

1 **Measuring group and individual relationship between**
2 **patterns in sedentary behaviour and glucose in type 2**
3 **diabetes adults**

4 Kathryn A. McMillan^{1,2}, Aye C. Paing³, Alison F. Kirk¹, Allan Hewitt¹, Sandra
5 MacRury⁴, Andrew Collier³, Sebastien F.M. Chastin^{3,5}

6 **Author affiliations:** ¹Physical Activity for Health Group, School of Psychological Sciences
7 and Health, University of Strathclyde, Glasgow, UK. ²Digital Health and Wellness Group,
8 Department of Computer and Information Science, University of Strathclyde, Glasgow, UK.

9 ³School of Health and Life Sciences, Glasgow Caledonian University, Glasgow, UK.

10 ⁴Highland Diabetes Institute, University of Highlands and Islands, Inverness, UK.

11 ⁵Department of Movement and Sports Science, Ghent University, Ghent, Belgium

Kathryn Anne McMillan, Ph.D Digital Health and Wellness Group LT14.14a Livingstone Tower University of Strathclyde Glasgow kathryn.mcmillan@strath.ac.uk 0141 548 4101	Aye Chan Paing School of Health and Life Sciences Room-257, Govan Mbeki Building Glasgow Caledonian University Glasgow AyeChan.Paing@gcu.ac.uk 0141 331 3357
Dr Alison Kirk, Ph.D Physical Activity for Health Group Room 532 Graham Hills Building University of Strathclyde Glasgow alison.kirk@strath.ac.uk 0141 548 4153	Dr Allan Hewitt, Ph.D Physical Activity for Health Group Room 538 Graham Hills Building University of Strathclyde Glasgow allan.hewitt@strath.ac.uk 0141 548 3255
Professor Sandra MacRury, MD Highland Diabetes Institute University of Highlands and Islands Inverness sandra.mcarury@uhi.ac.uk 01463 279 583	Professor Andrew Collier School of Health and Life Sciences Govan Mbeki Building Glasgow Caledonian University Glasgow Collier, andrew.collier@aaaht.scot.nhs.uk
Professor Sebastien Chastin School of Health and Life Sciences Govan Mbeki Building Glasgow Caledonian University Glasgow sebastien.chastin@gcu.ac.uk	

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1 **Corresponding author:** Kathryn Anne McMillan, Room LT1414a, Livingston Tower, 16
2 Richmond Street, Glasgow, G1 1XQ. E-mail address: kathryn.mcmillan@strath.ac.uk

3 **Abbreviations:** (FGM) Flash Glucose Monitoring, (UEC) University Ethics Committee,
4 (COV) Coefficient of variation, (BMI) Body Mass Index

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17

1 **Abstract**

2 **Aims:** Explore the relationship between patterns in sedentary behaviour and glucose in adults
3 with Type 2 diabetes.

4 **Methods:** 37 adults with Type 2 diabetes managed with diet and/or anti-diabetes medication
5 (not insulin) were recruited. Participants wore an activPAL accelerometer and FreeStyle
6 Libre flash glucose monitor for continuous measurement of activity and glucose for
7 24hours/day for 3-14days whilst documenting sleep, food and medication. The relationship
8 between daily patterns of sedentary behaviour and sedentary breaks with glucose was
9 investigated using correlation analysis. Regression analysis was used to investigate these
10 relationships at an individual level.

11 **Results:** Participants (mean age 62.8 ± 10.5 yrs, BMI 29.6 ± 6.8 kg/m²) spent 64% of their day
12 sedentary, 44.7% of sedentary bouts were 30-60 minutes in duration and mean bout duration
13 was 47.2 minutes. No association between mean glucose and sedentary proportion (total
14 sedentary time) was identified. Mean glucose and glucose standard deviation were positively
15 correlated with sedentary bout duration (both $p < 0.05$). Individual regression analysis showed
16 increased sedentary time is associated with increased mean glucose in 25 (68%) of the
17 participants, with a negative association being shown in 12 (32%) of the participants.

18 **Conclusions:** In analysis of the whole group, sedentary bout duration but not sedentary
19 proportion was associated with mean glucose and glucose variability. Individual regression
20 analysis identified a different relationship pattern for the majority of participants. This is the
21 first study to identify an individualised response to activity behaviour and highlights the
22 importance of conducting individual analysis when using continuous measurement methods.

1 **Key Points:**

- 2 1. A reduction in prolonged bouts of sedentary behaviour are beneficial to good
3 glycaemic control in people with Type 2 diabetes.
- 4 2. There is no relationship between proportion of time spent sedentary and mean
5 glucose.
- 6 3. Longer bouts of sedentary behaviour is associated with increased glucose variability.
- 7 4. There is an individual nature in the relationship between sedentary behaviour and
8 glucose.
- 9 5. Further research is required using digital wearable technologies to explore these
10 individual relationships in more detail and to understand how the technology and
11 information obtained can be used to support and tailor health care interventions.

1 **Introduction**

2 There is substantial evidence documenting the benefits of frequent physical activity for
3 people with Type 2 diabetes [1, 2, 3] including improvements in glycaemic control and
4 insulin sensitivity [2, 3]. Sedentary behaviour, characterised as any waking behaviour in a
5 sitting or reclined posture with a resultant energy expenditure of ≤ 1.5 metabolic equivalents
6 [4], has been associated with poorer glucose outcomes, independent of physical activity
7 levels [5]. In adults with Type 2 diabetes, regular physical activity breaks in sedentary time of
8 3-minutes of light intensity walking or 3-minutes of simple resistance activities every 30
9 minutes significantly reduced glucose, compared to continuous prolonged sitting during an 8-
10 hour lab period [6]. This pattern of reducing prolonged periods of sedentary behavior is
11 recommended in current American Diabetes Association guidelines; however, the current
12 guidelines surrounding sedentary behaviour are quite broad and do not suggest a specific
13 dose, but rather just to minimise time spent sedentary [7]. Studies to date have objectively
14 measured physical activity and sedentary behaviour in people with Type 2 diabetes in a free-
15 living setting [8]. Others have examined the relationship between objectively measured
16 physical activity and sedentary behaviour and continuously measured glucose in a lab setting
17 [6, 9, 10], but identifying associations in a freelifing setting are important for transferability
18 of future interventions and to enable more specific guidelines [11].

19 Advances in technology have led to the development of mobile technologies, which
20 continuously monitor lifestyle behaviours and health outcomes. Flash Glucose Monitoring
21 (FGM) is one of the newest methods of glucose monitoring, providing multiple continuous
22 glucose readings compared with conventional ad hoc capillary blood glucose data or 3-month
23 averaged glucose with HbA_{1c}. Further benefits of FGM include the lack of need for regular
24 calibrations and the low cost compared to continuous glucose monitors, making these devices
25 accessible and minimally invasive. FGM has been validated against capillary blood glucose

1 sampling [12] and have been used in previous research to continuously measure glucose
2 [13,14]. Using mobile technologies that continuously measure behaviour and health outcomes
3 within research opens opportunity to explore in detail group and individual patterns and
4 associations between these outcomes.

5 The aim of this study was to examine relationship between patterns in sedentary behavior and
6 glucose at group and individual levels when continuously measured using mobile
7 technologies in people with Type 2 diabetes.

8 **Methods**

9 **Participants**

10 Eligible participants were adults (>18yrs) with Type 2 diabetes, receiving diet modifications
11 and/or anti-diabetes medication (not insulin). Exclusion criteria were pregnancy, cancer,
12 alcohol or substance misuse and hepatic or renal function impairment. Participants were
13 recruited by distributing posters and emails around the University of Strathclyde and
14 Glasgow Caledonian University, visiting local diabetes support groups and an advert
15 appeared in Diabetes UK Balance magazine. The study was approved by the University
16 Ethics Committee of the University of Strathclyde and conformed to the Declaration of
17 Helsinki. Written informed consent was received from all participants.

18 **Study procedures**

19 This intensive longitudinal study was conducted between February 2016 and February 2017
20 and consisted of two visits. At the first, demographic data were recorded including: age,
21 gender, height, weight, waist circumference, anti-diabetes medication, retirement status and
22 duration of diabetes. Participants were fitted with a FreeStyle Libre flash glucose monitor
23 (Abbott FreeStyle Libre, Abbott Diabetes Care, CA, USA) with a sensor inserted into the
24 subcutaneous tissue at the back of the upper arm. Participants were also fitted with a

1 waterproofed activPAL3 activity monitor (PAL Technologies, Glasgow, UK) on the front of
2 the right thigh midway between the knee and the hip [15]. Participants were requested to
3 wear both devices 24 hours/day for a minimum of 3 and up to 14 days of normal daily living.
4 A minimum of three days was decided in order to comply with recommendations from
5 previous activity monitoring research [16]. At the time of this study there were no published
6 recommendations for glucose and therefore the same observational time frame was used.
7 Measurement was limited to a maximum of 14 days by the capacity of the FreeStyle Libre
8 sensors. Participants were provided with dietary, medication and sleep recall forms. This
9 allowed for average daily carbohydrate intake to be calculated for each participant using the
10 Carbs & Cals Counter [17]. After 3-14 days, participants attended a second visit to remove
11 the devices. If participants lived further away and were unable to attend the University, a
12 postal method was used. In this instance, the devices were initialised and waterproofed, ready
13 to be attached, and posted to participants with instructions on how to attach and remove the
14 devices and complete the demographic questionnaire and the recall forms. Participants were
15 also asked to self-report weight, height and waist circumference.

16 **Outcome measures**

17 *Flash glucose monitor - Abbott FreeStyle Libre*

18 The Abbott FreeStyle Libre records interstitial glucose every 15 min for up to 14 days.
19 Glucose data are retrieved wirelessly by placing the glucose reader close to the sensor for a
20 few seconds. Due to the limited memory in the sensor, the reader must be scanned at least
21 every 8 hours. The raw glucose data were extracted using the FreeStyle Libre software
22 (version 1.0). Glucose summary data extracted included: Wake time mean glucose (mmol/l)
23 and commonly used measures of glucose variability; standard deviation (SD), range

1 (difference between minimum and maximum glucose value) and coefficient of variation
2 (COV)[18].

3 *Sedentary behaviour - PAL Technologies ActivPAL3*

4 The activPAL3 accelerometer was used to measure sedentary behaviour. The activPAL3
5 records time spent sitting/lying, standing and stepping, in addition to step count and sit to
6 stand transitions, for up to 14days. After 3-14 days of wear time, the data were downloaded
7 using activPAL3™ software (version 7.2.32). To determine the total daily sedentary time,
8 the time spent in sitting/lying posture for each day (hours and % of day) was calculated, after
9 excluding the sleep manually using a sleep diary. For each participant, the average time (h)
10 and proportion (%) per day spent sitting and total sit to stand transitions over the monitored
11 days were computed. A day was defined by self-reported wake time to self-reported sleep
12 time. Using the activPAL events output file, individual sedentary bouts were identified and
13 categorised by duration (≤ 30 minutes, 30-60 minutes and >60 minutes).

14 *Data Alignment*

15 Once the raw data had been extracted, the first and last days of recording were removed from
16 the dataset. Sleep was removed and the datasets were combined using Matlab. Only data from
17 participants with three days of matched data were included in the analysis. The process of
18 data alignment and analysis has been published previously [19].

19 **Statistical analysis**

20 Sample size calculations were based on reported associations between breaks in sedentary
21 time and high 2-h plasma glucose ($R^2 = 0.21$) [20]. Assuming a statistical power of 85%, an
22 alpha of 0.05 and six predictors, we estimated that 37 participants would be required to detect
23 significant associations between sedentary time and glucose measures.

1 Data processing was conducted using Matlab (MathWorks, USA) and Microsoft Excel
2 (Microsoft, USA). Data analysis was conducted using R (R Foundation, USA). Descriptive
3 data of participants were described as numbers and mean with standard deviation (SD).
4 Pearson correlation analysis was used to examine the association between sedentary
5 behaviour patterns and wake time glucose patterns at a group level. The models were
6 adjusted for confounding factors (age, BMI, gender, waist circumference, duration of
7 diabetes diagnosis, medication status, retirement status, mean daily carbohydrate intake,
8 mean sleep, mean step count and mean glucose). Thresholds for correlation coefficient >0.7
9 and Variance Inflation Factor >10 were used to determine the presence of multi-collinearity
10 between independent variables [21]. In this study, no evidence of multi-collinearity was
11 detected between independent variables (Correlation coefficients <0.7 , Variance Inflation
12 Factors <5). Individual regression analysis was used to examine these relationships at an
13 individual level by looking at day-to-day variation within an individual. This method
14 addresses the multi-level nature of the data, where multiple days of data per participant were
15 collected. Significance was identified at $p < 0.05$.

16 **Results**

17 **Participant characteristics**

18 Participants ($n=37$) had a mean age of 62.8 ± 10.5 years, mean BMI (body mass index) of
19 29.6 ± 6.8 kg/m² and mean diabetes duration of 6.61 ± 5.2 years. Most participants were female
20 ($n=23$, 62.2%), just over half ($n=20$, 54.1%) of participants were retired and most ($n=25$,
21 67.6%) were taking anti-diabetes medication (Table 1). Several participants reported their last
22 known HbA_{1c} ($n=22$, mean= 47.7 ± 10.6 mmol/mol) and waist circumference ($n=28$,
23 Mean= 99.8 ± 13.7 cm). HbA_{1c}, as estimated by the FreeStyle Libre, was available for most
24 participants ($n=34$, Mean= 42.5 ± 11.1 mmol/mol).

1 **Habitual sedentary behaviour and glycaemic control**

2 Mean concurrent wear time for the activPAL3 and FreeStyle Libre was 10 ± 3.4 days, once the
3 first and last days were removed. Participants spent, on average, 10.1 ± 2.4 hours per day
4 sitting/lying (64% of waking day). Mean sit to stand transitions were 49 ± 16 per day. Waking
5 mean glucose was 7.5 ± 1.7 mmol/l (minimum 4.5 mmol/l (M=4.9mmol/l, S =1.4mmol/l),
6 maximum 13.6 mmol/l (M =11.04, SD =2.3mmol/l)). Group wake time glucose variability
7 patterns were calculated for several measures of variability including range, SD and COV
8 (Table 2).

9 Mean duration of sedentary bout was 47.2 ± 27.6 minutes (Table 3). In total 31.6% of bouts
10 were less than 30 minutes, 44.7% bouts were between 30 to 60 minutes and 23.7% bouts
11 were greater than 60 minutes.

12 **Group association of sedentary behaviour with glycaemic control**

13 Pearson product correlation analysis was conducted and adjusted for confounders, and the
14 results are shown in Table 4. Sedentary proportion was not positively associated with mean
15 glucose, glucose range and glucose standard deviation. Sedentary bout duration was
16 positively associated with glucose range ($r=0.47, p <0.05$), glucose standard deviation
17 ($r=0.25, p <0.05$) and glucose coefficient of variation ($r=0.27, p <0.05$). There was a very
18 weak positive relationship between sedentary bout duration and mean glucose ($r=0.06, p$
19 <0.05). Sit to stand transitions were negatively associated with glucose range ($r=-0.41, p$
20 <0.05) and glucose coefficient of variation ($r=-0.40, p <0.05$).

21 **Individual association of sedentary behaviour with glycaemic control**

1 Figures 1 (a-b), Figure 2 (a-b) and Figure 3 (a-b) illustrate the associations of glucose with
2 sedentary time (%), sedentary bout duration and daily sit to stand transitions, respectively.
3 Each coloured line represents the regression line for an individual participant.

4 *Mean glucose*

5 In 25 participants, increased sedentary time was associated with increased mean glucose. In
6 22 participants, increased sedentary bout duration was associated with increased mean
7 glucose. In 21 participants, increased daily sit to stand transitions were associated with
8 increased mean glucose.

9 *Glucose variability*

10 The relationship between sedentary time and glucose variability measures were similar to that
11 of sedentary time and mean glucose (standard deviation: 21 positive, 16 negative; range: 20
12 positive, 17 negative). This differs from the relationship between sedentary bout duration and
13 glucose variability. In 33 of the 37 participants, there was a positive association between
14 sedentary bout duration and glucose standard deviation. In all participants, there was a
15 positive association between sedentary bout duration and glucose range. The relationship
16 between daily sit to stand transitions and glucose variability measures was less consistent
17 between participants than sedentary bout duration (standard deviation: 18 positive, 19
18 negative; range: 22 positive, 15 negative).

19 To identify any characteristics that may explain the two groups with differing relationships
20 between glucose and sedentary behaviour, individual participant characteristics were
21 examined. An example of the relationship between sedentary time (%) and mean glucose
22 (mmol/l) is displayed in Table 5 (Supplementary File A). It appears that those with the
23 expected positive relationship (increased sitting is associated with increased mean glucose)

1 have a lower carbohydrate intake, sleep less, have a higher daily step count and have a lower
2 mean glucose.

3 **Discussion**

4 Analysis of the sedentary behaviour showed participants were spending almost two thirds of
5 their waking day (64%), or just over 10 hours, sedentary, and breaking their sedentary time
6 an average of 49 times/day. This is consistent with findings from the MAASTRICHT study
7 [8], which involved adults (40-75 years) with Type 2 diabetes ($n=714$) wearing an activPAL
8 accelerometer for 8 days and found that those with Type 2 diabetes spent 64.5% (10 hours) of
9 their waking day sedentary and 53 sedentary breaks per day, with the average duration of a
10 sedentary bout 12.62 minutes [8]. The current study found mean sedentary bout duration was
11 47.2(± 27.6) minutes long. The mean wake time glucose was 7.48mmol/l, which is within the
12 recommended <8.5 mmol/l target for people with diabetes [22], suggesting glucose was
13 relatively well controlled in this group. This could be reflected in the recruitment methods
14 used in this study, which may have led to participants who are more motivated and
15 committed to managing their glucose. Additionally, the sample did not include those on
16 insulin therapy and mean diabetes duration was relatively short, both of which could have an
17 impact on mean glucose.

18 The correlation analysis was conducted to identify whether there was a generic relationship
19 between sedentary behaviour and glucose. Increased proportion of time spent sedentary had
20 no association with mean glucose when adjusted for confounders. In contrast, lab-based
21 studies have found interrupting prolonged sitting time in those with Type 2 diabetes lead to
22 significantly lower mean glucose, which persisted for up to 22 hours [6, 12, 13]. Similarly, a
23 longitudinal, descriptive study found increased sedentary time was predictive of increased
24 time spent in hyperglycaemia in people with Type 2 diabetes ($n=86$) [22]. Dunstan et al [24]
25 found regular activity breaks in sedentary behaviour lead to significant ($p < 0.01$) reductions

1 in glucose area under the curve. Kingsnorth et al. (2018) found that sedentary time was
2 positively associated with higher mean glucose and glucose variability in nondiabetic adults
3 over 13 days [11]. The difference in study design and participants involved could explain the
4 differences in findings between the current study and those discussed [6, 9, 10, 11, 23, 24].
5 The previous studies were controlled lab-based studies in which sedentary behaviour was
6 manipulated, what sedentary behaviour was broken up with was controlled for and
7 participants were provided with standardised meals. The current study was conducted in a
8 free-living setting.

9 Increased sedentary bout duration was associated with significantly increased mean glucose
10 and glucose variability, implying that if sedentary time is accumulated in fewer, but longer
11 bouts, it is associated with poorer glycaemic control. To examine these relationships further,
12 and account for the multi-level data, individual regression analysis was conducted. This is the
13 first time this relationship has been analysed in this way and has presented some novel and
14 interesting findings. The individual analysis showed a different glucose response to sedentary
15 behaviour. The individuality is quite clearly shown in figures 1, 2 and 3, as there is noticeable
16 variability between participants who have the same direction of relationship. Participant
17 characteristics were checked in an attempt to identify anything that may explain the different
18 relationships. An example of this is presented in supplementary file A and interestingly, those
19 participants in the group whose mean glucose increased the more time they spent sedentary
20 were more active, slept less, had a lower daily carbohydrate intake and had a lower daily
21 mean glucose. Further examination is required; however, differences in baseline fitness, other
22 medical conditions, the glycaemic index of meals, the timing of meals and medication may be
23 some individual factors influencing these relationships.

24 A similar individual glucose response was reported in a large cohort ($n=800$) study
25 examining the effect of meal content on glucose [25]. Participants in this study did not have

1 Type 2 diabetes. The response to identical meals were assessed and high variability was
2 shown between participants. Additionally, four sub-types of Type 2 diabetes have recently
3 been identified and Ahlqvist et al [26] have suggested that different sub-types may respond
4 differently to food, activity and medication, but acknowledged that further research is
5 required to understand this fully. This is the first study to identify an individualised response
6 to activity behaviour as suggested by Ahlqvist and colleagues [26].

7 There is growing evidence to support a more personalised approach to diabetes care [25, 26]
8 and incorporating mobile technology could provide a mechanism for this tailored approach.

9 A recent pilot study examined the use of personalised glucose feedback to change activity
10 behaviour in nondiabetic adults ($n=33$) and found that the feedback resulted in reduced
11 sedentary time at follow-up. This is an example of how digital health may be used to promote
12 behaviour change and self-management in the future [27]. More research is required using
13 these technologies to further understand the relationships identified in the current study and
14 explore how this information can be used to provide a personalised prescription [28, 29, 30].

15 **Strengths**

16 The key strength of this study is the free-living context combined with objective and
17 continuous measurement of sedentary behaviour and glucose and the inclusion of self-
18 reported food intake. This, along with a sample size of 37 and average wear time of 10 days
19 per participant, enabled a large amount of data to be collected and thereby increasing the
20 rigor of our findings. This also presented a significant challenge for data processing and
21 analysis which has previously been discussed [19].

22 **Limitations**

23 The free-living design of the study allowed no control over participant meal content and
24 timing or medication dose and timing; however, participant food and medication diaries were

1 collected and this data was controlled for in the analysis. Although average carbohydrate
2 intake was calculated and controlled for in the analysis, the glycaemic index of meals, which
3 indicates how quickly a carbohydrate is absorbed, was not. This should be considered in
4 future research examining these relationships. Participant fitness levels and other health
5 conditions were not collected, both of which have been shown to influence glycaemic control
6 in previous research. Similarly, the focus of this paper was sedentary behaviour and breaks in
7 sedentary behaviour so standing and stepping time were not included in the analysis. Future
8 analysis focusing on the types of behaviour during a sedentary break would provide valuable
9 insight into what behaviours would be most beneficial to break sedentary behaviour with.
10 Participants were not blinded to the feedback provided by the FreeStyle Libre and therefore
11 there is a possibility that they altered their behaviour based on this feedback.

12 **Conclusions**

13 Findings from this study highlight the individualised nature of the relationship between
14 sedentary behaviour and glucose in adults with Type 2 diabetes emphasising that lifestyle
15 modification will have different results in different individuals. This is an important finding
16 given the current advances in technology. There are an increasing number of devices
17 providing objective and continuous measurement of lifestyle behaviours and health
18 outcomes. Further research is required to explore these individual relationships further and to
19 understand how the technology and information obtained can be used to adopt individualised
20 precision prescription of lifestyle modification.

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Table 1: Participant Descriptive Statistics

<i>n</i> = 37	Mean (SD)	<i>n</i> (%)
Age (Years)	62.8 (±10.5)	
BMI (kg/m ²)	29.6 (±6.8)	
Male sex		14 (37.8)
Waist circumference (cm)	99.8 (±13.7)*	
Duration since diagnosis (Years)	6.61 (±5.2)	
Work hours per week (hours)	11.6 (±15.4)	
Self-Reported HbA _{1c} (mmol/mol (%))	47.7 (±10.6) (6.5%)**	
FreeStyle Libre HbA _{1c} (mmol/mol (%))	42.5 (±11.1) (6%)***	
Retired		20 (54.1)
Carbohydrate intake (g/day)	125.3(±21.1)	
Anti-Diabetes Medication		
No medication/ diet controlled		12
Metformin		18
Metformin + sulfonylurea		5
Metformin + gliptin		1
Metformin + sulfonylurea + gliptin		1

Note. **n* = 28, ***n* = 22, ****n* = 34

Table 2: Daily sedentary behaviour and glucose during waking time

	Mean (SD)
<i>Sedentary Behaviour</i>	
Sitting/lying (h)	10.1 (\pm 2.4)
Sitting/lying (%)	64.0 (\pm 13.2)
Sit to Stand Transitions	48.6 (\pm 16.4)
Sedentary Bout Duration (mins)	47.2 (\pm 27.6)
Stepping (h)	1.6 (\pm 0.6)
Sleeping (h)	8.3 (\pm 1.4)
<i>Glucose</i>	
Mean (mmol/l)	7.5 (\pm 1.7)
Min (mmol/l)	4.9 (\pm 1.4)
Max (mmol/l)	11.04 (\pm 2.3)
SD	1.6 (\pm 0.5)
Range	6.2 (\pm 1.9)
COV	0.2 (\pm 0.1)

Table 3: Sedentary bout patterns

<i>n</i>= 2434	Total number of bouts	Proportion of bouts (%)
≤30 minutes	770	31.6
>30 minutes ≤60 minutes	1088	44.7
>60 minutes	576	23.7

Table 4: Association of physical activity and sedentary behaviour with glucose

	Mean Glucose	Glucose SD	Glucose Range	Glucose COV	Glucose CONGA_n
Sedentary Time (%)	0.06	0.12	0.04	0.31	0.03
Sedentary Time (h)	0.05	0.12	0.04	0.32	0.03
Sit to Stand	-0.07	-0.24	-0.41*	-0.40*	-0.26
Sedentary Bout Duration	0.06*	0.25*	0.47*	0.27*	--

Note. * = $p < 0.05$