Full title: Diurnal patterns of objectively measured sedentary time and interruptions to sedentary time are associated with glycaemic indices in type 2 diabetes.

Abstract

Objectives: To investigate diurnal patterns of sedentary time and interruptions to sedentary time and their associations with achievement of pre-meal glucose, post-meal glucose, bedtime glucose and the dawn phenomenon targets and with duration of hypoglycaemia, euglycaemia, hyperglycaemia and above target range.

Design: Intensive longitudinal study.

Methods: In 37 adults with type 2 diabetes, the FreeStyle Libre and activPAL3 were used to monitor glucose and sedentary time and interruptions to sedentary time in the morning (07:00-12:00), afternoon (12:00-17:00) and evening (17:00-23:00) for 14 days. Diurnal patterns of sedentary behaviour and associations with glycaemic indices were assessed using repeated measures ANOVA and linear regressions.

Results: Sedentary time was significantly higher in the evening (43.47±7.37 min/h) than the morning (33.34±8.44 min/h) and afternoon (37.26±8.28 min/h). Interruptions to sedentary time were significantly lower in the evening (2.64±0.74 n/h) than the morning (3.69±1.08 n/h) and afternoon (3.06±0.87 n/h). Sedentary time in the morning and afternoon was associated with lower achievement of the dawn phenomenon target. Sedentary time in the evening was associated with lower achievement of post-lunch glucose target. Interruptions to sedentary time in the morning and afternoon were associated with higher achievement of pre-dinner glucose target. Interruptions to sedentary time in the evening showed beneficial associations with achievement of post-dinner glucose and bedtime glucose targets and euglycaemia.

This is a peer-reviewed, accepted author manuscript of the following article: Paing, A. C., McMillan, K. A., Kirk, A. F., Collier, A., Hewitt, A., Dunstan, D., Owen, N., & Chastin, S. F. M. (2020). Diurnal patterns of objectively measured sedentary time and breaks in sedentary time are associated with glycaemic indices in Type 2 diabetes. Diabetic Medicine, 23(11), 1074-1079. https://doi.org/10.1016/j.jsams.2020.06.003

Conclusions: Prolonged sedentary behaviour is high in the evening. Interruptions to sedentary time, particularly in the evening, have beneficial associations with glycaemic indices. Interventions targeting interruptions to sedentary time in the evening may be more clinically relevant.

Keywords: Glucose; Physical activity; Sedentary behaviour; Type 2 diabetes.

Practical implications

- There are diurnal variations in sedentary time and interruptions to sedentary time, and prolonged uninterrupted sedentary behaviour is high in the evening.
- Interruptions to sedentary time in the morning and afternoon are beneficially associated with pre-dinner glucose.
- Interruptions to sedentary time in the evening have beneficial associations with post-dinner glucose, bedtime glucose and euglycaemia.
- Interrupting prolonged sedentary behaviour, especially in the evening, should be considered for promoting glucose control.

1. Introduction

Sedentary behaviour, defined as time spent sitting or reclining during waking hours, has been shown to be associated with poorer glucose control in those with type 2 diabetes (T2D), whereas interruptions to sedentary time can predict better glucose control.[1] Brief physically-active interruptions of sedentary time have been advocated for improving glucose control.[2,3] In free-living settings, distribution of sedentary time and interruptions to sedentary time may vary throughout the day.[4,5]

In the context of glycaemic control in T2D, understanding diurnal patterns of sedentary time and interruptions to sedentary time may help to understand the potential benefits of targeting specific times of the day in which there may be periods of high uninterrupted sedentary time. For example, there may be options to reduce potential burden for those with T2D if they were to interrupt their sedentary time primarily at specific points in the day at which there would be more optimal benefits for glycaemic control. The potential of such approaches could be informed by evidence on the diurnal patterns of sedentary time and interruptions to sedentary time and their associations with glycaemic indices.

There is experimental evidence that physical activity at different times of the day (morning vs. afternoon) can have differential effects on glycaemic indices, and this may be influenced by diurnal variations in behavioural patterns, insulin sensitivity and glucose metabolism.[6–9] Potentially, there may be such relationships for sedentary time and interruptions to sedentary time. Understanding whether this might be the case may be approached through identifying whether there are associations of free-living sedentary time and interruptions to sedentary time at different times of the day (morning, afternoon and evening) with glycaemic indices.

We objectively measured concurrent and continuous glucose and activity data in free-living settings in adults with T2D and examined diurnal patterns of sedentary time and interruptions to sedentary time and their associations with glycaemic indices.

2. Methods

The University Ethics Committee (UEC) of University of Strathclyde approved this intensive longitudinal study.[10] This study conformed to the Declaration of Helsinki. Written informed consent was obtained from all participants.

Participants were recruited between February 2016 and February 2017 from the Glasgow community. Inclusion criteria were diagnosed T2D, age ≥18 years and diet modification±oral glucose-lowering medications. Individuals with insulin therapy, age <18 years, alcohol and substance abuse, pregnancy, liver and renal diseases and cancer were excluded.

Forty-six adults with T2D were recruited and assessed. After excluding a participant with misdiagnosed T2D and eight participants with less than 3 days of glucose and activity data, total thirty-seven participants were included in the final analyses.

In this study, two visits to the University laboratory or convenient location (participant's home) were included. At the first visit, participants' demographic data, glucose-lowering medication use and body mass index (BMI) were collected. A sensor of Flash glucose monitoring system (Abbott FreeStyle Libre) and an activPAL3 activity monitor (PAL Technologies, Glasgow, UK) were attached, and participants then returned home and followed normal daily life for up to 14 days. To record habitual waking time, bedtime, mealtime, dietary intake and medication, sleep diary and 24-hour Dietary Recall Form were provided. At the end of study period, participants attended a second visit to return the devices, sleep diary and 24-hour Dietary Recall Form.

To estimate carbohydrate intake in each day, 24-hour Dietary Recall Form and Carbs & Cals Counter were used.[11] Average daily carbohydrate intake (g/day) was then calculated for each participant.

After the activPAL3 was waterproofed, it was attached to the anterior aspect of the right thigh using hypoallergenic dressing. This is a validated device that accurately measures sedentary time and number of

transitions from sitting or lying condition to standing or stepping condition, defined as interruptions to sedentary time, for 14 days.[12] The data from this device were downloaded using the activPAL3™ software (version 7.2.32). The data from 00:00 to 00:00 h of two consecutive days were used to get the 24-h data, but the first and final days with less than 24-h recording and sleeping time were excluded.[13] For each participant, average minutes of sedentary time per hour (min/h) and average numbers of interruptions to sedentary time per hour (n/h) in the morning (07:00-12:00 h), afternoon (12:00-17:00 h) and evening (17:00-23:00 h) were calculated using the activPAL summary file. A valid hour was defined as an hour with full 60 min of waking time data. There was no limitation regarding the number of valid hours per day. Average daily sedentary time (h/day), interruptions to sedentary time (n/day), walking time (h/day), steps per interruption, moderate to vigorous physical activity (MVPA) time (min/day) and energy expenditure (MET x h/day) were also calculated for each participant. A cadence value of ≥100 steps/min was classified as MVPA.

The Flash glucose monitoring system consists of a sensor and a reader, and the system accurately measures interstitial glucose every 15 min for 14 days.[14] The sensor was attached to the back of the upper arm, and the reader was used to scan and retrieve glucose data at least every 8 h. FreeStyle Libre software (version 1.0) was used to download the data from the system. The first and final days with less than 24-h recording were not included in analyses. Global guideline for T2D by the International Diabetes Federation was used to define targets for pre-meal glucose (≤6.5 mmol/L) and post-meal glucose (≤9 mmol/L) and thresholds for hypoglycaemia (<3.9 mmol/L), euglycaemia (3.9-7.8 mmol/L), hyperglycaemia (>7.8 mmol/L) and above target range (>9 mmol/L).[15] This is an evidence-based guideline, which targets HbA1c <7% (53 mmol/mol) to reduce diabetes-related complications. Thresholds for bedtime glucose ≤8.5 mmol/L and the dawn phenomenon ≤1.1 mmol/L have been suggested to achieve HbA1c <7% (53 mmol/mol);[16,17] therefore, these thresholds were used for bedtime glucose and the dawn phenomenon.

For each day, pre-breakfast glucose, pre-lunch glucose and pre-dinner glucose were defined as glucose values before the start of breakfast, lunch and dinner, respectively.[18] Post-breakfast glucose, post-lunch glucose and post-dinner glucose were calculated from glucose values during 2-h from the start of breakfast, lunch and dinner.[18] Bedtime glucose and the dawn phenomenon were defined as glucose value at bedtime and the increase in glucose value from the nocturnal nadir glucose to pre-breakfast glucose, respectively.[16] The dawn phenomenon was recorded as zero when all nocturnal glucose values were higher than pre-breakfast glucose value.[19] Across all participants, 4.2% of data points for these glucose profiles (451 of 10614 glucose data points) were missing, and within-individual mean substitution, which is accurate and effective to deal with ≤10% of missing data, was applied.[20] The percentages of pre-meal glucose, post-meal glucose, bedtime glucose and the dawn phenomenon profiles achieving targets were then calculated for each participant (e.g. The percentages of pre-breakfast glucose profiles achieving target = [Number of pre-breakfast glucose profiles ≤6.5 mmol/L/Total number of pre-breakfast glucose profiles] x 100%).

Average daily time in hypoglycaemia, euglycaemia and hyperglycaemia and time above target range were calculated for each participant.[15] Each missing glucose data point represents 15 min missing data time; therefore, normalisation method was applied and time in different glucose ranges were reported as % of recording h/day (e.g. Time in hypoglycaemia = [Average daily time in hypoglycaemia/(24 h - Average daily missing data time)] x 100). Self-reported HbA1c from participants' last visits to diabetes specialist nurse, general practitioner and diabetes clinic was also obtained.

Sample size calculations were based on a previous study, which found the association between interruptions to sedentary time and high 2-h plasma glucose (R^2=0.21).[21] Allowing for a statistical power of 85%, an alpha of 0.05 and six predictors, we estimated that we would need 37 participants to detect significant association between interruptions to sedentary time and glycaemic indices. Repeated measures ANOVA was used to assess the diurnal patterns of sedentary time and interruptions to sedentary time, and

differences between morning, afternoon and evening were investigated with *post hoc* Fisher LSD test.[22] Time periods (morning, afternoon and evening) were treated as within-subject factors, and the assumption of sphericity was assessed using Mauchly's test. Linear regression models were used to identify the associations of sedentary time and interruptions to sedentary time during the morning, afternoon and evening with the percentages of glucose profiles achieving targets and time in different glucose ranges. Model 1 was adjusted for age, sex, energy expenditure and glucose-lowering medication dose (mg/day). Model 2 was adjusted for variables in Model 1 plus walking time (h/day), steps per interruption, carbohydrate intake and BMI. Model 2 investigating the associations between interruptions to sedentary time and glycaemic indices was also adjusted for sedentary time (h/day). Normal distribution of the data was confirmed by visual inspection of the residual plots. The presence of multicollinearity between independent variables was determined by thresholds for correlation coefficient >0.7 and Variance Inflation Factor >10.[23] There was no evidence of multicollinearity in the regression models (Correlation coefficients <0.6, Variance Inflation Factors <3). The results are reported as mean with standard deviation (SD) and standardised coefficient (β) with 95% confidence interval (CI) unless otherwise stated. The level of statistically significant was set at p value ≤0.05. Microsoft Excel 2016 and IBM SPSS Statistics software (version 24.0) were used to prepare data and conduct statistical analyses, respectively.

A sensitivity analysis was conducted to examine whether the associations of sedentary time and interruptions to sedentary time during the morning, afternoon and evening with glycaemic indices were affected by stratifying the data according to carbohydrate intake <130 g/day (low-carbohydrate intake) and ≥130 g/day (high-carbohydrate intake).

3. Results

Characteristics of the sample are reported in Table 1.

153 The diurnal patterns of sedentary time and interruptions to sedentary time are described in Supplemental
154 Fig. 1. The assumption of sphericity was not violated for both sedentary time ($X^2(2)=5.22$, p=0.07) and
155 interruptions to sedentary time ($X^2(2)=3.57$, p=0.17). Therefore, corrections for degrees of freedom were
156 not needed, and repeated measures ANOVA showed that the diurnal patterns of sedentary time ($F(2,$
157 $72)=31.94$, p<0.001) and interruptions to sedentary time ($F(2, 72)=34.35$, p<0.001) are different between
158 time periods. Sedentary time was higher in the evening (43.47±7.37 min/h) compared with the morning
159 (33.34±8.44 min/h, p<0.001) and afternoon (37.26±8.28 min/h, p<0.001). Sedentary time was also
160 different between the morning and afternoon (p=0.001). Conversely, interruptions to sedentary time were
161 lower in the evening (2.64±0.74 n/h) than the morning (3.69±1.08 n/h, p<0.001) and afternoon (3.06±0.87
162 n/h, p<0.001). Interruptions to sedentary time during the morning were higher than the afternoon
163 (p<0.001).

164 Table 2 shows standardised regression of sedentary time in the morning, afternoon and evening with
165 glycaemic indices. Model 1 showed association between sedentary time in the morning and lower
166 achievement of the dawn phenomenon target (p=0.04). Associations of lower achievement of the dawn
167 phenomenon target with sedentary time in the morning (p=0.03) and afternoon (p=0.02) were found in
168 Model 2. Model 2 also showed association between sedentary time in the evening and lower achievement
169 of post-lunch glucose target (p=0.03).

170 Standardised regression coefficients of interruptions to sedentary time in the morning, afternoon and
171 evening with glycaemic indices are reported in Table 3. In Model 1, interruptions to sedentary time in the
172 morning (p=0.03) and afternoon (p=0.04) were associated with higher achievement of pre-dinner glucose
173 target. Interruptions to sedentary time in the evening were associated with higher achievement of post-
174 dinner glucose (p=0.02) and bedtime glucose (p=0.04) targets and higher time in euglycaemia (p=0.04).
175 There were trends towards beneficial associations of interruptions to sedentary time in the evening with
176 higher achievement of pre-breakfast glucose (p=0.08), pre-lunch glucose (p=0.06), pre-dinner glucose

(p=0.06) and post-breakfast glucose (p=0.06) targets and lower time in hyperglycaemia (p=0.08) and time above target range (p=0.07). No associations between interruptions to sedentary time in the morning, afternoon and evening and glycaemic indices were observed in Model 2.

A sensitivity analysis showed that the associations between sedentary patterns and glycaemic indices could be dependent of carbohydrate intake. The association between sedentary time in the morning and increased time in hypoglycaemia was found in participants with low-carbohydrate intake (Supplemental Table 1) but not in those with high-carbohydrate intake (Supplemental Table 3). Interruptions to sedentary time in the morning were associated with lower time in hypoglycaemia in participants with low-carbohydrate intake (Supplemental Table 2). In participants with high-carbohydrate intake, there were beneficial associations of interruptions to sedentary time in the evening with achievement of bedtime glucose target and interruptions to sedentary time in the morning with achievement of pre-dinner glucose, post-breakfast glucose, post-dinner glucose and bedtime glucose targets and time in euglycaemia and hyperglycaemia (Supplemental Table 4).

4. Discussion

Our findings provide new insights into the diurnal patterns of sedentary time and interruptions to sedentary time and their associations with glycaemic indices in T2D. Our participants spent some 43 min sedentary in each hour in the evening, whereas they spent about 33 min and 37 min sedentary in each hour in the morning and afternoon, respectively. During the morning, there were on average 3.7 interruptions to sedentary time each hour, and this decreased throughout the day, with 3.1 and 2.6 interruptions per hour in the afternoon and evening, respectively. There were associations of sedentary time in the morning and afternoon with lower achievement of the dawn phenomenon target and sedentary time in the evening with lower achievement of post-lunch glucose target. Interruptions to sedentary time in the morning and afternoon were associated with achievement of pre-dinner glucose target. Interruptions to sedentary time in the evening had beneficial associations with achievement of post-dinner glucose and

bedtime glucose targets and time in euglycaemia. Interruptions to sedentary time in the evening also showed potential trends towards beneficial associations with achievement of pre-breakfast glucose, pre-lunch glucose, pre-dinner glucose and post-breakfast glucose targets and time in hyperglycaemia and time above target range.

The diurnal patterns of sedentary time and interruptions to sedentary time in those with T2D in this study are in agreement with previous studies conducted in older adults without T2D.[5,24,25] There is evidence that those with T2D can spend longer periods of time sedentary than do their healthier counterparts.[26] Our findings suggest that prolonged uninterrupted sedentary time in the evening could be the main contribution to this sedentary behaviour because more sedentary time and fewer interruptions to sedentary time were observed in the evening than the morning and afternoon. This highlights that behavioural change interventions may benefit from a focus on reducing sedentary time and promoting interruptions to sedentary time in the evening. Consequently, this may be more acceptable and may require minimal efforts of people with T2D. Take the intervention involving prompts or suggestions to interrupt sedentary time for example, if people receive prompts or suggestions constantly throughout the day, they tend to be agitated and discouraged, and thus lowering the effectiveness of the intervention.[27] Therefore, there may be importance of delivering intervention when it is most needed and the individual is most receptive to it, and the findings from this study could be helpful to develop such intervention.

Our findings suggest that reducing sedentary time in the evening with regular activity breaks may be more clinically relevant because interruptions to sedentary time in the evening showed beneficial associations and potential trends towards beneficial associations with almost all glycaemic indices while interruptions to sedentary time in the morning and afternoon only showed the associations with pre-dinner glucose. This is supported by previous experimental findings, which suggested that physical activity in the evening could be more effective than physical activity in the morning.[6,7] This may be due to diurnal pattern of insulin sensitivity, which tends to be higher in the afternoon and evening,[9] and the accumulative effect of

all activity breaks performed throughout the day.[3,6] Therefore, experimental studies investigating the effects of interruptions to sedentary time with the same intensity, frequency and duration performed at different times of the day (morning vs. afternoon vs. evening) should be considered to confirm cause-effect relationship. We also suggest future studies to investigate temporal relationships of sedentary time and interruptions to sedentary time during the morning, afternoon and evening with glycaemic indices in free-living settings using larger sample size and more-sophisticated statistical models.

The findings from sensitivity analysis suggest that the associations between interruptions to sedentary time and glycaemic indices could be more pronounced in those with high-carbohydrate intake, and this is supported by previous experimental studies, which showed that the effect of physical activity on glucose can be strong when carbohydrate intake is high.[6,8,28] The mechanism for this is unclear, and we suggest future experimental studies to explore this.

A major strength of the present study was the use of continuous and concurrent activity and glucose data assessed by the activPAL3 and Flash glucose monitoring system. The assessment of the associations between the diurnal patterns of sedentary time and interruptions to sedentary time and glucose profiles throughout the day were only possible with the use of these devices, and this study design could be less reliable or could not be achieved with periodic blood glucose measurements using laboratory tests or finger-prick tests and self-reported sedentary time.[14,29] This allowed us to evaluate the diurnal patterns or dynamic pictures of sedentary time, interruptions to sedentary time and glucose profiles.

A limitation of this study was a relatively small sample size, and the study might not provide enough power to detect the associations with some glycaemic indices. We therefore suggest future studies with larger sample size despite cost and burden of the Flash glucose monitoring system. Moreover, meals were not standardised among participants, which could influence glycaemic indices.[30] Furthermore, sociodemographic data such as age, gender, marital status and education level could influence sedentary

patterns,[4,24] and this should be evaluated in T2D in future studies. Finally, sedentary patterns between week and weekend days could be different.[4] However, 27% of participants provided 3-6 days of data, and differences between week and weekend days were not evaluated.

5. Conclusion

Prolonged uninterrupted sedentary behaviour is high in the evening, and interruptions to sedentary time, particularly in the evening, show beneficial associations with glycaemic indices. Interrupting sedentary time, particularly in the evening, added to glucose-lowering medications should be considered as a time phased combined treatment for improving glucose control, and future experimental studies should explore this.

Acknowledgements

The authors would like to thank participants who volunteered and devoted their time to the study. The authors also thank Kathryn Anne McMillan who put significant effort on recruitment of participants. This work was supported by School of Psychological Sciences and Health, University of Strathclyde, UK; PAL technologies Ltd (Glasgow, UK), and School of Health and Life-Sciences, Glasgow Caledonian University, UK. Professor Neville Owen is supported by a National Health and Medical Research Council of Australia (NHMRC) Centre of Research Excellence Grant (#1057608), NHMRC Senior Principal Research Fellowship (#1118225), and the Victorian Government's Operational Infrastructure Support Program. The funding agencies did not play any role in preparing and writing up manuscript, and in making a decision to submit manuscript.

Declaration of interest: none.

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340

Characteristics	
Total sample (Men/Women) (n)	37 (14/23)
Age (years)	62.8±10.5
BMI (kg/m^2)	29.6±6.8
Duration of diabetes (years)	5.9±4.7
Diabetes management (n)	
No medication/diet modification alone	12
Metformin	18
Metformin + sulphonylurea	5
Metformin + gliptin	1
Metformin + sulphonylurea + gliptin	1
Carbohydrate intake (g/day)	125.3±21.1
The activPAL3 and Flash glucose monitoring system recording time (days)	10±3.4
Energy expenditure (MET x h/day)	33.6±1.3
Sedentary time (h/day)	9.8±1.8
Interruptions to sedentary time (n/day)	52±13
Walking time (h/day)	1.6±0.6
Steps per interruption	150.9±78.9
MVPA time (min/day)	32.1±22.7
HbA1c (%), (n=15 missing)	6.6±0.9
HbA1c (mmol/mol), (n=15 missing)	48±10.6
24-h mean glucose (mmol/L)	7.03±1.64
Glucose profiles achieving targets (%)	
Pre-breakfast glucose target (≤6.5 mmol/L)	55.7±44.9
Pre-lunch glucose target (≤6.5 mmol/L)	62.5±37.7
Pre-dinner glucose target (≤6.5 mmol/L)	55.0±35.3
Post-breakfast glucose target (≤9 mmol/L)	59.1±38.3
Post-lunch glucose target (≤9 mmol/L)	77.5±28.2
Post-dinner glucose target (≤9 mmol/L)	69.7±35.9
Bedtime glucose target (≤8.5 mmol/L)	81.2±25.5
The dawn phenomenon target (≤1.1 mmol/L)	33.7±27.6
Time in glucose ranges (% of recording h/day)	
Time in hypoglycaemia (<3.9 mmol/L)	3.7±6.9
Time in euglycaemia (3.9-7.8 mmol/L)	64.7±25.5
Time in hyperglycaemia (>7.8 mmol/L)	32.1±27.4
Time above target range (>9 mmol/L)	19.2±20.8

341 Data are means±SD or number (n) or (%). BMI, body mass index; MET, metabolic equivalent task;
342 MVPA, moderate to vigorous physical activity.

343

344 **Table 1**

345 Characteristics of the sample.

346

Glycaemic indices	Model	Morning sedentary		Afternoon sedentary		Evening sedentary	
		β **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**
Glucose profiles achieving targets (%)							
Pre-breakfast glucose target	1	-0.06 (-0.56, 0.43)	0.79	-0.04 (-0.49, 0.41)	0.86	-0.26 (-0.64, 0.10)	0.15
	2	-0.17 (-0.69, 0.34)	0.51	-0.31 (-0.83, 0.22)	0.23	-0.28 (-0.67, 0.11)	0.15
Pre-lunch glucose target	1	-0.01 (-0.05, 0.48)	0.96	0.02 (-0.44, 0.48)	0.92	-0.24 (-0.63, 0.13)	0.19
	2	-0.14 (-0.64, 0.36)	0.57	-0.26 (-0.79, 0.26)	0.32	-0.26 (-0.65, 0.13)	0.18
Pre-dinner glucose target	1	0.21 (-0.29, 0.71)	0.39	0.26 (-0.19, 0.71)	0.24	0.05 (-0.034, 0.44)	0.78
	2	0.03 (-0.36, 0.42)	0.87	-0.08 (-0.52, 0.35)	0.71	0.06 (-0.27, 0.39)	0.71
Post-breakfast glucose target	1	-0.06 (-0.54, 0.42)	0.80	0.01 (-0.42, 0.44)	0.96	-0.23 (-0.59, 0.15)	0.20
	2	-0.18 (-0.67, 0.31)	0.45	-0.23 (-0.72, 0.28)	0.37	-0.27 (-0.64, 0.10)	0.14
Post-lunch glucose target	1	0.03 (-0.46, 0.52)	0.90	-0.03 (-0.48, 0.43)	0.90	-0.33 (-0.70, 0.03)	0.07
	2	-0.09 (-0.58, 0.40)	0.71	-0.24 (-0.75, 0.28)	0.35	**-0.40 (-0.76, -0.04)**	**0.03**
Post-dinner glucose target	1	0.02 (-0.51, 0.54)	0.94	0.13 (-0.32, 0.59)	0.55	-0.09 (-0.49, 0.30)	0.61
	2	-0.16 (-0.63, 0.31)	0.48	-0.19 (-0.69, 0.30)	0.43	-0.12 (-0.48, 0.23)	0.49
Bedtime glucose target	1	-0.07 (-0.57, 0.44)	0.79	-0.01 (-0.47, 0.45)	0.96	-0.16 (-0.54, 0.22)	0.40
	2	-0.22 (-0.70, 0.25)	0.34	-0.39 (-0.87, 0.08)	0.10	-0.16 (-0.53, 0.20)	0.37
The dawn phenomenon target	1	**-0.48 (-0.96, -0.98)**	**0.04**	-0.34 (-0.78, 0.09)	0.11	-0.21 (-0.59, 0.17)	0.28
	2	**-0.57 (-1.07, -0.07)**	**0.03**	**-0.61 (-1.12, -0.10)**	**0.02**	-0.23 (-0.65, 0.19)	0.27
Time in glucose ranges (% of recording h/day)							
Time in hypoglycaemia	1	0.38 (-0.13, 0.88)	0.09	0.18 (-0.18, 0.45)	0.38	-0.11 (-0.58, 0.23)	0.52
	2	0.34 (-0.11, 0.79)	0.34	-0.01 (-0.00, 0.00)	0.95	-0.14 (-0.70, 0.28)	0.45
Time in euglycaemia	1	-0.24 (-0.80, 0.28)	0.32	-0.11 (-0.61, 0.39)	0.63	-0.17 (-0.53, 0.22)	0.38
	2	-0.38 (-0.63, 0.10)	0.12	-0.43 (-0.96, 0.07)	0.08	-0.15 (-0.60, 0.24)	0.41
Time in hyperglycaemia	1	0.12 (-0.36, 0.60)	0.63	0.05 (-0.63, 0.76)	0.84	0.17 (-0.22, 0.59)	0.37
	2	0.25 (-0.25, 0.75)	0.30	0.38 (-0.12, 0.60)	0.12	0.17 (-0.23, 0.57)	0.37
Time above target range	1	0.08 (-0.45, 0.61)	0.74	-0.03 (-0.32, 0.29)	0.90	0.17 (-0.19, 0.53)	0.39
	2	0.23 (-0.23, 0.69)	0.23	0.32 (-0.80, 0.80)	0.19	0.17 (-0.20, 0.54)	0.34

347 Model 1 was adjusted for age, sex, energy expenditure and glucose-lowering medication dose. Model 2 was adjusted
348 for variables in Model 1 and walking time, steps per interruption, carbohydrate intake and body mass index. Data are
349 presented as standardised coefficient (*β*) with 95% confidence interval (CI).
350 Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).
351
352
353 **Table 2**

354 Standardised regression of sedentary time in the morning, afternoon and evening with glycaemic indices.

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Glycaemic indices	Model	Morning interruptions		Afternoon interruptions		Evening interruptions	
		β (95% CI)	p value	*β* (95% CI)	p value	*β* (95% CI)	p value
Glucose profiles achieving targets (%)							
Pre-breakfast glucose target	1	0.19 (-0.16, 0.53)	0.28	0.09 (-0.28, 0.47)	0.60	0.33 (-0.05, 0.71)	0.08
	2	0.11 (-0.54, 0.76)	0.73	-0.07 (-0.68, 0.54)	0.81	0.50 (-0.31, 1.31)	0.21
Pre-lunch glucose target	1	0.23 (-0.12, 0.60)	0.19	0.17 (-0.20, 0.55)	0.36	0.37 (-0.01, 0.75)	0.06
	2	0.12 (-0.56, 0.80)	0.71	-0.02 (-0.52, 0.48)	0.93	0.43 (-0.38, 1.24)	0.28
Pre-dinner glucose target	1	**0.37 (0.02, 0.72)**	**0.03**	**0.36 (0.00, 0.73)**	**0.04**	0.36 (-0.02, 0.74)	0.06
	2	0.15 (-0.45, 0.75)	0.61	0.25 (-0.33, 0.83)	0.38	0.09 (-0.69, 0.87)	0.81
Post-breakfast glucose target	1	0.17 (-0.18, 0.52)	0.33	0.10 (-0.26, 0.47)	0.57	0.34 (-0.02, 0.71)	0.06
	2	0.06 (-0.58, 0.70)	0.84	-0.05 (-0.63, 0.53)	0.86	0.53 (-0.23, 1.29)	0.16
Post-lunch glucose target	1	0.11 (-0.25, 0.48)	0.53	0.06 (-0.32, 0.45)	0.75	0.31 (-0.06, 0.70)	0.10
	2	-0.08 (-0.67, 0.51)	0.78	-0.20 (-0.81, 0.41)	0.50	0.30 (-0.47, 1.07)	0.43
Post-dinner glucose target	1	0.29 (-0.07, 0.65)	0.11	0.29 (-0.07, 0.67)	0.11	**0.44 (0.07, 0.82)**	**0.02**
	2	0.05 (-0.55, 0.65)	0.86	0.16 (-0.43, 0.75)	0.58	0.42 (-0.34, 1.18)	0.26
Bedtime glucose target	1	0.27 (-0.08, 0.63)	0.13	0.30 (-0.06, 0.66)	0.10	**0.38 (0.01, 0.76)**	**0.04**
	2	0.05 (-0.52, 0.62)	0.85	0.26 (-0.31, 0.83)	0.35	0.28 (-0.47, 1.03)	0.45
The dawn phenomenon target	1	0.17 (-0.19, 0.54)	0.34	0.01 (-0.36, 0.39)	0.94	0.19 (-0.13, 0.65)	0.19
	2	0.29 (-0.35, 0.93)	0.35	-0.09 (-0.71, 0.40)	0.76	0.41 (-0.39, 1.21)	0.30
Time in glucose ranges (% of recording h/day)							
Time in hypoglycaemia	1	-0.18 (-0.52, 0.15)	0.28	-0.07 (-0.42, 0.27)	0.68	-0.08 (-0.44, 0.29)	0.65
	2	-0.40 (-1.20, 0.30)	0.20	0.12 (-0.48, 0.72)	0.68	0.18 (-0.62, 0.95)	0.64
Time in euglycaemia	1	0.24 (-0.12, 0.60)	0.18	0.23 (-0.15, 0.60)	0.23	**0.39 (0.01, 0.77)**	**0.04**
	2	0.13 (-0.52, 0.78)	0.69	0.07 (-0.45, 0.57)	0.82	0.40 (-0.37, 1.23)	0.27
Time in hyperglycaemia	1	-0.16 (-0.52, 0.20)	0.37	-0.18 (-0.55, 0.19)	0.34	-0.33 (-0.71, 0.05)	0.08
	2	-0.01 (-0.66, 0.64)	0.96	-0.10 (-0.73, 0.53)	0.73	-0.44 (-1.24, 0.33)	0.25
Time above target range	1	-0.19 (-0.55, 0.17)	0.29	-0.17 (-0.56, 0.20)	0.34	-0.35 (-0.73, 0.03)	0.07
	2	-0.04 (-0.65, 0.55)	0.89	-0.06 (-0.64, 0.52)	0.83	-0.43 (-1.18, 0.32)	0.25

359 Model 1 was adjusted for age, sex, energy expenditure and glucose-lowering medication dose. Model 2 was adjusted
360 for variables in Model 1 and walking time, sedentary time, steps per interruption, carbohydrate intake and body
361 mass index. Data are presented as standardised coefficient (*β*) with 95% confidence interval (CI).
362 Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).
363
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365 **Table 3**

366 Standardised regression of interruptions to sedentary time in the morning, afternoon and evening with

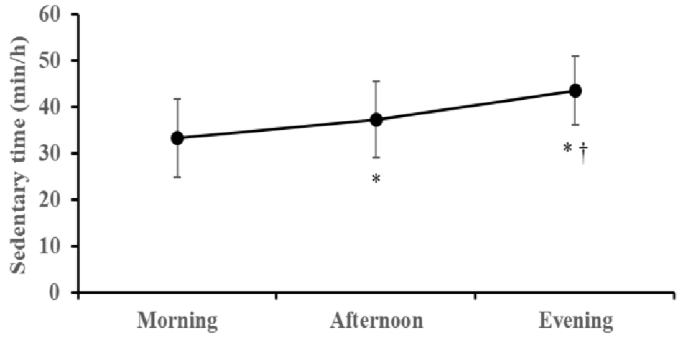
367 glycaemic indices.

368

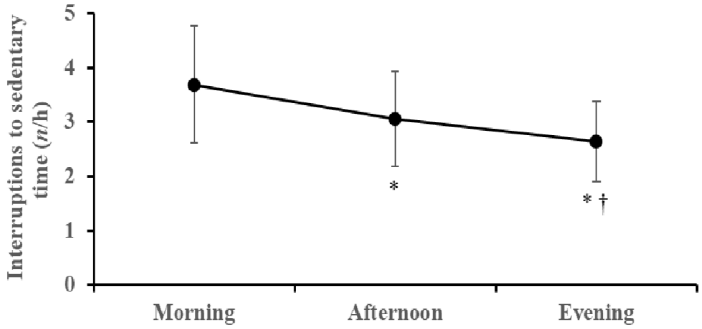
Figure legends

Supplemental Fig. 1. Diurnal patterns of (a) sedentary time and (b) interruptions to sedentary time, showing differences between the morning, afternoon and evening. Data represent means±SD. *Significantly different compared with the morning ($p \leq 0.001$). †Significantly different compared with the afternoon ($p < 0.001$).

(a)


Sedentary time (min/h)
60
50
40
30
20
10
0
Morning
Afternoon
Evening
*
* †

(b)


Interruptions to sedentary time (n/h)
5
4
3
2
1
0
Morning
Afternoon
Evening
*
* †

Glycaemic indices	Morning sedentary		Afternoon sedentary		Evening sedentary	
	β **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**
Glucose profiles achieving targets (%)						
Pre-breakfast glucose target	0.13 (-0.32, 0.59)	0.55	0.01 (-0.44, 0.46)	0.96	0.01 (-0.29, 0.31)	0.94
Pre-lunch glucose target	0.28 (-0.15, 0.72)	0.19	0.15 (-0.30, 0.60)	0.49	0.22 (-0.21, 0.65)	0.29
Pre-dinner glucose target	0.26 (-0.17, 0.69)	0.22	0.13 (-0.29, 0.55)	0.52	0.21 (-0.23, 0.65)	0.32
Post-breakfast glucose target	0.15 (-0.30, 0.60)	0.49	0.06 (-0.37, 0.49)	0.77	0.01 (-0.00, 0.00)	0.99
Post-lunch glucose target	0.16 (-0.28, 0.60)	0.45	-0.01 (-0.36, 0.33)	0.94	-0.03 (-0.48, 0.42)	0.89
Post-dinner glucose target	0.01 (-0.25, 0.27)	0.93	-0.01 (-0.38, 0.36)	0.95	0.02 (-0.31, 0.35)	0.89
Bedtime glucose target	-0.09 (-0.53, 0.35)	0.66	-0.24 (-0.67, 0.19)	0.25	-0.06 (-0.53, 0.40)	0.78
The dawn phenomenon target	-0.01 (-0.34, -0.32)	0.95	-0.05 (-0.46, 0.36)	0.79	0.09 (-0.35, 0.53)	0.67
Time in glucose ranges (% of recording h/day)						
Time in hypoglycaemia	**0.44 (0.00, 0.88)**	**0.03**	0.30 (-0.10, 0.70)	0.15	0.06 (-0.36, 0.42)	0.78
Time in euglycaemia	-0.03 (-0.30, 0.39)	0.89	-0.05 (-0.38, 0.30)	0.80	0.08 (-0.20, 0.40)	0.70
Time in hyperglycaemia	-0.10 (-0.33, 0.33)	0.63	-0.03 (-0.30, 0.39)	0.86	-0.11 (-0.37, 0.18)	0.60
Time above target range	-0.05 (-0.50, 0.45)	0.82	-0.01 (-0.01, 0.01)	0.93	-0.07 (-0.42, 0.30)	0.73

Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).

Supplemental Table 1

Standardised regression of sedentary time in the morning, afternoon and evening with glycaemic indices in participants with carbohydrate intake <130 g/day (n=23).

Glycaemic indices	Morning interruptions		Afternoon interruptions		Evening interruptions	
	β **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**
Glucose profiles achieving targets (%)						
Pre-breakfast glucose target	-0.12 (-0.56, 0.32)	0.57	-0.11 (-0.53, 0.31)	0.59	0.13 (-0.29, 0.55)	0.52
Pre-lunch glucose target	0.04 (-0.36, 0.44)	0.83	-0.03 (-0.52, 0.45)	0.89	0.12 (-0.31, 0.55)	0.57
Pre-dinner glucose target	0.22 (-0.21, 0.65)	0.29	0.19 (-0.25, 0.63)	0.38	0.19 (-0.25, 0.63)	0.38
Post-breakfast glucose target	-0.18 (-0.62, 0.26)	0.40	-0.18 (-0.63, 0.27)	0.41	0.08 (-0.34, 0.50)	0.69
Post-lunch glucose target	-0.02 (-0.48, 0.44)	0.92	-0.06 (-0.47, 0.35)	0.76	0.20 (-0.23, 0.63)	0.34
Post-dinner glucose target	0.08 (-0.36, 0.52)	0.71	-0.002 (-0.60, 0.60)	0.99	0.18 (-0.24, 0.61)	0.38
Bedtime glucose target	-0.01 (-0.31, 0.29)	0.94	0.09 (-0.34, 0.52)	0.66	0.15 (-0.23, 0.49)	0.46
The dawn phenomenon target	0.02 (-0.38, 0.42)	0.91	-0.16 (-0.58, 0.26)	0.44	0.11 (-0.33, 0.55)	0.61
Time in glucose ranges (% of recording h/day)						
Time in hypoglycaemia	**-0.41 (-0.82, -0.00)**	**0.05**	-0.27 (-0.81, 0.14)	0.21	-0.24 (-0.84, 0.24)	0.26
Time in euglycaemia	0.004 (-0.40, 0.42)	0.98	-0.03 (-0.47, 0.40)	0.89	0.15 (-0.27, 0.60)	0.46
Time in hyperglycaemia	0.12 (-0.28, 0.56)	0.55	0.11 (-0.40, 0.62)	0.61	-0.07 (-0.67, 0.49)	0.75
Time above target range	0.08 (-0.48, 0.72)	0.71	0.09 (-0.32, 0.54)	0.65	-0.08 (-0.52, 0.36)	0.68

Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).

Supplemental Table 2

Standardised regression of interruptions to sedentary time in the morning, afternoon and evening with glycaemic indices in participants with carbohydrate intake <130 g/day (n=23).

Glycaemic indices	Morning sedentary		Afternoon sedentary		Evening sedentary	
	β **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**
Glucose profiles achieving targets (%)						
Pre-breakfast glucose target	-0.04 (-0.66, 0.58)	0.88	0.17 (-0.44, 0.79)	0.56	-0.29 (-0.89, 0.31)	0.31
Pre-lunch glucose target	-0.25 (-0.86, 0.36)	0.38	-0.06 (-0.68, 0.56)	0.83	-0.51 (-1.04, 0.02)	0.06
Pre-dinner glucose target	0.05 (-0.51, 0.61)	0.85	0.25 (-0.34, 0.85)	0.37	-0.04 (-0.66, 0.57)	0.88
Post-breakfast glucose target	0.09 (-0.49, 0.67)	0.74	0.33 (-0.26, 0.92)	0.24	-0.16 (-0.77, 0.45)	0.57
Post-lunch glucose target	0.14 (-0.48, 0.76)	0.63	0.09 (-0.52, 0.71)	0.75	-0.43 (-0.99, 0.13)	0.12
Post-dinner glucose target	-0.12 (-0.75, 0.51)	0.68	0.14 (-0.45, 0.74)	0.61	-0.25 (-0.86, 0.36)	0.38
Bedtime glucose target	-0.38 (-0.96, 0.20)	0.17	-0.04 (-0.59, 0.51)	0.87	-0.34 (-0.93, 0.25)	0.23
The dawn phenomenon target	-0.40 (-0.97, 0.17)	0.15	-0.19 (-0.80, 0.42)	0.51	-0.29 (-0.88, 0.30)	0.30
Time in glucose ranges (% of recording h/day)						
Time in hypoglycaemia	0.33 (-0.33, 0.99)	0.24	0.23 (-0.35, 0.69)	0.42	-0.01 (-0.50, 0.50)	0.96
Time in euglycaemia	-0.40 (-0.80, 0.20)	0.15	-0.13 (-0.65, 0.33)	0.64	-0.37 (-0.82, 0.21)	0.19
Time in hyperglycaemia	0.29 (-0.33, 0.91)	0.31	0.06 (-0.30, 0.60)	0.82	0.35 (-0.23, 0.78)	0.35
Time above target range	0.22 (-0.40, 0.88)	0.44	-0.02 (-0.20, 0.32)	0.92	0.29 (-0.29, 0.83)	0.31

Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).

Supplemental Table 3

Standardised regression of sedentary time in the morning, afternoon and evening with glycaemic indices in participants with carbohydrate intake ≥130 g/day (n=14).

Glycaemic indices	Morning interruptions		Afternoon interruptions		Evening interruptions	
	β **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**	***β*** **(95% CI)**	**p value**
Glucose profiles achieving targets (%)						
Pre-breakfast glucose target	0.53 (-0.00, 1.06)	0.051	0.15 (-0.44, 0.74)	0.59	0.28 (-0.32, 0.88)	0.32
Pre-lunch glucose target	0.47 (-0.08, 1.02)	0.09	0.19 (-0.40, 0.78)	0.49	0.36 (-0.22, 0.95)	0.20
Pre-dinner glucose target	**0.55 (0.03, 1.07)**	**0.04**	0.35 (-0.24, 0.94)	0.22	0.32 (-0.26, 0.90)	0.25
Post-breakfast glucose target	**0.54 (0.01, 1.07)**	**0.04**	0.13 (-0.47, 0.73)	0.64	0.23 (-0.36, 0.82)	0.41
Post-lunch glucose target	0.15 (-0.47, 0.77)	0.61	-0.003 (-0.67, 0.66)	0.99	0.22 (-0.39, 0.83)	0.44
Post-dinner glucose target	**0.62 (0.13, 1.11)**	**0.02**	0.38 (-0.20, 0.96)	0.17	0.45 (-0.10, 1.00)	0.10
Bedtime glucose target	**0.70 (0.25, 1.15)**	**0.01**	0.41 (-0.16, 0.99)	0.15	**0.53 (0.00, 1.07)**	**0.05**
The dawn phenomenon target	0.35 (-0.23, 0.93)	0.21	0.12 (-0.49, 0.73)	0.67	0.09 (-0.48, 0.66)	0.73
Time in glucose ranges (% of recording h/day)						
Time in hypoglycaemia	-0.01 (-0.34, 0.32)	0.95	0.02 (-0.30, 0.40)	0.93	0.07 (-0.56, 0.70)	0.80
Time in euglycaemia	**0.59 (0.10, 1.08)**	**0.02**	0.26 (-0.35, 0.91)	0.35	0.43 (-0.11, 1.00)	0.12
Time in hyperglycaemia	**-0.53 (-1.11, -0.01)**	**0.04**	-0.23 (-0.84, 0.35)	0.42	-0.40 (-0.97, 0.17)	0.16
Time above target range	-0.51 (-1.13, 0.03)	0.06	-0.19 (-0.86, 0.43)	0.51	-0.36 (-1.00, 0.20)	0.19

Morning (07:00–12:00 h), afternoon (12:00–17:00 h) and evening (17:00–23:00 h).

Supplemental Table 4

Standardised regression of interruptions to sedentary time in the morning, afternoon and evening with glycaemic indices in participants with carbohydrate intake ≥130 g/day (n=14).