Sleep extension and metabolic health in male overweight/obese short sleepers: A randomised controlled trial

Title: Sleep extension and metabolic health in males with overweight/obesity and short sleep: A randomized controlled trial

Running head: Sleep extension for metabolic health

Authors:

Iuliana Hartescu*[1], PhD

David J. Stensel[1,2], PhD

Alice E. Thackray[1,2], PhD

James A. King[1,2], PhD

James L. Dorling[1, 4] , PhD

Eva N. Rogers[1], MSc

Andrew P. Hall[5], MA FRCP(Edin) FRCA FFICM

Emer M. Brady[3], PhD

Melanie J. Davies[3] , CBE, MB, ChB, MD, FRCP, FRCGP

Thomas Yates[2,3] PhD

Kevin Morgan[1], PhD

Affiliations:

[*]Corresponding author: Dr Iuliana Hartescu, School of Sport, Exercise and Health Sciences, Loughborough University, Epinal Way, Loughborough, LE11 3TU, UK i.hartescu@lboro.ac.uk ; Tel: 004(0)1509222760

[1] School of Sport, Exercise and Health Sciences, Loughborough University, Loughborough, UK

[2] National Institute for Health Research (NIHR), Leicester Biomedical Research Centre, Leicester, UK

[3] Diabetes Research Centre, University of Leicester, Leicester, UK

[4] Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA

[5] The Hanning Sleep Laboratory, University Hospitals of Leicester NHS Trust, Leicester, UK

The trial location was Loughborough University, School of Sport, Exercise and Health Sciences.

All authors have seen and approved the manuscript.

Acknowledgement:

This research was supported by the NIHR Leicester Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Disclosure of funding and conflict of interest

The trial was funded by Loughborough University and the Biomedical Research Centre.

The authors have no conflict of interest to report.

Contribution to the manuscript:

1. **Conception or design of the work: IH, KM, DJS, JAK, APH, EMB, MJD, TY**
2. **Data collection: IH, DJS, AET, JAK, JLD, ENR**
3. **Data analysis and interpretation: IH, KM, DJS, AET, TY**
4. **Manuscript preparation: IH, KM, DJS, AET, JAK, JLD, ENR, APH, EMB, MJD, TY.**

CLINICAL TRIAL REGISTRATION:

Registry: ClinicalTrials.gov; Title: Sleep Extension for Metabolic Health; Identifier: NCT04467268; URL: https://clinicaltrials.gov/ct2/show/NCT04467268

No. of tables: 4

No. of figures: 2

Manuscript word count: 5000 words

References count: 40

Abstract

While limited evidence suggests that longer sleep durations can improve metabolic health in habitual short sleepers, there is no consensus on how sustained sleep extension can be achieved. Eighteen male (mean age 41 ±9), overweight/obese (mean BMI 30±3 kg/m2), short sleepers at increased risk of type 2 diabetes were randomized to a 6-week sleep extension programme based on cognitive behavioural principles (n=10) or a control (n=8) group. The primary outcome was 6-week change in actigraphic TST. Fasting plasma insulin, insulin resistance (HOMA-IR), blood pressure, appetite-related hormones from a mixed-meal tolerance test, and continuous glucose levels were also measured. Baseline to 6-week change in TST was greater in the sleep extension group (79 min, 95% CI 68.90, 88.05 min vs. 6 min, 95% CI -4.43, 16.99 min). Change in the sleep extension and control groups respectively also showed: lower fasting insulin (-11.03 pmol/L, 95% CI -22.70, 0.65 vs. 7.07 pmol/L, 95% CI -4.60, 18.74); lower systolic (-11.09 mmHg, 95% CI -17.49, -4.69 vs. 0.76 mmHg, 95% CI -5.64, 7.15) and diastolic blood pressure (-12.16 mmHg, 95% CI -17.74, -6.59 vs. 1.38 mmHg, 95% CI -4.19, 6.96); lower mean amplitude of glucose excursions (0.34 mmol/L, 95% CI -0.57, -0.12 vs. 0.05 mmol/L, 95% CI -0.20, 0.30); lower fasting peptide YY levels (-18.25 pg/mL, 95%CI -41.90, 5.41 vs. 21.88 pg/mL, 95% CI -1.78, 45.53), and improved HOMA-IR (-0.51 95% CI -0.98, -0.03 vs. 0.28 95% CI -0.20, 0.76). Our protocol increased TST and improved markers of metabolic health in male overweight/obese short sleepers.

Key words: short sleep duration; insufficient sleep; cardiovascular health; metabolic health

Introduction

Epidemiologic evidence shows a cross-sectional association between shorter sleep durations (<7 hours/night) and a higher prevalence of type 2 diabetes, obesity, cardiovascular disease, impaired glucose regulation (Lou et al., 2014), and, in middle-aged men, elevated waist circumference and metabolic syndrome (Kim et al., 2018). Prospective studies have also reported independent associations between shorter sleep durations and elevated risks for: weight gain (Patel & Hu, 2008); impaired fasting glucose (Rafalson et al., 2010); and type 2 diabetes (Kita et al., 2012).

Such associations may be mediated by sleep-related changes in glucose metabolism and appetite regulation. Using both intravenous and oral glucose tolerance tests, experimental studies have shown that reducing sleep to ≤5.5 hours/night impairs glucose tolerance, lowers glucose effectiveness, and reduces the acute insulin response to glucose in healthy individuals (Buxton et al., 2010; Spiegel, Leproult, & Van Cauter, 1999). Sleep restriction has also been shown to reduce circulating leptin, and increase hunger (Spiegel et al., 2004), and stimulate the consumption of carbohydrate-rich foods (Brondel et al, 2010). Shorter sleep in individuals who are overweight is also accompanied by daytime sleepiness and fatigue, inhibiting physical activity and compounding energy imbalance (Bromley, Booth III, Kilkus, Imperial, & Penev, 2012).

Among some at-risk groups, therefore, sleep extension offers the theoretical benefit of reduced cardiometabolic risk (Brady & Hall, 2016) through improved glucose tolerance and superior appetite regulation (e.g. Buxton et al, 2010; Spiegel et al, 2004; Tasali et al, 2014). However, since extending sleep presents a greater challenge than restricting sleep, credible extension studies must demonstrate protocols which are practical, robust, and replicable. To date, modest sleep extension (20-40 minutes) has been reported in controlled comparisons of

cardiometabolic outcomes in participants who are healthy (Al Khatib et al., 2018), overweight (Haack et al., 2013), or diagnosed with metabolic syndrome (Lucassen et al., 2014). None of these studies assessed post-prandial glucose tolerance, and may not have tested the potential benefits of approximating a sleep duration in line with the recommended minimum of ≥7 hour/night (Hirshkowitz et al., 2015). However, improved glucose metabolism as measured by an oral glucose tolerance test (OGTT) has been reported in non-overweight habitually sleep-restricted adults (who slept <6hr/night on weekdays, but >7hr/night at weekends) who extended weekday total sleep time (TST) to above 6 hours (So-ngern et al, 2019).

In emphasising the need for further studies of sleep extension and metabolic health, a feasibility review by (Pizinger, Aggarwal, & St-Onge, 2018) also shows that sleep extension interventions tend to be vaguely described (inhibiting replication), with most limited to 'sleep hygiene' protocols. To date, no study has assessed the utility of deploying formal cognitive-behavioural strategies in promoting and maintaining sleep extension in overweight or obese short sleepers. Responding to these points, the present study was designed: 1) to develop and test the feasibility of a replicable sleep extension protocol, based on cognitive-Behavioral principles, which aimed to extend TST among short sleepers by an average of 60 min/night; and 2) to evaluate the impact of such sleep extension on the appetite and metabolic profiles of men who are overweight or obese, show increased risk of type 2 diabetes, but who report no symptoms of sleep disorder. An exemplar sample of men was selected; patterns of shorter sleep tend to be more stable in males, with less evidence of weekend compensation than in females (Killick et al, 2015).

METHODS

Study design and participants

The 2-arm randomized controlled trial (RCT) was conducted in the East Midlands, UK. Participants, recruited via media advertisements and screened using online questionnaires, met the following inclusion criteria: men aged 25 to 55 years; body mass index (BMI) > 25 kg/m^2; habitual short sleepers (with actigraphy-measured sleep duration of ≤ 6.5 hours per night); stable sleep/wake schedules. Increased risk of incident type 2 diabetes was assessed using items from the personal variables prediction model developed for the Framingham Offspring Study (gender, age, BMI, and parental history of diabetes) (Wilson et al., 2007). Exclusion criteria were: current diagnosis of a sleep disorder or cardiometabolic disease (including type 2 diabetes); reporting symptoms consistent with DSM-5 insomnia disorder; reporting symptoms of Restless Legs Syndrome (RLS) using 'essential diagnostic criteria' for RLS (Allen et al., 2003); high risk of obstructive sleep apnoea (OSA), using the Epworth Sleepiness Scale (Johns, 1991) and STOP Bang (Chung, Abdullah, & Liao, 2016); disrupted sleep schedules arising from (for example) frequent time-zone travel; the presence of young children in the home; shift work; or taking medications known to influence the study outcomes. Ethical approval was obtained from the Loughborough University Ethics Approvals (Human Participants) Sub-Committee, and all participants provided written informed consent before study participation.

Randomization

After baseline measurements, participants were randomized 1:1 (by researchers not involved in the study) into the 6-week sleep extension group or the control group using the method of minimization with BMI as a stratifying variable. Participants, and staff involved in administering the intervention were aware of group allocation. Staff involved in performing biochemical analyses were blinded to group allocation.

Procedures

Laboratory visits

Eligible participants attended the laboratory at Loughborough University for baseline questionnaire completion and assessments of: anthropometry; arterial blood pressure; fasting and postprandial glucose, insulin, and appetite-related hormone concentrations. The baseline visit was followed by a 2-week period of continuous free-living sleep and blood glucose monitoring. After this period, participants were randomized and received notification of their group allocation. All participants returned to the laboratory 6 weeks after randomization, and the baseline assessments were repeated.

Sleep extension intervention

Since none of the participants met DSM-5 criteria for insomnia disorder, or reported symptoms consistent with RLS or moderate/severe OSA, no assumptions were made about pathological mechanisms underlying their short sleep. Nevertheless, our sleep extension programme utilized behaviour-change principles already established in cognitive behavioural therapy for insomnia (Perlis, Jungquist, Smith, & Posner, 2006) and was designed around four assumptions: 1) that among habitual short sleepers, extending time in bed (TIB) represents a significant departure from routine; 2) that for practical purposes (accommodating personal, family and work schedules) extended time in bed is best anchored against typical rise-times; 3) that sleep onset may represent a particular challenge for those advancing habitual bed-times by over 1 hour each night; and 4) that in consenting to the trial, participants were motivated to make and sustain behavioural change.

Each intervention group participant met with an experienced sleep scientist to discuss and agree changes to their sleep and personal schedules. Discussions lasted 60-90 minutes, were

informed by sleep assessments from the baseline period, and aimed to increase TST by ≥1 hour/night. After a review of the participant's 24-hour routines, barriers to adopting a longer TIB were considered, and alternative sleep schedules were discussed. Typically, TIB was then anchored at the participant's usual rise time, and an earlier bedtime agreed. To support these behavioural changes: 1) opportunities to improve sleep hygiene were identified and discussed; 2) challenges which might arise from the revised schedule (particularly in relation to early evening routines, pre-bedtime practices and possible sleep onset problems) were discussed; and 3) the value of pre-sleep de-arousal strategies (specifically reducing cognitive activity, managing 'worry' thoughts, and pre-sleep relaxation techniques) were explained. The structure and information content of these discussions closely followed the "About Sleep", "Sleep Hygiene" and "Thoughts and Sleep" components of the online Sleepful application (Morgan, Hartescu, & Tomeny, 2017), a self-help sleep improvement programme. Advice was supported by the provision of self-help booklets addressing sleep hygiene and the management of pre-sleep cognitions which had been successfully trialled in an intervention for insomnia symptoms (Morgan, Gregory, Tomeny, David, & Gascoigne, 2012). In addition, participants were directed to the relaxation component (Step 6, Activity 3) of the online Sleepful programme and encouraged to download the accompanying MP3 recording of progressive muscle relaxation instructions. Finally, to capitalize on the participant's motivation at recruitment, and optimize adherence, the newly agreed sleep schedule was written into an agreement which the participant was asked to sign, simulating a 'therapeutic contract'. Schedules were reviewed by telephone at the end of the first week and revised if required.

Control group

Participants in the control group were asked to continue with their habitual sleep schedule. At the end of the study, this group was provided with the same written advice and online resources that had been offered to the intervention group.

Outcomes

The primary outcome was change from baseline to 6 weeks in total sleep time in the sleep extension group relative to the control group. Secondary outcomes included changes in biochemical measures of glucose tolerance, insulin resistance and appetite-related hormones, blood pressure, sleepiness and fatigue, and physical activity.

Sleep

Sleep parameters were assessed according to current guidelines (Ancoli-Israel et al., 2015): continuously for 14 days, starting on the evening of the baseline and follow-up laboratory visits, using actigraphs (MotionWatch 8, CamNTech, Cambridge, UK) set to record in 30-second epochs and worn on the non-dominant wrist. During this period, participants also completed a daily sleep diary recording bedtimes, rise times, any daytime naps, and any actigraph non-wear times. Actigraphy data were processed using the proprietary software MotionWare (v. 1.2.14, CamNTech, Cambridge, UK). Sleep variables assessed were: time in bed (time between getting into and getting out of bed, adjusted from the participants' sleep diaries), total sleep time (actual time spent asleep), sleep onset latency (time elapsed between 'lights out' and actigraphic sleep onset), wake after sleep onset (time awake after the first sleep period), and sleep efficiency (total sleep time expressed as a percentage of time in bed).

Glucose tolerance, insulin resistance and appetite-related hormones

At the baseline and follow-up laboratory visits, glucose tolerance was assessed using a mixed meal tolerance test (MMTT). Participants were required to refrain from vigorous physical activity for 72 hours, and refrain from alcohol and caffeine consumption for 48 hours prior to attendance. In the 24 hours before the test, participants consumed and recorded their regular meals. The final evening meal (a cheese and tomato pizza of approximately 900 calories) was provided by the study and delivered to the participant's home. On arrival at the laboratory between 08.00 – 09.00 after an overnight fast, participants were fitted with an intravenous cannula by a trained member of staff prior to consuming a standardized breakfast (comprising 17% protein; 53% carbohydrates; 30% fat and 600 kcal energy) within 15 minutes of arrival. Venous blood samples were collected immediately prior to the test meal (0 minutes), and at 30, 60, 90, 120, 150, and 180 minutes after completion of breakfast.

Continuous glucose monitoring

Following the MMTT, a continuous glucose monitoring (CGM; Freestyle Libre, Abbott Laboratories Ltd, UK) sensor was fitted on participants non-dominant upper arm by a trained member of the research team. Participants were asked to wear the device for up to 14 continuous days commencing immediately after the baseline and follow-up laboratory visits. The CGM sensor penetrates subcutaneous tissue and transmits information on interstitial fluid glucose concentration every minute. The wireless receiver, the size of a small cell phone, displays and retains the transmitted glucose levels. The device is unobtrusive, water proof, requires little training and minimal set-up, and has been validated in clinical populations (Terada et al., 2014). CGM delivered two measurements: mean blood glucose concentration (averaged over the monitoring period); and Mean Amplitude of Glycaemic Excursions (MAGE: mean blood glucose values exceeding one standard deviation of the 24-hour arithmetic average across the monitoring period).

Anthropometry and resting systolic and diastolic blood pressure

Measurements at baseline and follow-up visits included: height, quantified to the nearest 0.5 cm (Seca stadiometer, Hamburg, Germany); body mass, measured in a fasting state to the nearest 0.1 kg (Tanita digital scales, West Drayton, UK); waist circumference at the midpoint between the lower costal margin and the iliac crest to the nearest 0.5 cm, and neck circumference measured at mid-neck, between the midcervical spine and the midanterior neck, just below the prominence.

At both visits, three measurements of arterial blood pressure were taken, each after resting in a supine position for at least 10 minutes in a fasting state, between 8am and 9am. An upper arm fully automatic blood pressure monitor was used (Omron M5-1, Matsusaka Co., Japan). The average of the last two measurements are reported.

Sleep quality and fatigue

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a 19-item self-report questionnaire evaluating sleep schedules and disturbances over the previous month. The scale delivers a global score ranging from 0 to 21, with higher values indicative of poorer sleep. Levels of daytime fatigue were quantified using the Multidimensional Assessment of Fatigue (MAF), a 16-item scale which captures the degree, timing, associated distress and daily impact of fatigue over the previous week.

Habitual physical activity levels

Physical activity was measured over 14 consecutive days starting at 18:00 on the evening of the baseline and follow-up laboratory visits. Participants were asked to wear an Actigraph accelerometer (GTX3+, Actigraph, US) on the dominant hip side during wake time only. Participants were also asked to record the wear time and removal times of the device, and the time and duration of daytime naps, in a section of the sleep diary. Activity data were recorded as minutes of moderate to vigorous physical activity (MVPA) per week, using counts ≥2020 as the threshold (Troiano et al., 2008). Valid days for inclusion in analyses required at least 10 hours of wear, for at least 7 days, with non-wear time defined as 60 consecutive 0 counts.

Biochemical analyses

To eliminate inter-assay variation, samples from each participant were analysed in the same run. Plasma acylated ghrelin (SPI BIO, Montigny le Bretonneux, France), total peptide YY (PYY), (Millipore, Billerica, MA, USA), leptin (R&D Systems, Minneapolis, MN, USA) and insulin (Mercodia, Uppsala, Sweden) concentrations were determined by enzyme-linked immunosorbent assays. Plasma glucose concentrations were determined spectrophotometrically using a commercially available kit on a benchtop analyser (Pentra 400, HORIBA Medical, Montpellier, France). The within-batch coefficient of variation for each assay were: 4.0% for acylated ghrelin, 2.9% for total PYY, 4.2% for leptin, 3.4% for insulin and 0.5% for glucose. Fasting blood values were used to calculate HOMA-IR (Homeostatic Model Assessment for Insulin Resistance; Matthews, Hosker, Rudenski, Naylor, Treacher, & Turner, 1985) as: insulin (mU/ml) x glucose (mmol/l)/22.5.

Statistical analyses

A power calculation was based on the main outcome of total sleep time from actigraphy. Using an expected mean difference and standard deviation derived from previous study using a similar clinical population (Haack et al., 2013) of 31 minutes (SD = 22 minutes), alpha set at 0.05, and beta at 0.8, 9 participants per group were required.

The main analyses were conducted on an intention to treat (ITT) basis. Data are reported as means and standard deviations, or as median and interquartile range for skewed distributions. Time-averaged total area under the curve (AUC) values are calculated using the trapezium rule. Data distribution was visually inspected on histograms and q-q plots, and confirmed with Shapiro-Wilks tests. ANCOVA assumptions for residuals distribution normality, linearity of relationship between covariate and the dependent variables, and homogeneity of variance and regression slopes, were checked and met. General linear models were fitted with change scores from baseline to post-intervention as the dependent variable, group allocation (control or intervention) as a fixed factor, and baseline values of the dependent variable and BMI as covariates. Secondary outcomes were analysed using the same model specifications as for the primary outcome. Models were then repeated in exploratory per protocol analyses which excluded intervention participants whose average TST change scores were <40 minutes and control participants whose average TST change scores were >20 minutes. Outcomes are reported as adjusted differences in means. SPSS v.23 (IBM Corp., USA) and EasyGV (v. 9.0.R2, Hill, UK) were used for all analyses; two-tailed tests with alpha set at $p < 0.05$ (and 95% confidence intervals) are presented throughout.

Results

Participants

After the baseline measurements, 18 participants were randomized to the intervention (n = 10) or control (n = 8) group (Figure 1). Participant characteristics at baseline are shown in

Table 1: all participants were overweight or obese, showed relatively low levels of physical activity, and slept for <6.5 hours/night (mean actigraphy TST at baseline was 5.7 hours/night). Blood sampling and analyses were unsuccessful or not included for 3 participants in the study. In 2 participants this was due to failed intravenous cannula insertions. In a third participant results were clinically judged to be indicative of diagnosable diabetes and the values were withdrawn. Biochemical analyses are presented for 15 participants (sleep extension group n = 8; control group n = 7).

Adherence to sleep extension intervention

Adherence was defined at post-intervention as: an extension of time in bed of ≥ 60 minutes/night (intervention group); or a change of no more than 10% in time in bed (control group). Actigraphy, confirmed with sleep diaries, showed high adherence to the sleep extension programme with 90% of sleep extension participants increasing time in bed by at least 60 minutes/night at post-intervention. In the control group 75% adhered to the study protocol for their time in bed at post-intervention, with 25% of control participants showing an increase in time in bed of over 10% of their baseline values, after 6 weeks. In the general linear models, time in bed change from baseline to post-intervention showed a mean increase of 100.01 minutes/night (95% CI 74.85, 125.17 minutes/night) in the intervention group, and 3.61 minutes/night (95% CI -24.81, 32.04 minutes/night) in the control group.

Effectiveness of sleep extension intervention

Main trial outcome – total sleep time (ITT analysis)

There was a significant effect of the sleep extension intervention on total sleep time change from baseline to post-intervention, with the intervention group extending their sleep by an average of 72.19 minutes/night (95% CI 57.77, 86.62 minutes/night) compared to the control

group. Within the intervention group 60% of participants achieved the current total sleep guidelines of at least 7 hours per night at post-intervention, while 30% of participants were within 5% or less (20 minutes or less) of the current guidelines, after the 6-week intervention. Unadjusted values for baseline to post-intervention change are shown in Figure 2.

Secondary trial outcomes (ITT analyses)

All ITT trial outcomes from the general linear models are presented in Table 3. No significant treatment-control differences were found in sleep onset latency, wake after sleep onset, or sleep efficiency. There was a significant effect of the sleep extension intervention on PSQI global scores with the intervention group showing improved sleep quality compared to the control group: -2.99 (95% CI -5.59, -0.38). There were no significant effects of the sleep extension intervention on depression (HADS-Depression) and anxiety (HADS-Anxiety) scores.

The adjusted models showed significant reductions in both systolic and diastolic blood pressure in the intervention group compared to the control group (-11.85 mmHg (95% CI -21.05, -2.64 mmHg) and -13.55 mmHg (-21.45, -5.64 mmHg) respectively). There was also a significant effect of sleep extension on post-intervention fasting insulin levels and on the HOMA-IR measure of insulin resistance, with lower insulin levels (-18.09 pmol/L; 95% CI -34.74, -1.44 pmol/L) and lower HOMA-IR values (-0.79; 95% CI -1.47, -0.11) present in the intervention group, compared to the control group. However, no significant post-intervention effects were found for insulin time-adjusted AUC (Table 3). Sleep extension did impact change in fasting total PYY, and time averaged AUC models, with significant decreases shown in the intervention group (-40.13 pg/mL (95% CI -74.93, -5.32 pg/mL), and -26.24 pg/mL/h (95% CI -46.22, -6.25 pg/mL/h) respectively).

While mean glucose values from the continuous glucose monitoring systems (CGMs) showed no significant post-intervention differences, adjusted models did show a significant effect of the intervention on change in mean amplitude of glucose excursions (from CGMs) with a reduction in the variability measure in the intervention group, compared to the change in the control group: -0.40 N (95%CI -0.73, -0.06 N). No significant post intervention effects were found for: fasting glucose, and time-averaged glucose AUC; fasting ghrelin, and ghrelin time-adjusted AUC; or fasting leptin levels. Neither group showed significant changes in mean body weight during the study (baseline to 6-week follow-up means respectively: sleep extension group 94.08 kgs vs. 94.05 kgs; control group 94.47kg vs. 92.42 kgs).

Only 1 intervention (mean sleep extension = 25 minutes) and 2 control participants (mean sleep extension = 21 and 32 minutes) were excluded from the per protocol analyses which, overall, showed the same pattern of significant/nonsignificant results as those obtained from ITT models (Table 4).

Discussion

This trial achieved its objective of developing and testing a replicable protocol which successfully extended total sleep time (TST), and favourably impacted key indices of metabolic health in male overweight or obese habitual short sleepers. Both the average extension of TST (72 minutes), and the degree of adherence obtained within the intervention group (90%) are superior to values reported for earlier studies using sleep extension to improve metabolic health (Al Khatib et al., 2018; Haack et al., 2013; Lucassen et al., 2014; Leproult et al, 2015; So-ngern et al, 2019). At follow-up 60% of intervention participants reported average sleep durations within the current recommended guidelines (7-9 hours per night), with a further 30% of participants being within 5% of the minimum recommended

guidelines. All intervention group participants accessed the recommended online resources, with patterns of use showing multiple individual logins. It is reasonable to conclude, therefore, that the success of the protocol was due in part to the initial introduction to, and to the subsequent availability of cognitive behavioural strategies for managing the earlier scheduling of sleep onset times. Unlike earlier reported sleep extension studies, increased TST was not achieved at the cost of compromised sleep efficiency and continuity (e.g. (Al Khatib et al., 2018)). Despite an increase in sleep duration in the sleep extension group, no significant changes in sleep latency, wake after sleep onset, sleep efficiency, were observed across the intervention period. Furthermore, the increase in self-reported sleep quality (measured by the PSQI) in response to the sleep extension intervention suggests an overall positive response to the intervention. These conclusions are supported by the per protocol findings (Table 4) which used an inclusion threshold (average sleep extension ≥40 minutes) approximating the maximum extension reported in earlier studies. This threshold excluded only 1 intervention group participant, and resulted in a pattern of exploratory outcomes similar to those obtained from the ITT models. While these analyses are not without limitations (see below) they do demonstrate the high levels of adherence, and consequent separation of control-intervention TST values, achieved by the present sleep extension protocol.

Given the consistency of change achieved in intervention group sleep duration, the present results both extend, and address inconsistencies in earlier research findings. Evidence to date about the role of extending sleep on glucose and insulin regulation has been equivocal. In an uncontrolled study of healthy young adult short sleepers, for example, Leproult et al (2015) reported positive changes in fasting glucose, insulin, and insulin sensitivity (HOMA-IR) following a 6-week intervention achieving an average of 1 hour/night of sleep extension. In contrast, Al Khatib et al (2018) showed no changes in fasting insulin, glucose, leptin, or

ghrelin concentrations in healthy participants whose sleep was extended by approximately 20 min/night in a 4-week intervention. The present findings, showing a pattern of positive changes in glucose and insulin outcomes, and improved insulin resistance, support a conclusion that both the amount of additional sleep, and the duration of sleep extension, may be critical in obtaining positive metabolic health outcomes.

The present finding that variability measures from 13-day continuous glucose monitoring showed significant reductions in the intervention group also complements results from earlier studies of glucose regulation. High glucose variability has been found to increase the risk of hypoglycaemia, especially when the mean glucose concentration is close to normal values (Škrha, Šoupal, & Prázný, 2016) as was the case among present participants. It is also relevant that MVPA levels were not significantly altered by the sleep extension intervention, suggesting that the present metabolic health outcomes are not attributable to changes in activity-related energy expenditure.

Reductions in systolic and diastolic resting blood pressure reported in the present study after sleep extension are also consistent with earlier reported results. In a 6-week sleep extension study which achieved an average increase in TST of 35 min/night, Haack et al (2013) found that hypertensive and pre-hypertensive participants showed an average decrease in beat-by-beat systolic blood pressure of 14 mm/Hg, and a diastolic decrease of 8 mm/Hg. Our study showed similar decreases when assessed at a single timepoint before, and after the intervention. Significant reductions in systolic and diastolic blood pressure were also reported by Baron et al (2019) following a 6-week technology-assisted sleep extension programme which achieved an average increase of 47 min/night among hypertensive adults originally sleeping <7 hr/night. Since the baseline values of blood pressure in our participants showed a profile of pre-hypertensive individuals (combined average for both groups of 136/85 mm/Hg), these post-intervention changes have implications for cardiovascular health. These

results are similar to other Behavioral interventions which reduce blood pressure e.g. (Börjesson, Onerup, Lundqvist, & Dahlöf, 2016), such as a 6-week moderate intensity physical activity intervention in hypertensive individuals (Yakasai, Maharaj, Nuhu, & Danazumi, 2020).

Shorter sleep has been robustly associated with significant reductions in leptin and reciprocal increases in ghrelin, accompanied by increased hunger ratings (Spiegel et al, 2004; Taheri et al, 2004). Given the rigorous protocol employed in our study (a fasting mixed-meal tolerance test with post-ingestion blood samples every 30 minutes), our failure to detect appetite-related hormone changes after our intervention may have been due to the low sample size, compounded by wide variability in hormone concentrations between participants. Nevertheless, this study does allow for the derivation of standard variability measures for larger studies, the identification of trends in main outcome changes, and the feasibility of the intervention and measures used. As such, our sample size was adequate for these aims.

The biochemical analyses did show counterintuitive changes in total PYY, with a decrease in the hormone, indicating decreased satiety in the sleep extension group. As dietary intake was not analysed in our study, it is not known whether the changes in PYY would be accompanied by the respective dietary intake changes. A previous study of acute sleep extension in healthy male short sleepers showed a similar decrease in PYY, which was not accompanied by corresponding expected dietary intake changes (Killick et al., 2015). A calorimetry study of sleep duration manipulation for 2 weeks showed that changes in levels of PYY were not accompanied by expected changes in eating behaviour (Markwald et al., 2013), with both short and long sleepers. Further larger studies need to elucidate the direction of change for PYY with sleep extension, as well as its relevance for dietary intake.

Limitations to our study are acknowledged. While adequately powered for the principal outcome, the sample size was small; consideration of the secondary outcomes should recognize the wide confidence intervals. Caution is also appropriate in interpreting the per protocol analyses. Conducted to assess the robustness of the present protocol, and to allow comparisons with earlier studies, these exploratory analyses further diminished sample sizes and likely amplified Type 1 error rates.

In addition, our study methodology did not adequately capture dietary intake. While the present participants were asked to record their dietary intake at the baseline and follow-up periods, the quality of reports proved inconsistent, and inadequate for reliable analyses. Current dietary assessments tools in research are generally unreliable, which makes the accurate assessment of dietary intake inherently challenging (Dhurandhar et al., 2015). As a result, the present study was unable to identify possible changes in dietary composition.

The procedure for measuring blood pressure was standardized across conditions at timepoints; however, one point in the day measures are prone to significant variations unrelated to the study condition (O'brien et al., 2003), and we did not control for cuff size, emotional state, or bladder fullness. Larger studies, using validated 24-hour blood pressure measures over a sustained period, and assessing dietary intake using precise and acceptable (to participants) measures, are warranted. That the present study included only men is also a limitation; future studies addressing sleep extension and metabolic health should include males and females.

In conclusion, this study demonstrates that a protocol which increases TIB through a negotiated rescheduling of sleep, recognizes and addresses possible barriers to sleep-behaviour change, and provides evidence-based cognitive behavioural resources to overcome sleep onset difficulties, can achieve significant and sustained sleep extension in overweight

habitual short sleepers which favourably impacts blood pressure control and insulin regulation. These findings extend earlier research and offer both a methodological and scientific justification for larger scale controlled trials in this important area.

REFERENCES

Al Khatib, H. K., Hall, W. L., Creedon, A., Ooi, E., Masri, T., McGowan, L., . . . Pot, G. K. (2018). Sleep extension is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. *The American journal of clinical nutrition, 107*(1), 43-53. doi:10.1093/ajcn/nqx030

Allen, R. P., Picchietti, D., Hening, W. A., Trenkwalder, C., Walters, A. S., & Montplaisi, J. (2003). Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology: A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep medicine, 4*(2), 101-119. doi:https://doi.org/10.1016/S1389-9457(03)00010-8

Ancoli-Israel, S., Martin, J. L., Blackwell, T., Buenaver, L., Liu, L., Meltzer, L. J., . . . Taylor, D. J. (2015). The SBSM guide to actigraphy monitoring: clinical and research applications. *Behavioral Sleep Medicine, 13*(sup1), S4-S38.

Börjesson, M., Onerup, A., Lundqvist, S., & Dahlöf, B. (2016). Physical activity and exercise lower blood pressure in individuals with hypertension: narrative review of 27 RCTs. *British journal of sports medicine, 50*(6), 356-361. doi:10.1136/bjsports-2015-095786

Brady, E. M., & Hall, A. P. (2016). Sleep and type 2 diabetes mellitus. *Pract Diabetes, 33*, 23-26.

Bromley, L. E., Booth III, J. N., Kilkus, J. M., Imperial, J. G., & Penev, P. D. (2012). Sleep restriction decreases the physical activity of adults at risk for type 2 diabetes. *Sleep, 35*(7), 977.

Buxton, O. M., Pavlova, M., Reid, E. W., Wang, W., Simonson, D. C., & Adler, G. K. (2010). Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes, 59*(9), 2126-2133.

Chung, F., Abdullah, H. R., & Liao, P. (2016). STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. *Chest, 149*(3), 631-638.

Dhurandhar, N. V., Schoeller, D., Brown, A. W., Heymsfield, S. B., Thomas, D., Sørensen, T. I., . . . Allison, D. B. (2015). Energy balance measurement: when something is not better than nothing. *International Journal of Obesity, 39*(7), 1109-1113.

Haack, M., Serrador, J., Cohen, D., Simpson, N., Meier-Ewert, H., & Mullington, J. M. (2013). Increasing sleep duration to lower beat-to-beat blood pressure: a pilot study. *Journal of sleep research, 22*(3), 295-304.

Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., . . . Adams Hillard, P. J. (2015). National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health: Journal of the National Sleep Foundation, 1*(1), 40-43.

Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep, 14*(6), 540-545.

Killick, R., Hoyos, C. M., Melehan, K. L., Dungan, G. C., 2nd, Poh, J., & Liu, P. Y. (2015). Metabolic and hormonal effects of 'catch-up' sleep in men with chronic, repetitive, lifestyle-driven sleep restriction. *Clin Endocrinol (Oxf), 83*(4), 498-507. doi:10.1111/cen.12747

Kim, C. E., Shin, S., Lee, H.-W., Lim, J., Lee, J.-k., Shin, A., & Kang, D. (2018). Association between sleep duration and metabolic syndrome: a cross-

sectional study. *BMC Public Health, 18*(1), 720. doi:10.1186/s12889-018-5557-8
Kita, T., Yoshioka, E., Satoh, H., Saijo, Y., Kawaharada, M., Okada, E., & Kishi, R. (2012). Short sleep duration and poor sleep quality increase the risk of diabetes in Japanese workers with no family history of diabetes. *Diabetes care, 35*(2), 313-318.
Lou, P., Chen, P., Zhang, L., Zhang, P., Chang, G., Zhang, N., . . . Qiao, C. (2014). Interaction of sleep quality and sleep duration on impaired fasting glucose: a population-based cross-sectional survey in China. *BMJ open, 4*(3), e004436.
Lucassen, E. A., Piaggi, P., Dsurney, J., de Jonge, L., Zhao, X.-c., Mattingly, M. S., . . . Cizza, G. (2014). Sleep extension improves neurocognitive functions in chronically sleep-deprived obese individuals. *PloS one, 9*(1), e84832.
Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences, 110*(14), 5695-5700.
Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412–419.
Morgan, K., Gregory, P., Tomeny, M., David, B. M., & Gascoigne, C. (2012). Self-Help Treatment for Insomnia Symptoms Associated with Chronic Conditions in Older Adults: A Randomized Controlled Trial. *Journal of the American Geriatrics Society, 60*(10), 1803-1810.
Morgan, K., Hartescu, I., & Tomeny, M. (2017). Sleepful (v2.0) [Mobile application software]. Retrieved from https://sleepful.me/.Sleepful
O'brien, E., Asmar, R., Beilin, L., Imai, Y., Mallion, J.-M., Mancia, G., . . . Palatini, P. (2003). European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *Journal of hypertension, 21*(5), 821-848.
Patel, S. R., & Hu, F. B. (2008). Short sleep duration and weight gain: a systematic review. *Obesity, 16*(3), 643-653.
Perlis, M. L., Jungquist, C., Smith, M. T., & Posner, D. (2006). *Cognitive behavioral treatment of insomnia: A session-by-session guide* (Vol. 1): Springer Science & Business Media.
Pizinger, T. M., Aggarwal, B., & St-Onge, M.-P. (2018). Sleep Extension in Short Sleepers: An Evaluation of Feasibility and Effectiveness for Weight Management and Cardiometabolic Disease Prevention. *Frontiers in Endocrinology, 9*(392). doi:10.3389/fendo.2018.00392
Rafalson, L., Donahue, R. P., Stranges, S., Lamonte, M. J., Dmochowski, J., Dorn, J., & Trevisan, M. (2010). Short sleep duration is associated with the development of impaired fasting glucose: the Western New York Health Study. *Ann Epidemiol, 20*(12), 883-889.
Škrha, J., Šoupal, J., & Prázný, M. (2016). Glucose variability, HbA1c and microvascular complications. *Reviews in Endocrine and Metabolic Disorders, 17*(1), 103-110.
Spiegel, K., Leproult, R., L'Hermite-Balériaux, M., Copinschi, G., Penev, P. D., & Van Cauter, E. (2004). Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol,

and thyrotropin. *The Journal of clinical endocrinology & metabolism, 89*(11), 5762-5771.
Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *The Lancet, 354*(9188), 1435-1439.
Terada, T., Loehr, S., Guigard, E., McCargar, L. J., Bell, G. J., Senior, P., & Boule, N. G. (2014). Test-retest reliability of a continuous glucose monitoring system in individuals with type 2 diabetes. *Diabetes Technol Ther, 16*(8), 491-498. doi:10.1089/dia.2013.0355
Troiano, R. P., Berrigan, D., Dodd, K. W., Mâsse, L. C., Tilert, T., & McDowell, M. (2008). Physical activity in the United States measured by accelerometer. *Medicine and science in sports and exercise, 40*(1), 181-188.
Wilson, P. W. F., Meigs, J. B., Sullivan, L., Fox, C. S., Nathan, D. M., & D'Agostino, R. B., Sr. (2007). Prediction of Incident Diabetes Mellitus in Middle-aged Adults: The Framingham Offspring Study. *Archives of Internal Medicine, 167*(10), 1068-1074. doi:10.1001/archinte.167.10.1068
Yakasai, A. M., Maharaj, S. S., Nuhu, J. M., & Danazumi, M. S. (2020). Moderate intensity endurance exercise: a beneficial intervention for relative cardiovascular parameters of primary and secondary hypertensive patients. Randomised controlled trial. *European Journal of Physiotherapy*, 1-7. doi:10.1080/21679169.2020.1720800

Table 1 Participants characteristics at baseline in the sleep extension study

Characteristics at baseline	Control Group N=8	Intervention Group N=10
	Mean (SD) or Frequency (N or %)*	
Age (years)	43.00 (10.12)	39.89 (8.79)
Education (% Higher[1])	90%	80%
Ethnic origin % White	80%	80%
% Asian/British Asian	20%	20%
Marital status (% Married/Partnership)	80%	80%
Body mass index (kg/m^2)	29.88 (4.15)	29.26 (1.64)
Waist circumference (cm)	105 (9)	103 (7)
Fatigue (MAF[2] score)	24.57 (3.61)	29.47 (2.99)
Sleepiness (ESS[3] score)	11.77 (6.39)	12.77 (5.23)
EQ5D[4] (Visual Analogue Score)	81.66 (7.90)	74.77 (20.01)
MEQ[5] Type (N)		
Morning Type	1	2
Intermediate Type	3	4
Evening Type	5	3

*** Data are presented as means (standard deviation), or frequency (count or percentage)**

[1]Degree level or equivalent tertiary education; [2]MAF – Multidimensional Assessment of Fatigue; [3]ESS – Epworth Sleepiness Scale; [4]EQ5D Visual Analogue Score range 0-100; [5]MEQ - Horne & Ostberg Morningness-Eveningness Questionnaire

Table 2 Baseline values for primary and secondary outcomes in the sleep extension study

Study outcomes	Control Group N=8	Intervention Group N=10
	Mean (SD) or Median (IQR)*	
Primary outcome		
Total sleep duration[1] (min)	349.00 (29.25)	344.20 (46.83)
Secondary outcomes		
Time in Bed[1] (min)	431.63 (46.07)	398.40 (40.16)
Sleep Onset Latency[1] (min)	13.00 (11.96)	8.90 (4.93)
Wake After Sleep Onset[1] (min)	54.63 (20.54)	85.83 (22.03)
Sleep Efficiency[1] (%)	80.73 (6.93)	85.83 (7.52)
Sleep Quality (PSQI[2] Global Score)	9.44 (2.65)	10.76 (3.07)
Depression (HADS[3] score)	6.11 (3.48)	7.56 (4.30)
Anxiety (HADS[3] score)	7.67 (2.12)	6.89 (4.31)
Physical Activity[4] (MET/Week)[5]	1142.00 (1107)	960 (1981)
Blood pressures systolic[6] (mmHg)	135 (9)	136 (10)
Blood pressure diastolic[6] (mmHg)	84 (9)	84 (10)
Glucose[7] (fasting) (mmol/L)	5.55 (0.34)	5.72 (0.70)
Glucose[8] (TA-AUC) (mmol/L/h)	6.24 (0.74)	5.65 (1.14)
Insulin[7] (fasting) (pmol/L)	62 (25)	52 (30)
Insulin[8] (TA-AUC) (pmol/L/h)[5]	349.00 (329.20, 394.20)	308.10 (194.98, 427.43)
Acylated Ghrelin[7] (Fasting) (pg/mL)[5]	46.90 (34.40, 129.60)	49.30 (34.70, 77.70)
Acylated Ghrelin[8] (TA-AUC) (pg/mL/h)[5]	25.60 (22.60, 68.10)	28.60 (18.85, 53.30)
Total PYY[7] (fasting) (pg/mL)	186.36 (69.35)	151.24 (45.73)
Total PYY[8] (TA-AUC) (pg/mL/h)[5]	244.70 (199.80, 247.00)	183.45 (147.35, 234.93)
Leptin[7] (ng/mL) (fasting)[5]	7.24 (5.02, 14.38)	10.30 (6.99, 11.51)
Mean Daily Glucose (CGMs)[9] (mmol/L)	5.80 (0.36)	5.82 (1.25)
MAGE[10] (CGMs)[9] (N)	2.65 (0.54)	2.73 (0.97)
HOMA-IR[11]	2.36 (1.46, 3.42)	2.15 (1.0, 2.94)

***Data are presented as mean (standard deviation) or median (interquartile range)**

1 Data derived from sleep actigraphy from an average of 14 continuous valid nights monitoring at baseline, adjusted with sleep diary time in bed anchor points. 2 PSQI – Pittsburgh Sleep Quality Index. 3 HADS – Hospital Anxiety and Depression Scale. 4 Data derived from GTX3+ accelerometers worn for an average of 11.12 valid days at baseline (SD=1.8). 5 Data presented as median (interquartile range). 6 Blood pressure measures recorded after resting in a supine position for 10 minutes in a fasting state, using a random-zero sphygmomanometer. 7 Fasting blood samples were obtained after a standardised meal the night before blood sampling, and overnight fasting (min 8 hours fasting). 8 Blood samples were obtained after a standardised breakfast at 0, 30, 60, 90, 120, 150 and 180min), and time-averaged area under the curve was calculated using the trapezium rule. 9 Data derived from continuous glucose monitoring devices worn for an average of 12.01 valid days (SD=0.84) at baseline. 10 MAGE – Mean Amplitude of Glycaemic Excursions, data derived from continuous glucose monitoring device, and calculated as an arithmetic average of either the upward or downward of all glycaemic excursions exceeding the threshold (standard deviation of blood glucose (SDBG) obtained from all blood glucose concentrations within 24-hour period. 11 Homeostatic Model Assessment for Insulin Resistance calculated as: fasting serum insulin (mU/ml) x fasting plasma glucose (mmol/l)/22.5

Table 3 Change in outcomes at 6 weeks in the control and intervention group and associated intervention effect (intention to treat analyses)

	Control Group	Intervention Group	Intervention effect Intervention vs control**
	Change value (95% CI)*		
Primary outcome	*N = 8*	*N = 10*	
Total sleep duration[1] (min)	6.28 (-4.43, 16.99)	78.48 (68.90, 88.05)	**72.19 (57.77, 86.62)**
Secondary outcomes	N = 8	N = 10	
Time in Bed[1] (min)	3.61 (-24.81, 32.04)	100.01 (74.85, 125.17)	**96.40 (56.73, 136.06)**
Sleep Onset Latency[1] (min)	1.65 (-9.78, 13.08)	9.38 (-0.80, 19.56)	7.73 (-7.84, 23.30)
Wake after sleep onset[1] (min)	-4.61 (-20.45, 11.23)	5.89 (-8.18, 19.95)	10.50 (-11.38, 32.38)
Sleep Efficiency[1] (%)	0.68 (-3.33, 4.70)	-0.18 (-3.74, 3.39)	-0.86 (-6.42, 4.70)
Sleep Quality (PSQI Global Score[2])	-2.56 (-4.38, -0.75)	-5.55 (-7.36, -3.74)	**-2.99 (-5.59, -0.38)**
Depression (HADS-D Score[3])	-1.34 (-3.58, 0.90)	-2.44 (-4.68, -0.20)	-1.10 (-4.32, 2.13)
Anxiety (HADS-A Score[3])	-0.75 (-2.74, 1.24)	-1.25 (-3.24, 0.74)	-0.51 (-3.33, 2.32)
Physical Activity (MET/Week)[4]	788.52 (-351.94, 1298.28)	-99.28 (-1239.74, 1041.19)	-887.80 (-2507.39, 731.80)
Blood Pressure Systolic[6] (mmHg)	0.76 (-5.64, 7.15)	-11.09 (-17.49, -4.69)	**-11.85 (-21.05, -2.64)**
Blood Pressure Diastolic[6] (mmHg)	1.38 (-4.19, 6.96)	-12.16 (-17.74, -6.59)	**-13.55 (-21.45, -5.64)**
Secondary outcomes (biochemical)	*N = 7*	*N = 7*	
Glucose (fasting)[7] (mmol/L)	-0.03 (-0.19, 0.13)	0.10 (-0.07, 0.26)	0.12 (-0.11, 0.35)
Glucose TA-AUC[8] (mmol/L/h)	-0.10 (-0.71, 0.52)	-0.28 (-0.85, 0.30)	-0.18 (-1.04, 0.68)
Insulin (fasting[7]) (pmol/L)	7.07 (-4.60, 18.74)	-11.03 (-22.70, 0.65)	**-18.09 (-34.74, -1.44)**
Insulin TA-AUC[8] (pmol/L/h)	32.31 (-55.70, 120.33)	-13.68 (-95.90, 68.55)	-45.99 (-167.54, 75.56)

Acylated Ghrelin (fasting)[7] (pg/mL)	11.23 (-5.68, 28.14)	17.92 (1.01, 34.82)	6.69 (-17.44, 30.82)
Acylated Ghrelin (TA-AUC)[8] (pg/mL/h)	5.63 (-2.36, 13.61)	9.74 (2.28, 17.20)	4.11 (-6.94, 15.16)
Total PYY (fasting)[7] (pg/mL)	21.88 (-1.78, 45.53)	-18.25 (-41.90, 5.41)	**-40.13 (-74.93, -5.32)**
Total PYY TA-AUC[8] (pg/mL/h)	20.40 (6.23, 34.57)	-5.84 (-19.03, 7.36)	**-26.24 (-46.22, -6.25)**
Leptin (fasting)[7] (ng/mL)	-1.41 (-4.31, 1.48)	0.34 (-2.56, 3.23)	1.75 (-2.35, 5.85)
HOMA-IR[9]	0.28 (-0.20, 0.76)	-0.51 (-0.98, -0.03)	**-0.79 (-1.47, -0.11)**
	N = 8	*N = 10*	
Mean Daily Glucose (CGMs)[10] (mmol/L)	-0.20 (-0.58, 0.18)	-0.09 (-0.43, 0.24)	0.11 (-0.40, 0.61)
MAGE[11] (CGMs)[10] (n)	0.05 (-0.20, 0.30)	-0.34 (-0.57, -0.12)	**-0.40 (-0.73, -0.06)**

***Data as adjusted means change between baseline and post-intervention (95% CI).**

****Bold values indicate significant (p < 0.05) differences between groups in change from baseline, in ANCOVA models, adjusted for baseline values, and baseline body mass index, as covariates.**

1 Data derived from sleep actigraphy, adjusted with sleep diary time in bed anchor points. 2 PSQI – Pittsburgh Sleep Quality Index. 3 HADS – Hospital Anxiety and Depression Scale. 4 Data derived from GTX3+ accelerometer. 6 Blood pressure measures recorded after resting in a supine position for at least 10 minutes, in a fasting state, using a random-zero sphygmomanometer. 7 Fasting blood samples were obtained after a standardised meal the night before blood sampling, and overnight fasting (min 8 hours fasting). 8 Blood samples were obtained after a standardised breakfast at 0, 30, 60, 90, 120, 150 and 180min), and time-averaged area under the curve was calculated using the trapezium rule. 9 Homeostatic Model Assessment for Insulin Resistance calculated as: fasting serum insulin (mU/ml) x fasting plasma glucose (mmol/l)/22.5. 10 Data derived from continuous glucose monitoring devices. 11 MAGE – Mean Amplitude of Glycaemic Excursions, data derived from continuous glucose monitoring devices, and calculated as an arithmetic average of either the upward or downward of all glycaemic excursions exceeding the threshold (standard deviation of blood glucose (SDBG) obtained from all blood glucose concentrations within 24-hour period).

Table 4 Change in outcomes at 6 weeks in the control and intervention group and associated intervention effect (per protocol analyses*)

	Control Group	Intervention Group	Intervention effect Intervention vs control***
	Change value (95% CI)**		
Primary outcome	*N = 6*	*N = 9*	
Total sleep duration[1] (min)	5.30 (-7.53, 18.12)	80.58 (70.22, 90.94)	**75.29 (58.40, 92.17)**
Secondary outcomes	N = 6	N = 9	
Time in Bed[1] (min)	0.97 (-33.19, 35.13)	94.80 (67.82, 121.78)	**93.83 (46.97, 140.69)**
Sleep Onset Latency[1] (min)	2.63 (-12.40, 17.66)	6.91 (-5.20, 19.02)	4.28 (-15.63, 24.19)
Wake after sleep onset[1] (min)	-8.97 (-28.34, 10.39)	4.204 (-11.48, 19.89)	13.18 (-12.21, 38.57)
Sleep Efficiency[1] (%)	1.97 (-3.03, 6.97)	0.632 (-3.40, 4.66)	-1.34 (-7.96, 5.29)
Sleep Quality (PSQI Global Score[2])	-3.28 (-5.60, -0.95)	-5.63 (-7.80, -3.47)	**-2.36 (-5.63, 0.91)**
Depression (HADS-D Score[3])	-1.70 (-4.53, 1.12)	-2.76 (-5.39, -.012)	-1.05 (-4.98, 2.88)
Anxiety (HADS-A Score[3])	-0.67 (-3.22, 1.87)	-1.17 (-3.54, 1.21)	-0.50 (-3.97, 2.98)
Physical Activity (MET/Week)[4]	1191.07 (-87.58, 2469.71)	-343.03 (-1537.92, 851.85)	-1534.10 (-3297.01, 228.80)
Blood Pressure Systolic[6] (mmHg)	1.63 (-6.25, 9.50)	-12.30 (-19.66, -4.94)	**-13.93 (-24.80, -3.05)**
Blood Pressure Diastolic[6] (mmHg)	1.38 (-5.73, 8.49)	-12.20 (-18.86, -5.56)	**-13.59 (-23.33 -3.838**
Secondary outcomes (biochemical)	*N = 5*	*N = 6*	
Glucose (fasting)[7] (mmol/L)	0.05 (-0.15, 0.25)	0.04 (-0.15, 0.22)	-.012 (-0.30, 0.27)
Glucose TA-AUC[8] (mmol/L/h)	0.18 (-0.68, 1.04)	-0.35 (-1.05, 0.36)	-0.52 (-1.73, 0.69)
Insulin (fasting[7]) (pmol/L)	3.54 (-6.80, 13.89)	-14.58 (-23.93, -5.23)	**-18.12 (32.81, -3.43)**
Insulin TA-AUC[8] (pmol/L/h)	51.97 (-71.48, 175.42)	-31.06 (-133.03, 70.90)	-83.03 (-253.51, 87.44)

Acylated Ghrelin (fasting)[7] (pg/mL)	5.85 (-13.64, 25.34)	9.61 (-8.01, 27.22)	3.76 (-23.91, 31.43)
Acylated Ghrelin (TA-AUC)[8] (pg/mL/h)	2.96 (-7.23, 13.14)	2.83 (-5.58, 11.24)	-0.13 (-14.20, 13.94)
Total PYY (fasting)[7] (pg/mL)	34.42 (8.01, 60.84)	-27.44 (-51.24, -3.63)	**-61.86 (-99.83, -23.89)**
Total PYY TA-AUC[8] (pg/mL/h)	30.58 (13.04, 48.12)	-12.03 (-26.28, 2.22)	**-12.03 (-26.28, 2.22)**
Leptin (fasting)[7] (ng/mL)	-0.20 (-2.98, 2.59)	-0.60 (-3.12, 1.91)	-0.41 (-4.37, 3.56)
HOMA-IR[9]	0.18 (-0.31, 0.67)	-0.67 (-1.11, -0.23)	**-0.85 (-1.54, -0.15)**
	N = 6	*N = 9*	
Mean Daily Glucose (CGMs)[10] (mmol/L)	-0.25 (-0.73, 0.23)	-0.18 (-0.57, 0.21)	0.07 (-0.55, 0.69)
MAGE[11] (CGMs)[10] (n)	0.06 (-0.26, 0.38)	-0.40 (-0.66, -0.13)	**-0.46 (-0.87, -0.04)**

*Analyses exclude intervention participants whose TST change scores were <40 minutes, and control participants whose TST change scores were >20 minutes.

**Data as adjusted means change between baseline and post-intervention (95% CI).

***Bold values indicate significant ($p < 0.05$) differences between groups in change from baseline, in ANCOVA models, adjusted for baseline values, and baseline body mass index, as covariates.

1 Data derived from sleep actigraphy, adjusted with sleep diary time in bed anchor points. 2 PSQI – Pittsburgh Sleep Quality Index. 3 HADS – Hospital Anxiety and Depression Scale. 4 Data derived from GTX3+ accelerometer. 6 Blood pressure measures recorded after resting in a supine position for at least 10 minutes, in a fasting state, using a random-zero sphygmomanometer. 7 Fasting blood samples were obtained after a standardised meal the night before blood sampling, and overnight fasting (min 8 hours fasting). 8 Blood samples were obtained after a standardised breakfast at 0, 30, 60, 90, 120, 150 and 180min), and time-averaged area under the curve was calculated using the trapezium rule. 9 Homeostatic Model Assessment for Insulin Resistance calculated as: fasting serum insulin (mU/ml) x fasting plasma glucose (mmol/l)/22.5. 10 Data derived from continuous glucose monitoring devices. 11 MAGE – Mean Amplitude of Glycaemic Excursions, data derived from continuous glucose monitoring devices, and calculated as an arithmetic average of either the upward or downward of all glycaemic excursions exceeding the threshold (standard deviation of blood glucose (SDBG) obtained from all blood glucose concentrations within 24-hour period).