nutrition at the University of Auckland.

J. Brand-Miller: Principal investigator of the Sydney site, editing of the manuscript. Jennie Brand-Miller declares the following conflict of interest: I am the President of the Glycemic Index Foundation, Director of the Sydney University Glycemic Index Research Service and author of popular books about the glycemic index of foods

T. Larsen: Principal investigator of the Copenhagen site, editing of the manuscript. No conflict of interest to declare

G. Stratton: Study design and conception, supervision of physical activity analyses, editing of the manuscript. No conflict of interest to declare.

T. Handjieva-Darlenska: Principle investigator of the Sofia site, design of the, study, recruitment and implementation of the trial, data interpretation and approval of the draft. No conflict of interest to declare

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Table 1 Descriptive, metabolic and physical activity characteristics of 2,326 pre-diabetic adults from the PREVIEW study

Characteristics	Female (*n*=1570)	Male (*n*= 755)
Age (years)	51.6 ± 11.6	53.5 ± 11.6
Height (m)	1.64 ± 0.07	1.77 ± 0.07
Weight (kg)	95.88 ± 20.33	108.87 ± 20.98
BMI ($kg \cdot m^2$)	35.70 ± 6.76	34.55 ± 6.01
Fat (%)	46.45 ± 5.85	36.67 ± 6.92
Waist (cm)	107.7 ± 14.6	116.8 ± 14.5
Systolic BP (mmHg)	126.98 ± 5.88	133.10 ± 14.8
Diastolic BP (mmHg)	77.07 ± 11.15	80.88 ± 9.96
Fasting insulin ($mU \cdot l^{-1}$)	12.53 ± 6.54	14.03 ± 6.68
Fasting plasma glucose ($mmol \cdot l^{-1}$)	6.08 ± 0.67	6.33 ± 0.66
2 h plasma glucose ($mmol \cdot l^{-1}$)	7.64 ± 2.21	7.73 ± 2.24
HbA_{1c} ($mmol \cdot l^{-1}$)	36.61 ± 4.03	36.73 ± 4.06
HbA_{1c} (%)	5.50 ± 0.37	5.51 ± 0.37
HOMA-IR	3.44 ± 1.90	4.00 ± 2.01
Triglycerides ($mmol \cdot l^{-1}$)	1.45 ± 0.77	1.62 ± 0.82
Total cholesterol ($mmol \cdot l^{-1}$)	5.25 ± 0.99	5.03 ± 0.97
HDL-cholesterol ($mmol \cdot l^{-1}$)	1.33 ± 0.29	1.15 ± 0.23
LDL-cholesterol ($mmol \cdot l^{-1}$)	3.28 ± 0.84	3.16 ± 0.85
CRP (mg/l) ($mg \cdot l^{-1}$)	4.81 ± 4.02	3.46 ± 3.35
Accelerometer variables		
Waking wear Time ($minutes \cdot day^{-1}$)	933.10 ± 83.85	928.40 ± 83.37
Sleep ($minutes \cdot day^{-1}$)	474.69 ± 80.26	471.83 ± 85.16
Sedentary ($minutes \cdot day^{-1}$)	579.46 ± 91.76	617.54 ± 98.06
Light ($minutes \cdot day^{-1}$)	320.84 ± 82.62	280.12 ± 78.20
Moderate ($minutes \cdot day^{-1}$)	25.30 ± 6.88	30.33 ± 20.33
MVPA ($minutes \cdot day^{-1}$)	26.18 ± 17.03	31.58 ± 20.62
CPM ($counts \cdot minute^{-1}$)	294.30 ± 96.77	297.98 ± 17.28
Ethnicity		
Caucasian (%)	86.02	89.9
Asian (%)	2.66	2.71
Black (%)	1.82	1.2
Arabic (%)	0.2	0.3
Hispanic (%)	2.33	1.38
Other (%)	6.61	4.25
Smoking		
Yes (Daily) (%)	10.72	9.57
Sometimes (less than weekly) (%)	3.3	2.93
No (%)	85.98	87.48
Education		
No formal education (%)	0.5	--
Primary/junior school (%)	2.1	2.8
Secondary school (%)	15.1	14.2
Secondary vocational education (%)	17.7	19.2
Higher vocational education (%)	16.4	18.6
University education	40.5	35.6

Other	7.6	9.7
Household income (per year)		
less than £9360, (%)	8.8	5.3
£9360 - £12,479.99 (%)	5.8	2.9
£12,480 - £15,599.99 (%)	5.1	2.5
£15,600 - £18,719.99 (%)	6.5	3.5
£18,720 -£22,879.99 (%)	5.7	4.6
£22,880 - £27,559.99 (%)	8.1	5.9
£27,560 - £32,759.99 (%)	10.6	8.1
£32,760 – £41,079.99 (%)	11.2	10.9
£41,080 – £53,559.99 (%)	13.4	14.2
£53,560 or more (%)	24.9	42

BMI, body mass index; BP, blood pressure; HbA_{1c}, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein; MVPA, moderate to vigorous physical activity; CPM, counts per minute.

Table 2	**Standardized β coefficients for associations between total physical activity** (counts·minute^{-1}) **and cardio metabolic risk factor**			
Characteristics	***B***	***95% Confidence Interval***	***p***	***R^2***
Waist (cm)	-0.179	(-0.224, -0.134)	***	0.2057
Systolic BP (mmHg)	-0.033	(-0.074, 0.007)		0.1927
Diastolic BP (mmHg)	-0.02	(-0.057, 0.017)		0.3448
Fasting insulin (mU·l^{-1})	-0.139	(-0.183, -0.096)	***	0.1293
Fasting glucose (mmol·l^{-1})	-0.028	(-0.074, 0.018)		0.1647
2 h plasma glucose (mmol·l^{-1})	-0.088	(-0.131, -0.045)	***	0.1139
HbA_{1c} (%)	-0.049	(-0.098, -0.001)		0.1337
HOMA-IR	-0.151	(-0.194, -0.107)	***	0.1306
Triglycerides (mmol·l^{-1})	-0.117	(-0.162, -0.071)	***	0.0812
Total cholesterol (mmol·l^{-1})	-0.007	(-0.053, 0.038)		0.095
HDL (mmol·l^{-1})	0.088	(0.048, 0.129)	***	0.1856
LDL (mmol·l^{-1})	0.002	-0.045, 0.049)		0.0566
CRP (mg·l^{-1})	-0.104	(-0.146, -0.062)	***	0.2657

BP, blood pressure; HbA_{1c}, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein. Adjusted for age, sex, ethnicity, smoking, household income, education level, body fat%, wear time, sleep time and intervention centre. *****P<0.05; ******P<0.01; *******P<0.001

Table 3	**Standardized β coefficients for associations between MVPA** (minutes·day^{-1}) **and cardio metabolic risk factors**			
Characteristics	***B***	***95% Confidence Interval***	***p***	***R^2***
Model 1				
Waist (cm)	-0.177	(-0.122, -0.134)	***	0.2046
Systolic BP (mmHg)	-0.005	(-0.047, 0.083)		0.1915
Diastolic BP (mmHg)	-0.007	(-0.044, 0.031)		0.3441
Fasting insulin (mU·l^{-1})	-0.115	(-0.158, -0.072)	***	0.1237
Fasting glucose (mmol·l^{-1})	-0.028	(-0.072, 0.017)		0.1645
2 h plasma glucose (mmol·l^{-1})	-0.069	(-0.112, -0.025)	**	0.1108
HbA_{1c} (%)	-0.046	(-0.096, 0.004)		0.1334
HOMA-IR	-0.122	(-0.166, -0.078)	***	0.1235
Triglycerides (mmol·l^{-1})	-0.091	(-0.138, -0.044)	***	0.0762
Total cholesterol (mmol·l^{-1})	-0.01	(-0.056, 0.035)		0.0952
HDL (mmol·l^{-1})	0.055	(0.009, 0.101)	*	0.1808
LDL (mmol·l^{-1})	0.002	(-0.044, 0.048)		0.0567
CRP (mg·l^{-1})	-0.086	(-0.127, -0.045)	***	0.262
Model 2				
Waist (cm)	-0.127	(-0.173, -0.081)	***	0.2215
Systolic BP (mmHg)	0.02	(-0.026, 0.067)		0.1961
Diastolic BP (mmHg)	0.011	(-0.03, 0.053)		0.3467
Fasting Insulin (mU·l^{-1}) main effect	-0.078	(-0.127, -0.03)	**	0.1337
main effect				
25-45.9 years(reference)	-	-	-	-
46.0 -54.9 years	0.025	(-0.120, 0.170)		0.1313
55.0 -71 years	-0.098	(-0.195, -0.001)	*	0.1313
Fasting glucose (mmol·l^{-1})	-0.014	(-0.063, 0.035)		0.1659
2 h plasma glucose (mmol·l^{-1})	-0.053	(-0.1, -0.006)	*	0.1129
HbA_{1c} (%)	-0.036	(-0.095, 0.023)		0.1345
HOMA-IR	-0.08	(-0.129, -0.031)	**	0.1368
Triglycerides (mmol·l^{-1})	-0.067	(-0.117, -0.017)	**	0.0804
Cholesterol (mmol·l^{-1})	-0.013	(-0.064, 0.037)		0.0953
HDL (mmol·l^{-1})	0.028	(-0.081, 0.383)		0.1867
LDL (mmol·l^{-1})	0	(-0.053, -0.052)		0.0572
CRP (mmol·l^{-1})	-0.061	(-0.108, -0.015)	**	0.2665

Model MVPA, moderate to vigorous physical activity; BMI, body mass index; BP, blood pressure; HbA_{1c}, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein. Model1 adjusted for age, sex, ethnicity, smoking, household income, education level, body fat%, wear time, sleep time, and intervention centre. Model 2 additionally adjusted for sedentary time. *****P<0.05; ******P<0.01; *******P<0.001

Table 4	**Standardized β coefficients for associations between Sedentary time** (minutes·day^{-1}) **and cardio metabolic risk factors**			
Characteristics	***B***	***95% Confidence Interval***	***p***	***R^2***
Model 1				
Waist (cm)	0.215	(0.146, 0.267)	***	0.2088
Systolic BP (mmHg)	0.078	(0.026, 0.131)	**	0.1957
Diastolic BP (mmHg)	0.057	(0.007, 0.106)	*	0.3464
Fasting insulin (mU·l^{-1})	0.155	(0.092, 0.219)	***	0.1291
Fasting glucose (mmol·l^{-1})	0.052	-0.004, 0.108)		0.1656
2 h plasma glucose (mmol·l^{-1})	0.072	(0.015, 0.129)	*	0.1106
HbA_{1c} (%)	0.047	(-0.022, 0.117)		0.1332
HOMA-IR	0.175	(0.114, 0.236)	***	0.1316
Triglycerides (mmol·l^{-1})	0.106	(0.052, 0.16)	***	0.0766
Total cholesterol (mmol·l^{-1})	-0.006	(-0.062, 0.051)		0.0953
HDL (mmol·l^{-1})	-0.103	(-0.165, -0.042	***	0.1859
LDL (mmol·l^{-1})	-0.007	(-0.062, 0.048)		0.0568
CRP (mg·l^{-1})	0.106	(0.039, 0.172)	**	0.2632
Model 2				
Waist (cm)	0.165	(0.109, 0.221)	***	0.2215
Systolic BP (mmHg)	0.086	(0.028, 0.143)	**	0.1961
Diastolic BP (mmHg)	0.061	(0.006, 0.116)	*	0.3467
Fasting insulin (mU·l^{-1})	0.126	(0.055, 0.198)	**	0.1337
Fasting glucose (mmol·l^{-1})	0.047	(-0.014, 0.108)		0.1659
2 h plasma glucose (mmol·l^{-1})	0.053	(-0.009, 0.114)		0.1129
HbA_{1c} (%)	0.034	(-0.045, 0.113)		0.1345
HOMA-IR	0.145	(0.077, 0.213)	***	0.1368
Triglycerides (mmol·l^{-1})	0.08	(0.023, 0.138)	**	0.0804
Total cholesterol (mmol·l^{-1})	-0.011	(-0.074, 0.052)		0.0953
HDL (mmol·l^{-1})	-0.093	(-0.163, -0.022)	*	0.1867
LDL (mmol·l^{-1})	-0.007	(-0.069, 0.055)		0.0572
CRP (mg·l^{-1})	0.083	(0.01, 0.156)	*	0.2665

BMI, body mass index; BP, blood pressure; HbA_{1c}, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein; MVPA, moderate to vigorous physical activity. Model1 adjusted for age, sex, ethnicity, smoking, household income, education level, body fat%, wear time, sleep time, and intervention centre. Model 2 additionally adjusted for MVPA.
*****P<0.05; ******P<0.01; *******P<0.001