The Potential Impact of Displacing Sedentary Time in Adults with Type 2 Diabetes

Catherine L Falconer¹, Angie S Page², Rob C Andrews³, and Ashley R Cooper¹,²

¹National Institute for Health Research, Bristol Biomedical Research Unit in Nutrition, Diet and Lifestyle, Bristol, United Kingdom; ²Centre for Exercise, Nutrition and Health Sciences, School for Policy Studies, University of Bristol, Bristol, United Kingdom; ³School of Clinical Sciences, University of Bristol, Bristol, United Kingdom

Accepted for Publication: 24 February 2015
The Potential Impact of Displacing Sedentary Time in Adults with Type 2 Diabetes

Catherine L Falconer ¹, Angie S Page ², Rob C Andrews ³, and Ashley R Cooper ¹,²

¹National Institute for Health Research, Bristol Biomedical Research Unit in Nutrition, Diet and Lifestyle, Bristol, United Kingdom; ²Centre for Exercise, Nutrition and Health Sciences, School for Policy Studies, University of Bristol, Bristol, United Kingdom; ³School of Clinical Sciences, University of Bristol, Bristol, United Kingdom

Correspondence to:
Dr Catherine Falconer
NIHR Biomedical Research Unit in Nutrition, Diet and Lifestyle
Level 3, University Hospitals Bristol Education and Research Centre
Upper Maudlin Street
Bristol United Kingdom
BS2 8AE
Tel: 0117 3421759
Email: Catherine.falconer@bristol.ac.uk

The research was supported by the National Institute for Health Research (NIHR) Bristol Nutrition Biomedical Research Unit based at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The authors declare that there is no conflict of interest associated with this manuscript. Publication of these results of the present study does not constitute an endorsement by the American College of Sports Medicine.

Running title: Potential impact of displacing sedentary time
This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.
Abstract

**Purpose:** Sedentary time, in particular prolonged unbroken sedentary time is detrimental to health and displaces time spent in either light or moderate intensity physical activity. This cross-sectional study aims to identify the potential impact of reallocating time from sedentary behaviours to more active behaviours on measures of body composition and metabolic health in people with type 2 diabetes. **Methods:** Participants were 519 adults with newly diagnosed type 2 diabetes who had been recruited to the Early Activity in Diabetes (Early ACTID) randomised controlled trial. Waist-worn accelerometers were used to obtain objective measurement of sedentary time, light physical activity (LPA), and moderate-to-vigorous physical activity (MVPA) at baseline alongside clinical measurements and fasting blood samples to determine cholesterol, triglycerides, HOMA-IR and glucose. Isotemporal substitution modelling was performed to determine the potential impact of reallocating 30 minutes of sedentary time accumulated in a single bout (long-bout) with 30 minutes of interrupted sedentary time, LPA or MVPA. **Results:** Sedentary time accounted for 65% of the waking day, of which 45% was accumulated in prolonged (≥30 minute) bouts. Re-allocation of 30 minutes of long-bout sedentary time with 30 minutes of short-bout sedentary time was associated with lower BMI (adjusted β -0.60 95% CI: -1.00, -0.21) and waist circumference (WC) (adjusted β -1.16 95% CI -2.08, -0.25). Stronger effects were seen for LPA and MVPA. Re-allocation of 30 minutes of long-bout sedentary time with LPA was associated with higher HDL-cholesterol (adjusted β 0.02 95% CI 0.00, 0.03mmol/L). **Conclusions:** Encouraging adults with newly diagnosed type 2 diabetes to break up prolonged periods of sedentary time may be an effective strategy for improving body composition and metabolic health. **Keywords:** Sedentary, type 2 diabetes, physical activity, accelerometer, sedentary breaks.
Introduction

Regular physical activity is recommended for the prevention and management of type 2 diabetes due to its beneficial effects on weight control, glucose metabolism and lipid profiles (5, 18, 20). However, people with type 2 diabetes tend to have low levels of activity, with few achieving the recommended 30 minutes moderate-to-vigorous activity (MVPA) per day (6, 19). In addition, lifestyle interventions to increase physical activity often have weak effects, with most people failing to achieve increases in MVPA sufficient to confer health benefits (2). Recently, increasing emphasis has been placed on the role sedentary time may play in the aetiology of diabetes development (11, 26). Substantial cross-sectional and longitudinal evidence exists to support the association between sedentary time, impaired metabolic health, diabetes and mortality, associations which occur independently of time spent in MVPA (6, 9, 14, 21, 26). Furthermore, there is evidence to suggest that the pattern in which sedentary time is accumulated may be important, with interruptions in sedentary time being beneficial for health (6, 7) and prolonged bouts of unbroken sedentary time being particularly detrimental (15). However, the duration and frequency of bouts of continuous sedentary time in people with diabetes is not known.

During waking hours, individuals participate in a range of activities varying in intensity between sedentary, (defined as ‘any waking behaviour characterised by an energy expenditure of less than or equal to 1.5 metabolic equivalents while in a sitting or reclining posture” (25)), and those which are more vigorous in nature (23). Total time in a day is finite, and therefore these activities are inter-dependent; an increase in time spent in one activity displaces time spent in another activity. The benefit of a particular intensity of activity will be dependent not only upon the type of activity it is (sedentary, light or MVPA) but also on the activity intensity it displaces. Few
studies to date have considered this inter-dependency, instead using statistical adjustment to either present the effects of the activity intensities in isolation or estimates of the independent associations of the different activity intensities in turn.

Isotemporal substitution methods, originally developed in nutritional epidemiology, take into account the finite nature of time and the inter-relationships between activities, thus giving estimations of the effect of ‘substitution’ of one activity type for another (23, 24). For example these models allow you to examine the potential impact of reallocating 30 minutes of sedentary time with 30 minutes of MVPA, while keeping total time constant. Although these substitutions are often cross-sectional and therefore causality cannot be assumed, the interpretation is more readily interpretable to public health compared to a standard regression model. These methods have previously been applied to data from both the Whitehall II and National Health and Nutrition Survey (NHANES) cohorts to show the beneficial health effects of replacing prolonged sedentary time with MVPA or LPA (4, 12). The health enhancing effects of activities depend on the type of activity performed, the type of activity displaced and the population of interest. Adults with type 2 diabetes commonly spend a large portion of their day sedentary (6, 9), some of which is likely accumulated in prolonged bouts, considered to be more detrimental to health. The aims of this study are therefore to use isotemporal methods to examine the substitution effects of the different activity intensity types on metabolic health by artificially displacing a fixed duration of one activity intensity with a fixed duration of another. This type of analysis will allow understanding of the potential health benefits of reallocating sedentary time to alternative, more intense activities in a population with type 2 diabetes. Interventions to date have had limited success in increasing MVPA in people with type 2 diabetes, and therefore it is important
to consider whether there is a potential benefit of replacing sedentary time with light intensity activity.

Methods

This paper presents a cross-sectional, secondary data analysis from baseline data collected as part of the Early Activity in Diabetes (Early Actid) study, a randomised controlled trial of physical activity and diet in the early management of type 2 diabetes. This study has been described in detail previously (1). Briefly, participants with newly diagnosed type 2 diabetes were recruited through primary care in the South West of England. Eligible participants had been diagnosed with type 2 diabetes in the previous 6 months and were aged 30-80 years at diagnosis. Participants were excluded on the basis of uncontrolled diabetes (HbA1c > 10% [85.8mmol/mol]), blood pressure >180/100mmHg, LDL-cholesterol >4mmol/l, and body mass index (BMI) < 25kg/m² or body weight >180kg. Telephone screening was performed on 1,634 participants, of whom 712 were eligible for face-to-face screening and 593 were enrolled in the study. All participants provided written informed consent prior to participation and ethical approval was obtained from the Bath Hospital Research Ethics Committee (05/Q2001/5). This study is registered (number ISRCTN92162869).
Physical activity and sedentary time

Participants wore a uni-axial accelerometer (Actigraph GT1M; Actigraph LLC, Pensacola, FL, USA) set to record data every minute on a waist-worn belt for seven days during waking hours except when swimming or bathing. Accelerometer data were downloaded using Actilife software (version 1.0.52 Actigraph LLC) and were processed using Kinesoft (version 3.3.62; Kinesoft, Saskatoon, SK, Canada) to generate outcome variables (mean daily minutes of LPA, MVPA, total sedentary time, long-bout sedentary time and short-bout sedentary time). Long-bout sedentary time was defined as sedentary time accumulated in bouts of ≥30 consecutive minutes while short-bout sedentary time was calculated as sedentary time accumulated in bouts of <30 minutes. From these data, we calculated the average daily minutes in short and long-sedentary bouts, LPA and MVPA. For isotemporal analysis, data are expressed in units of 30 minutes per day.

For comparison with other studies, thresholds of ≥1,952 counts per minute (cpm) for MVPA, ≥100 and <1952 for light physical activity (LPA) and <100cpm for sedentary time were used to compute the average number of minutes spent in each behaviour (15, 16). The activity cut-points applied were developed and validated in a healthy adult population to reflect intensities of activity which equate to light (<3 Metabolic Equivalents (METs)), moderate (3-5.99 METs) and vigorous (6.0-8.99 METs) intensity (10). A cut-point of <100cpm was selected to classify sedentary time as this has previously been shown to include activities such as sitting or working quietly (15). Non-wear time was defined as a period of ≥60 minutes with continuous zero values, and days with at least 10 hours of measurement were considered valid. For inclusion in the analyses, participants were required to record at least three valid days of accelerometer data (6).
Metabolic, anthropometric and demographic outcomes

Body weight and height were measured to the nearest 0.1 kg and 0.5 cm, respectively with participants wearing light, indoor clothing and without shoes. Body Mass Index (BMI) was calculated as weight divided by height in metres squared (kg/m$^2$). Waist circumference was measured at the midpoint between the lowest rib and the anterior iliac. Blood pressure was measured in a seated position using an automated blood pressure monitor (Omron, Healthcare, Henfield, UK). Venous blood samples were obtained following an overnight fast for the measurement of HDL-cholesterol, triglycerides (TG), glucose and insulin levels, and HOMA of insulin resistance (HOMA-IR) was calculated using the HOMA-2 computer model (22). All metabolic and anthropometric measurements were performed in a fasted state, during a morning visit to the clinic.

Social deprivation was measured using the Index of Multiple Deprivation (IMD) score, a measure of local area deprivation based on residents postcode. Information on ethnicity and medication use was obtained by the research nurse.

Statistical analysis

Descriptive characteristics are presented as mean and standard deviation (SD) unless otherwise stated. Data were checked for normality using visual inspection of histograms.

Standard linear regression analyses were used to explore cross-sectional associations between long-bout sedentary time ($\geq$30 minutes continuous sedentary time) and short-bout sedentary time, LPA and MVPA with markers of metabolic health. Unstandardized regression coefficients
are presented. No significant interactions by gender were present and therefore results from pooled analysis are presented.

The isotemporal substitution regression approach is described in detail by Mekary et al (23). Firstly, each intensity of physical activity was fitted in isolation into a single model to give an estimation of the total association for each activity. Then, isotemporal substitution models were fitted for metabolic markers which had demonstrated an association with activity in the single activity models. A model is fitted which includes all activity intensities and a variable for total time. By eliminating one activity component from the model (e.g. long-bout sedentary time) at a time, the coefficient can be interpreted as the effect of substituting a specific duration of activity per day in a specific intensity with the same duration of another intensity. By holding total time constant and expressing the behaviours as a function of 30 minute time periods, the models estimate the effect of re-allocating a 30 minutes a day in a less intense activity (e.g. sedentary time) with 30 minutes/day in a more intense activity (e.g. MVPA) on metabolic markers. In this study, these models fit artificial cross-sectional associations and do not estimate causal associations of individuals replacing time at one intensity with another, instead providing estimates of the mean shift in the outcome that would be observed cross-sectionally when time spent in an active behaviour is artificially increased. All regression models were adjusted for age, sex, deprivation score, ethnicity, accelerometer wear-time, BMI (where appropriate) and relevant lipid, blood pressure or diabetes-lowering medication (dichotomised as medication yes/no). All analyses were conducted using STATA 13 (College Station, TX; StataCorp).
Results

A total of 593 participants were randomised to the Early-ACTID study. Of these, 519 (88%) fulfilled the accelerometer inclusion criteria and were included in the current analyses.

The baseline demographic, metabolic and physical activity characteristics of the participants are shown in Table 1 (n=519). On average participants spent 25.4 ± 18.9 minutes of the day in MVPA and 272.5 ± 75.4 minutes in LPA. Sedentary time accounted for 65% of the day, of which 46% was accrued in bouts >30 minutes in length.

The results of the regression analyses for long-bout sedentary time, short-bout sedentary time, LPA and MVPA are displayed in table 2. Following adjustment for confounders, long-bout sedentary time was associated with a higher BMI (adjusted β 0.41 95% CI; 0.26, 0.56), higher waist circumference (adjusted β 1.03 95% CI: 0.69, 1.37) and a lower HDL-cholesterol (adjusted β -0.02 95% CI -0.03, -0.01). No associations with other biomarkers were observed. Short-bout sedentary time, LPA and MVPA were all associated with a lower BMI with the strongest effect seen for MVPA (adjusted β -2.15 95% CI: -2.87, -1.44). Associations were also seen between short-bout sedentary time, LPA and MVPA and a lower waist circumference. There were suggestions of an association between LPA and HDL-cholesterol (adjusted β 0.21 95% CI: 0.01, 0.03). No other associations between LPA, MVPA and metabolic markers were observed.

The results of the isotemporal substitution analyses are displayed in table 3. Results are shown for BMI, waist circumference, and HDL-cholesterol as these biomarkers were associated with the activity spectrum in simple regression analyses. In cross-sectional analyses, re-allocating 30 minutes/day in long-bouts of sedentary time to 30 minutes of short-bout of sedentary time, LPA, or MVPA was associated with a lower BMI and waist circumference. The associations were
stronger than seen in the single activity models. Re-allocation of 30 minutes of long-bout sedentary time with 30 minutes of short-bout sedentary time was associated with a lower BMI (adjusted $\beta -0.60$ 95% CI: -1.00, -0.21) and waist circumference (adjusted $\beta -1.16$ 95% CI: -2.08, -0.25). Re-allocating 30 minutes of long-bout sedentary time with LPA was also associated with a higher HDL-cholesterol (adjusted $\beta 0.02$ 95% CI: 0.01, 0.03). Re-allocating 30 minutes of short-bout sedentary time and LPA with 30 minutes of MVPA were associated with a lower BMI and waist circumference.

**Discussion**

The results of this study demonstrate that adults with newly diagnosed type 2 diabetes spend 65% of the day sedentary, of which 46% of sedentary time is accumulated in prolonged bouts of more than 30 minutes. MVPA accounted for less than 4% of the waking day. Time spent in long-bout sedentary time ($\geq$30 minutes), was shown to be detrimentally associated with BMI and WC, while short-bout sedentary time, LPA and MVPA had health enhancing effects. The greatest effects were shown for MVPA. Light-intensity physical activity was shown to be beneficial for HDL-cholesterol.

Cross-section isotemporal substitution analysis suggested that reallocation of 30 minutes of long-bout sedentary time with 30 minutes of short-bout sedentary time, LPA or MVPA could have a beneficial effect on BMI and WC. The strongest associations were shown for MVPA; however, isotemporal regression suggests that reallocation of just 30 minutes/day long-bout sedentary time with 30 minutes of short-bout sedentary time, achieved through frequent breaks, may have a favourable inverse relationship with BMI and WC. This finding, although surprising, is in
agreement with previous research which found breaks in sedentary time to be beneficially associated with metabolic risk, independently of total time sedentary and MVPA (15). From a public health perspective this is an important message to people who perhaps struggle to increase levels of MVPA but would be able to break up prolonged periods of sitting with standing or light walking. Furthermore replacing 30 minutes long-bout sedentary time with LPA was associated with a lower HDL-cholesterol, an effect that was not observed for MVPA.

Previous research using these methods in a sample of healthy, older adults from the Whitehall II study, has shown that replacing 10 minutes of sedentary time with the equivalent amount of MVPA was associated with favourable effects on markers of metabolic health such as HbA1C and BMI (12). A further study in the National Health and Nutrition Survey (NHANES) cohort demonstrated that reallocation of sedentary time to sleep, LPA or MVPA was associated with improved health outcomes including reduced waist circumference, and improved triglycerides (TG) (4). The strongest effects were with MVPA suggesting that MVPA may be the most potent health enhancing activity (4). In contrast to this, we did not observe any associations between LPA, MVPA and triglycerides, HOMA, LDL or fasting plasma glucose. One potential explanation for the lack of effect observed for metabolic markers in the present study is that the previous research has been conducted on healthy populations, free from diabetes and with normal cardiovascular risk profiles (4, 12). In comparison, participants in the current study were more obese and had poorer metabolic risk profiles. Furthermore, the levels of physical activity observed in the current study were very low and it may be that the apparent lack of effect of MVPA demonstrated may be a reflection of the low levels of MVPA exhibited by participants.

The beneficial effects of LPA have previously been demonstrated in an older population with improvements in HRQOL observed following reallocation of sedentary time with LPA (3).
These results suggest that for some populations such as older people and people with type 2 diabetes, LPA might be sufficiently intense, if displacing prolonged sedentary time, to see health benefits. This supports experimental evidence obtained in a sample of healthy adults which suggested displacement of sitting time with regular light intensity exercise had a greater positive effect on insulin level and plasma lipids than a single 1 hour bout of more intense physical activity (8). The mechanisms by which sedentary behaviour exerts its detrimental effect on metabolic health are still disputed but possibilities include changes in lipoprotein lipase (LPL) activity, reduced fatty acid clearance and a loss of adenosine monophosphate-activate protein kinase (AMPK) activity (8, 13) as a result of reduced muscle activity. Although further experimental work is needed to fully understand the mechanisms involved, findings from the current study that breaking up prolonged sedentary time with frequent breaks and LPA is sufficient to confer metabolic benefits would support the mechanisms suggested.

This study has several strengths. The sample includes a relatively large number of adults with newly diagnosed type 2 diabetes with a large range of outcome measures including objectively measured physical activity and time spent in sedentary behaviour. However, objective measurement techniques such as accelerometers are still prone to measurement error, especially in the measurement of sedentary behaviours. Waist-worn accelerometers are limited by their inability to detect differences between sitting and standing, and therefore the measurement of sedentary time and specifically sedentary bout time may be overestimated in this sample. Furthermore, there is some discrepancy in the literature about the accelerometer thresholds used to define sedentary time (6, 12) and the data reduction techniques used to discard continuous periods of zero values, generally interpreted as time when the accelerometer has been removed. Sedentary behaviour refers to low-intensity activities and rest, therefore zero counts on the
accelerometer could in fact be a ‘real’ value. Decisions about the data reduction techniques are therefore particularly important when considering sedentary bout time to ensure that continuous zero counts discarded are in fact non-wear time and not continuous sedentary time.

This study is also limited by its cross-sectional design and inability to infer causality. For the single activity models in particular, there is a risk of reverse causality between BMI and activity behaviours. The cross-sectional isotemporal substitution methods control for total time in the models; however, the substitution that is performed is an artificial replacement of one activity type with another and therefore the results should be interpreted accordingly. We did not record time asleep, another discretionary behaviour; however, we assume the accelerometer is only worn during waking hours and continuous periods of zero counts are removed from the analysis and therefore this is unlikely to affect the current study. In addition, we did not include measures of dietary intake in the models. Sedentary behaviour may mediate some of its effect on body composition through dietary intake; there is some suggestion that sedentary behaviour is associated with increased consumption of high-fat, energy dense foods (17). The measure of social deprivation provides a measure of multiple deprivation experienced by people living within an area, therefore it is a population level measure and may have limitations when applied at the individual level.

In conclusion this study demonstrates an association between long-bout sedentary time and markers of metabolic health. Participants spent over 9 hours of the waking day sedentary, and there is accumulating evidence from this study and others (6, 15) that time spent in prolonged sedentary behaviours is particularly harmful. In the present study, artificial reallocation of long-bout sedentary time to either short-bout sedentary time, LPA and MVPA was associated with improvements in BMI and WC. Stronger associations were seen with MVPA but these results
estimate displacement of long-bout sedentary time with frequently interrupted, short-bout sedentary time could be sufficient for beneficial associations with BMI and WC in this population. Therefore, messages aimed at replacing long sedentary bouts with LPA or short-bout sedentary time through frequent breaks may be an alternative public health message for improving health in people with type 2 diabetes. Further work using prospective and experimental study designs is needed to identify the frequency and duration of breaks in sedentary time required for benefits to be seen.
Author contributions: CLF performed the statistical analysis, interpreted the data, drafted the manuscript and approved the final version to be published. ASP contributed to drafting the manuscript, read and approved the final manuscript. ARC and RCA conceived the project and participated in the design and coordination of the project. ARC contributed to the design of the analysis and drafting of the manuscript. All authors read and approved the final manuscript. ARC is the guarantor of this work, and as such, has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding source: The research was supported by the National Institute for Health Research (NIHR) Bristol Nutrition Biomedical Research Unit based at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Conflict of interest: The authors declare that there is no conflict of interest associated with this manuscript. Publication of these results of the present study does not constitute an endorsement by the American College of Sports Medicine.
References

1. Andrews RC, Cooper AR, Montgomery AA et al. Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. *The Lancet*. 378(9786):129-39.

2. Avery L, Flynn D, van Wersch A, Sniehotta FF, Trenell MI. Changing Physical Activity Behavior in Type 2 Diabetes: A systematic review and meta-analysis of behavioral interventions. *Diabetes Care*. 2012;35(12):2681-9.

3. Balboa-Castillo T, Leon-Munoz L, Graciani A, Rodriguez-Artalejo F, Guallar-Castillon P. Longitudinal association of physical activity and sedentary behavior during leisure time with health-related quality of life in community-dwelling older adults. *Health and Quality of Life Outcomes*. 2011;9(1):47.

4. Buman MP, Winkler EAH, Kurka JM et al. Reallocating Time to Sleep, Sedentary Behaviors, or Active Behaviors: Associations With Cardiovascular Disease Risk Biomarkers, NHANES 2005–2006. *American Journal of Epidemiology*. 2014;179(3):323-34.

5. Colberg SR, Sigal RJ, Fernhall B et al. Exercise and Type 2 Diabetes: The American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes care*. 2010;33(12):e147-e67.

6. Cooper AR, Sebire S, Montgomery AA et al. Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes. *Diabetologia*. 2012;55(3):589-99.

7. Dunstan DW, Kingwell BA, Larsen R et al. Breaking Up Prolonged Sitting Reduces Postprandial Glucose and Insulin Responses. *Diabetes care*. 2012;35(5):976-83.

8. Duvivier BMFM, Schaper NC, Bremers MA et al. Minimal Intensity Physical Activity (Standing and Walking) of Longer Duration Improves Insulin Action and Plasma Lipids.
More than Shorter Periods of Moderate to Vigorous Exercise (Cycling) in Sedentary Subjects When Energy Expenditure Is Comparable. *PLoS ONE*. 2013;8(2):e55542.

9. Falconer CL, Cooper AR, Walhin JP et al. Sedentary time and markers of inflammation in people with newly diagnosed type 2 diabetes. *Nutrition, Metabolism and Cardiovascular Diseases*. 2014;24(9):956-62.

10. FREEDSON PS, MELANSON E, SIRARD J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Medicine & Science in Sports & Exercise*. 1998;30(5):777-81.

11. Grøntved A HFB. Television viewing and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: A meta-analysis. *JAMA*. 2011;305(23):2448-55.

12. HAMER M, STAMATAKIS E, STEPTOE A. Effects of Substituting Sedentary Time with Physical Activity on Metabolic Risk. *Medicine & Science in Sports & Exercise*. 2014;46(10):1946-50 10.249/MSS.00000000000000317.

13. Hamilton MT, Hamilton DG, Zderic TW. Role of Low Energy Expenditure and Sitting in Obesity, Metabolic Syndrome, Type 2 Diabetes, and Cardiovascular Disease. *Diabetes*. 2007;56(11):2655-67.

14. Healy G, Wijndaele K, Dunstan D et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes care*. 2008;31:369 - 71.

15. Healy GN, Dunstan DW, Salmon J et al. Breaks in Sedentary Time: Beneficial associations with metabolic risk. *Diabetes care*. 2008;31(4):661-6.

16. Healy GN, Matthews CE, Dunstan DW, Winkler EAH, Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003–06. *European Heart Journal*. 2011;32(5):590-7.

17. Heinonen I, Helajärvi H, Pahkala K et al. Sedentary behaviours and obesity in adults: the Cardiovascular Risk in Young Finns Study. *BMJ Open*. 2013;3(6).
18. Hu FB, Stampfer MJ, Solomon C et al. Physical Activity and Risk for Cardiovascular Events in Diabetic Women. *Annals of Internal Medicine*. 2001;134(2):96-105.

19. Jakicic JM, Gregg E, Knowler W et al. Activity patterns of obese adults with type 2 diabetes in the look AHEAD study. *Medicine and science in sports and exercise*. 2010;42(11):1995.

20. Jeon C, Lokken R, Hu F, van Dam R. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes care*. 2007;30:744 - 52.

21. Katzmarzyk P, Church T, Craig C, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Med Sci Sport Exer*. 2009;41(5):998 - 1005.

22. Levy JC, Matthews DR, Hermans MP. Correct homeostasis model assessment (HOMA) evaluation uses the computer program. *Diabetes care*. 1998;21(12):2191-2.

23. Mekary R, Willett W, Hu F, Ding E. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol*. 2009;170:519 - 27.

24. Mekary RA, Lucas M, Pan A et al. Isotemporal Substitution Analysis for Physical Activity, Television Watching, and Risk of Depression. *American Journal of Epidemiology*. 2013;178(3):474-83.

25. Sedentary Behaviour Research Network. Standardized use of the terms 'sedentary' and 'sedentary behaviours' *Applied Physiology Nutrition and Metabolism*. 2012;37:540-2.

26. Wilmot EG, Edwardson CL, Achana FA et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia*. 2012;55(11):2895-905.
Table 1. Demographic, metabolic and physical activity characteristics of participants (n=519)

| Variable                               | Total (n=519)       |
|----------------------------------------|---------------------|
| Age                                    | 59.9 ± 9.9          |
| BMI (kg/m²)                            | 31.6 ± 5.7          |
| Waist circumference (cm)               | 106.9 ± 12.5        |
| IMD Score                              | 15.8 ± 11.9         |
| Ethnic group (%)                       |                     |
| White                                  | 96.0                |
| On diabetes medication (%)             | 38.1                |
| On lipid medication (%)                | 63.9                |
| On blood pressure medication (%)       | 61.9                |
| Accelerometer wear time (mins)         | 841.3 ± 73.2        |
| Mean MVPA/day (mins)                   | 25.4 ± 18.9         |
| Mean LPA/day (mins)                    | 272.5 ± 75.4        |
| Mean SED/day (mins)                    | 543.4 ± 83.3        |
| Mean long bout SED/day (mins) c,d      | 250.7 ± 93.7        |
| Mean short-bout SED/day (mins) c       | 169.0 ± 41.6        |
| HbA1c (%)                              | 6.7 ± 0.9           |
| HDL- cholesterol (mmol/l)              | 1.29 ± 0.3          |
| LDL-cholesterol (mmol/l)               | 2.3 ± 0.8           |
| Triglycerides                          | 1.7 ± 0.9           |
| Insulin (pmol/l)                       | 17.8 ± 10.6         |
| HOMA-IRf                               | 5.9 ± 3.8           |
| Fasting plasma glucose                 | 7.4 ± 1.5           |

*a* moderate to vigorous physical activity (MVPA); *b* Light physical activity (LPA); *c* Sedentary behaviour (SED) *d* at least 30 consecutive minutes of sedentary time; *e* Glycosylated haemoglobin (HbA1c); *f* Homeostatic model assessment of Insulin Resistance (HOMA-IR)
Table 2. Associations of each 30 minutes/day of long sedentary bouts (>=30 minutes in length), short-bout sedentary time, light intensity activity and MVPA with cardio-metabolic biomarkers in adults with newly diagnosed type 2 diabetes (n=519)

| Regression coefficients (95% CI) |
|---------------------------------|
|                                |
| **Sedentary bouts (>30 minutes)** | **Short bout (<30 minutes) sedentary time** | **Light intensity** | **MVPA** |
| Body Mass Index (kg/m²)^(a)     | 0.41 (0.26, 0.56) | -0.71 (-1.11, -0.33) | -0.41 (-0.61, -0.22) | -2.15 (-2.87, -1.44) |
| Waist circumference (cm)^(a)    | 1.03 (0.69, 1.37) | -1.63 (-2.51, -0.76) | -1.15 (-1.60, -0.70) | -4.49 (-6.16, -2.82) |
| HbA1c (%)^(b)                   | 0.01 (-0.02, 0.04) | 0.04 (-0.03, 0.11) | -0.02 (-0.06, 0.02) | -0.10 (-0.23, 0.04) |
| HDL-cholesterol (mmol/L)^(b)    | -0.02 (-0.03, -0.01) | 0.02 (-0.00, 0.04) | 0.02 (0.01, 0.03) | 0.03 (-0.01, 0.07) |
| LDL (mmol/L)^(b)                | 0.00 (-0.02, 0.02) | 0.02 (-0.03, 0.08) | -0.01 (-0.04, 0.02) | 0.07 (-0.04, 0.17) |
| Triglycerides (mmol/L)^(b)      | 0.01 (-0.01, 0.04) | -0.04 (-0.11, 0.03) | -0.02 (-0.06, 0.02) | -0.05 (-0.19, 0.09) |
| Fasting plasma glucose (mmol/L)^(b) | 0.00 (-0.04, 0.05) | 0.03 (-0.08, 0.15) | -0.01 (-0.07, 0.05) | -0.01 (-0.24, 0.21) |
| HOMA-IR^(b)                     | 0.06 (-0.04, 0.16) | 0.09 (-0.16, 0.34) | -0.11 (-0.24, 0.02) | -0.34 (-0.83, 0.15) |

^(a) adjusted for sex, age, ethnic group, IMD score and accelerometer wear time; ^(b) additionally adjusted for relevant diabetes or lipid-lowering drugs. Bold typeface indicates statistical significance at the p<0.05 level.
Table 3. Estimated impact of reallocating 30 minutes/day of less active behaviours for 30 minutes/day of more active behaviours in adults with newly diagnosed type 2 diabetes (n= 519)

| Replace sedentary bouts with | Body Mass Index (kg/m²) | Waist circumference (cm) | HDL-cholesterol (mmol/L) |
|------------------------------|-------------------------|--------------------------|--------------------------|
| Sedentary non-bouts          | -0.60 (-1.0, -0.21)     | -1.16 (-2.08, -0.25)     | 0.01 (-0.02, 0.03)       |
| Light intensity              | -0.26 (-0.47, -0.05)    | -0.87 (-1.35, -0.39)     | 0.02 (0.01, 0.03)        |
| MVPA                         | -2.19 (-2.89, -1.49)    | -4.56 (-6.19, -2.93)     | 0.03 (-0.01, 0.08)       |

Replace sedentary non-bouts with

| Light intensity              | -0.01 (-0.38, 0.36)     | -0.44 (-1.30, 0.41)      | 0.01 (-0.01, 0.04)       |
| MVPA                         | -1.87 (-2.59, -1.14)    | -3.97 (-5.65, -2.28)     | 0.03 (-0.02, 0.07)       |

Replace light with

| MVPA                         | -2.00 (-2.74, -1.26)    | -3.93 (-5.65, -2.21)     | 0.02 (-0.03, 0.06)       |

\(^a^{adjusted for sex, age, ethnic group, IMD score and accelerometer wear time; \(^b^{additionally adjusted for relevant diabetes or lipid-lowering drugs. Bold typeface indicates statistical significance at the p<0.05 level.}