Sleep duration, obesity and insulin resistance in a multi-ethnic UK population at high risk of diabetes

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Abstract

Aims: Investigating the association between sleep duration, obesity, adipokines and insulin resistance (via Leptin:Adiponectin ratio (LAR)), in those at high risk of type 2 diabetes mellitus (T2DM). **Methods:** Adults with impaired glucose regulation (IGR) were included. Fasting bloods for inflammatory biomarkers and glycaemic status, 2-hour glucose, anthropometrics, objective physical activity, and self-reported sleep were collected. The average number of hours slept in a 24 hour period was categorised as ≤5.5, 6-6.5, 7-7.5, 8-8.5, and ≥9 hours. Regression models were fitted with sleep (linear and quadratic) and logistic regression used for IGR and adjusted for age, sex, ethnicity, body mass index, waist circumference and objective physical activity. **Results:** 2848 participants included (593 with inflammatory marker data). Short sleep and long sleep duration were significantly independently associated with higher body mass index ($P<0.001$), body weight ($P<0.01$), and waist circumference ($P<0.001$). 6-7 hours of sleep/24 hours is associated with the lowest obesity measures. Fasting insulin and LAR were positively associated with sleep duration. Adiponectin levels were negatively associated with sleep duration. **Conclusions:** These results support the evidence of an association between short and long sleep duration and indices of obesity. We demonstrate an independent relationship between long sleep duration and insulin resistance.

Key Words: Sleep duration, insulin resistance, adipokines, obesity

Introduction

The prevalence of both obesity and diabetes have reached epic proportions; in England alone, 23% of all adults are classified as obese,[1] and 6% have been diagnosed with Type 2 Diabetes Mellitus (T2DM).[2] Principal contributors to the incidence of these conditions are changes in societal and behavioural patterns, such as high-fat poor-quality diets [3] and low levels of physical activity.[4] Increasingly, sleep time and sleep quality have been identified as plausible contributors to this major public health issue.[5] Sleep was originally thought to be a passive process, the quiescent part of our daily lives; however, it is now understood to be a dynamic and crucial process essential for good health and bodily function. It has been shown to directly affect numerous metabolic, immune and hormonal processes.[6, 7] Although it is recognised that there is no 'magic number' for the optimal hours of sleep, the national sleep foundation recommends that adults sleep between 7-9 hours/day.[8] However, voluntary sleep restriction is becoming increasingly common due to societal demands and pressures, with an estimated third of all British adults now sleeping just 5-6 hours/day.[9] Both laboratory and epidemiological studies have linked this non-traditional lifestyle factor to the current epidemic of diabetes and obesity,[5, 10] but the data remain inconsistent.[11, 12] Interestingly, this putative relationship appears to be non-linear with evidence of a 'u-shaped' correlation, with both short and long durations of sleep being detrimental to health.[13] This has been recently illustrated in a systematic review and meta-analysis by Cappuccio et al[14] who reported both short and long duration sleep to be associated with greater risk of developing or dying from coronary heart disease and stroke. Further, an association between clinically identified impaired glucose tolerance (IGT; where glucose levels are high, but below the threshold for diagnosis of diabetes) and short sleep time (≤5 hours/day), independent of socio-demographic characteristics and health behaviours, has been demonstrated.[15]

It is well recognised that T2DM and cardiovascular disease are states of subclinical inflammation likely to be driven by visceral fat accumulation. It is now recognised that adipose tissue is an endocrine organ in its own right. The hormones adiponectin and leptin are both secreted by the adipocyte with circulating levels responding reciprocally to increasing adiposity[16] and both reported to improve insulin resistance.[17, 18] Thus the ratio of leptin to adiponectin (LAR) is a useful indicator of obesity and adipocyte dysfunction, and could act as a useful marker for metabolic disease. Recently the LAR has been identified as a surrogate marker for insulin resistance,[19, 20] in both those without hyperglycaemia[21] and those with T2DM.[22] In addition, partial and total sleep deprivation gives rise to a state of systemic subclinical inflammation.[23] Circulating levels of both leptin and adiponectin (adipokines (secreted by adipocytes)) are distorted by alterations in sleep duration.[24, 25] Thus the complex interrelationship between sleep, metabolic dysfunction and obesity warrants further exploration. Thus the aim of this study was to further investigate whether sleep duration is independently associated with insulin resistance, as measured by LAR, thus a potential manifestation of adipocyte dysfunction and sub-clinical inflammation driven by reduced sleep duration, in population at high risk of T2DM.

Subjects, Materials and Methods

These analyses used data from the screening phases of two cluster randomised controlled trials ('Let's Prevent Diabetes' [LP] and 'Walking Away from Diabetes' [WA]). Both studies screened multi-ethnic UK populations identified at high risk of developing T2DM. The rationale and design of these studies have been previously described.[26, 27] Briefly, after obtaining full local NHS research ethics and governance approval individuals at risk of IGT or T2DM were identified from general practices across Leicester, Leicestershire and Rutland, UK using an automated validated risk score utilising data routinely stored on individual general practice databases.

Participants attended the screening session having fasted for at least 8 hours prior to the visit. Upon providing written informed consent an oral glucose tolerance test was performed for all consenting participants. IGR was defined using the WHO criteria: fasting plasma glucose between 6.1 and 6.9 mmol/l and/or 2-hour glucose between 7.8 and 11.1 mmol/l.[28] Additionally, a fasting plasma sample for HbA1c was taken. Separate fasting blood samples were obtained for the measurement of a number of adipokines (leptin and adiponectin) on the same day. Anthropometric data and medical history were collected, a physical exam was performed, and a number of questionnaires were administered which included two sleep related questions: "How many hours sleep did you get last night?" and "On average, how many hours do you sleep in 24 hours". Only the answers to the latter question were used in these analyses as it is more pertinent to long-term biomedical characteristics. Physical activity was assessed objectively via pedometers in the LP study, and the triaxial Actigraph GT3X+ accelerometer (ActiGraph, Fort Walton Beach, Florida USA) in the WA study.

Anthropometric measurements

Anthropometric measurements, recorded by trained researchers following standard operating procedures, included height and weight (Tanita TBE 611, Tanita, West Drayton, UK). Waist circumference was measured at the point of minimal abdominal circumference located halfway between the navel and the lower end of the sternum. Hip measurement was measured at the greatest protrusion of the gluteal muscles as viewed from the side. Three separate blood pressure readings were taken (sitting without crossed legs at 5 minute intervals (Omron M5-1, HEM-757-E model)). The mean of the last two readings was then calculated and used in analyses.

Biochemical analyses

Venous blood samples were collected following an 8-hour fast. Quantitation of serum glycohaemoglobin (HbA1c) was performed using High Performance Liquid Chromatography (HPLC) on the automated glycohaemoglobin HLC-723G analyzer (Tosoh Bioscience Ltd, UK) and plasma glucose was measured using the Hexokinase method. These assays were undertaken in an accredited pathology laboratory within University Hospitals Leicester and repeated testing carried out if the coefficient of variance was ≥20%. Leptin, adiponectin and insulin assays were undertaken at Unilever Discover (Colworth Science Park, Bedford UK) and were available for participants from WA (n=593) only. Leptin analysis was carried out using ELISA kits (Mediagnost, Reutlingen, Germany). Adiponectin was analyzed using a time-resolved fluorescent immunoassay (Perkin Elmer, Turku,

Finland). Insulin was analyzed using a Perkin Elmer time-resolved fluoroimmunoassay on the AutoDELFIA (Perkin Elmer). All assays were conducted twice on the same occasion and the average value obtained. Coefficients of variation were less than 10%. All assays were conducted within the same laboratory under the same conditions.

Statistical analysis

The average number of hours slept in a 24 hour period was categorised for summary characteristics as ≤5.5, 6-6.5, 7-7.5, 8-8.5, and ≥9 hours. All reported averages fell within these category boundaries as there was a digit preference towards participants reporting hours slept in half or full hour increments. Descriptive characteristics are presented for each sleep category with continuous variables summarised as mean (standard deviation) and categorical variables as percentages. Differences in descriptive characteristics between sleep categories were tested using ANOVA for continuous variables and chi-squared tests for categorical variables. To investigate whether sleep was associated with anthropometric, glycaemic and inflammatory factors, each outcome of interest was first summarised by sleep category as mean (standard deviation) for continuous variables and as percentage for categorical variables. This suggested that some of the variables had a non-linear association with sleep. Therefore, for each continuous outcome of interest, a linear regression model was fitted with sleep (continuous; average hours slept in a 24 hour period) included as both a linear and quadratic term. Likewise, for each categorical outcome of interest, a logistic regression model was fitted with sleep included as both a linear and quadratic term. In all models, if the quadratic term was not significant at the 5% level then it was removed and only a linear term for sleep was included. Models were fitted both with and without adjustment for potential confounders: age (continuous), sex (male, female), ethnicity (White European, South Asian, Other), and objectively-measured physical activity (step count; continuous); non-anthropometric variables were additionally adjusted for body mass index (BMI; continuous) and waist circumference (continuous). To improve the fit of the models, sleep (7 hours) and age (60 years) were centred, and the quadratic sleep term was calculated from centred sleep. Sleep was centred at seven hours per 24-hours as this was the mean value. All analyses were conducted in Stata v14.0. All p-values shown are two sided and those less than 0.05 were taken to be statistically significant.

Results

In the two studies, 4283 participants were screened (833 from WA and 3450 from LP); the average sleep time was missing for 1412 participants who were excluded from these analyses. A further 23 were excluded as the average sleep time reported was more than 4 SDs from the mean and thus likely to be incorrectly reported (n=). A total of 2848 were therefore included in the analysis (758 from WA and 2090 from LP). Of these, 593 (all from WA) also provided additional blood samples for the quantification of leptin and adiponectin. There was not a significant difference between those who were included or excluded from the main analyses in terms of age (P=0.941), sex (P=0.053), or physical activity (P=0.051), but South Asians were more likely to be excluded from the analyses than White Europeans or other ethnic groups (P=0.037); data not shown.

Descriptive characteristics of those included in the analysis are shown in Table 1. In summary, there were no significant differences in gender, ethnicity between the average sleep time categories. From herein the term 'short sleeper' refers to <=5.5 hours sleep duration and 'long sleeper' to those sleeping >= 9 hours duration. However, age did differ significantly (p<0.001); short and long sleepers tended to be older on average.

The three indices of obesity (BMI, weight and waist circumference) showed a 'u-shaped' relationship with sleep duration (Table 2; please note statistically insignificant quadratic terms are not presented). Both short sleep and long sleep duration were significantly associated with higher BMI (P<0.001), body weight (P<0.01), and waist circumference (P<0.001), after adjustment for age, sex, ethnicity and objectively-measured physical activity (Figures 1-3). Specifically, people who reported having short and long sleep duration had a higher BMI, with the highest average BMI for those who slept for a maximum of 5.5 hours or for at least 9 hours (33.1 and 33.5kg/m^2, respectively) with a mean average difference of approximately one BMI unit from the reference range of 7-7.5 hours/24-hours. Data suggest that around 6-7 hours of sleep slept in a 24 hour period was associated with the lowest obesity measures.

Fasting glucose and 2-hour glucose showed a quadratic relationship with sleep duration (Table 2). Sleep duration was significantly positively associated with glucose levels, and this association was particularly strong amongst long sleepers (Figure 4). HbA1c levels were not significantly associated with sleep time in unadjusted or adjusted analyses. The percentage of individuals with IGT increased across the sleep categories with the highest percentage observed for ≥9 hours sleep in a 24 hour period at 33.8%, again a quadratic relationship with sleep duration was observed (Table 2).

Fasting insulin and LAR were positively associated with sleep duration independent of age, sex, ethnicity, BMI, waist circumference and objectively-measured physical activity; these relationships were modelled as linear as the quadratic term was not significant. Adiponectin levels were found to be negatively associated with sleep duration, independently of the same confounders.

Finally, a significant negative association between sleep hours in a 24 hour period and average steps per day was observed (P<0.05). In adjusted analyses, a reduction in step count across the sleep categories with those sleeping ≥9 hours in a 24 hour period exhibiting the lowest levels of activity (Table 2) was observed.

In the unadjusted models that only included sleep terms, the R^2 values were very low (≤0.02 for all outcomes) suggesting that sleep did not explain much of the variance in these outcomes and so readers should exercise caution when interpreting the results of the models (the scatter plot with curve over laid is provided in the supporting documents).

Discussion

This large cross-sectional analysis demonstrates that both short and long sleep appear to be associated with measures of obesity, and that this relationship appears to be independent of age, sex, ethnicity and objectively-

measured physical activity. Sleep duration is significantly positively associated with glucose levels, with the association being particularly strong among long sleepers in this cohort. Thus an individual sleeping longer could potentially benefit metabolically from reducing their sleep if a causal relationship exists. However, HbA1c (today used for the diagnosis and management of T2DM) was not significantly associated with sleep duration. This may reflect that nearly 70% of participants were normoglycaemic with the range of HbA1c values being fairly small. Insulin resistance, is a phenomenon occurring before dysglycaemia can be identified, and potentially of more clinical value; independent linear relationships between fasting insulin and sleep duration were observed. However, a u-shaped curve between sleep duration and insulin for fasting and 2-hour levels would be expected, but the quadratic term did not reach statistical significance, which may reflect inadequate power. The highest levels of fasting insulin was observed in those sleeping 9 hours or more and the lowest observed for between 7-7.5 hours/24-hours. These data also suggest that long-sleep duration may have a stronger impact on insulin secretion than short-sleep.

Insulin regulation and tissue sensitivity/resistance is a complex process with numerous contributing factors making quantification of insulin resistance, a key component in metabolic dysfunction, a difficult undertaking. A measure of insulin resistance provides more information on an individual's metabolic status than either the fasting or 2-hour insulin levels alone, subsequently a number of surrogate measures have been developed and validated. The data reported here did show a significant independent positive association between sleep duration and insulin resistance, as measured by LAR. With increasing LAR, the state of insulin resistance is higher; the highest level of insulin resistance in the long sleepers and again a trend towards a u-shaped relationship is observed. These data mirror the fasting insulin data, therefore suggesting that sleep could be directly affecting adipose tissue function and in turn exacerbate the obesity driven metabolic dysfunction. An association between sleep duration and leptin levels alone was not found but a statistically significant negative association between sleep duration and physical activity (average steps per day) is evident.

These results are in support of the growing body of evidence for the association between short sleep (<5.5 hours/24-hours) and obesity in both children and adults.[29, 30] Cappuccio's pooled regression suggests that a reduction of one hour in sleep/24-hours would be associated with a 0.35kg/m^2 increase in BMI; [30] these results suggest a greater impact of short sleep reduction on BMI. The prevalence of short sleep has been steadily increasing over the last 32 years [31] in parallel with that of obesity. Long sleep (≥9 hours/24-hours) has also been associated with obesity although the evidence is less convincing.[31] Diet and physical activity are at opposing ends of the energy balance equation, whereas sleep duration has the potential to affect both energy intake and expenditure. Firstly, Sleep deprivation may lead to excessive daytime sleepiness resulting in a reduction in physical activity, reduced energy expenditure and thus weight promoting – although the data presented here do not support this. Alternatively, over sleeping may lead to fatigue and lethargy coupled with overall increase in non-active time and increasing the likelihood of weight gain. Further, the presence of co-morbidities which could impact on both the duration of sleep (e.g. insomnia) and/or are themselves associated with measures of obesity and metabolic dysregulation (e.g. depression) should be acknowledged. For example long-sleepers may have sleep-related morbidities that promote long-sleep duration and are associated with

obesity, for example obstructive sleep apnoea, which disrupts sleep quality and thus the individual needs to sleep longer in a bid to achieve a refreshing feeling akin to a 'normal sleeper'. Secondly, the reported direct effects of sleep deprivation on the regulation of appetite hormones, such as ghrelin and leptin, leads to an increase in appetite and desire for energy dense foods which may increase energy intake. [7, 32, 33]. Therefore, sleep duration could be a contributing factor to the obesity epidemic, and potentially offers another modifiable risk factor to target.

A well debated concept is sub-clinical inflammation playing a fundamental role in the link between adiposity and metabolic dysfunction. Visceral fat accumulation, evident in obesity leads to a state of sub-clinical inflammation. The adipocytes express and secrete a large number of adipokines with dual metabolic and immuno-modulatory functions. Adipokines influence both local adipocyte biology, and systemic metabolism. Adiponectin and leptin are unique adipokines as they are secreted exclusively by adipocytes. Adiponectin is well characterized and is inversely correlated with adiposity. It has insulin-sensitising effects, with circulating levels significantly lower in insulin resistant states such as T2DM, in addition to both anti-inflammatory and anti-atherogenic properties. [34] Leptin is considered one of the most important adipose-derived hormones and appears to have both long acting and acute properties designed to maintain energy homeostasis. Serum levels are positively correlated with total adipose-tissue mass. [35] These adipokines are each other's opposite, but when considered together, as a ratio, they reflect adipose tissue function and provide a sensitive index of insulin action. [19] Subsequently, in the context of these analysis LAR was one of the most appropriate measure of insulin resistance to employ, in the absence of clamp data.

Data pertaining to leptin and sleep alone does not support the literature where short sleep has been shown to be associated with elevations in leptin. Hayes et al report a 7% increase in leptin levels with every 1-hour decrease in total sleep time. [23] This study may not have enough power to detect this as sleep time was self-reported, unlike Hayes' group who measured sleep using the gold standard objective measure of polysomnography. Differential relationships between self-reported habitual sleep and polysomnographically measured acute sleep on cytokines have been previously suggested, which may also explain these results.[36] We have demonstrated a statistically significant negative relationship between sleep duration and levels of adiponectin, the lowest levels observed for long sleepers suggesting again that the negative impact on the metabolism of long sleep is stronger than that of short sleep or indeed that the homeostatic response to short sleep is more protective.

Although the relationship between sleep and physical activity is still poorly understood, bidirectional effects linking sleep duration and physical activity have been reported,[37] and both short- and long-duration sleepers have been reported to have decreased activity levels. [38] These data do not show low activity with short-sleep however, whilst it is perceivable that a short sleeper may engage with higher levels of sedentary behaviours due to daytime-sleepiness or fatigue, it is equally plausible that a longer duration of wake-time per day the greater the likelihood of increased movement, which may explain the present results. Further, these results suggest

that it is not reduced physical activity driving the association between sleep duration and insulin resistance given the relationship remains statistically significant after adjusting for objectively-measured physical activity.

A major limitation of this study is the nature of the study itself as with cross-sectional analysis you cannot infer causality; indeed sleep duration may simply be a marker of unfavourable health status and lifestyle traits, which is accounted for to some extent by adjusting for measured confounders. Further, self-report was used for sleep in these analyses and is less robust than objective measures such as polysomnography. Further, no questions in the health questionnaire were included to capture 'nap-time' and therefore sleep duration is only reported per 24-hour period. The physiology of short bursts of sleep in addition to or in place of a continuous sleep period may differ, posing a further limitation of the present study. A further limitation is that participants were not screened for or a current diagnosis of obstructive sleep apnoea captured and therefore adjustment for this confounder could not be made. The possible impact of diet was not addressed in this study, this needs to be considered in future studies, particularly the consumption of caffeine and alcohol which impact on both sleep duration and quality. However, standard operational procedures were followed by the clinical measurement teams who were fully trained and competent at collecting this type of data. These data were adjusted for an objective measure of physical activity adding further strength to our findings. Finally, all blood samples were analysed in accredited National Health Service (NHS) pathology laboratories or at the Unilever Discover laboratories at Colworth Science Park in Bedford, UK. These are reliable, valid data that add to the growing evidence in sleep and health.

Sleep is a health behaviour that is more often over looked or dismissed particularly when in the absence of a specific sleep disorder. To recognise, prioritise and respond to your natural requirements for sleep above social demands has the potential to improve health and well-being. Sleep represents a potential modifiable lifestyle behaviour that is largely ignored in general health and well-being but also in the prevention of chronic diseases. The promotion of 'good' sleep and/or the inclusion of sleep hygiene measures, and the inclusion of benefits and risks of poor sleep in structured education programmes is potentially a feasible undertaking. Such low-cost interventions, could be incorporated into current prevention strategies for diabetes and other chronic diseases. Indeed, improved public awareness of the importance of sleep and strategies to improve personal patterns alone could help support better health outcomes as part of a balanced lifestyle and healthy diet.

Conclusion

Collectively these results add to the evidence base for an association between sleep duration and indices of obesity. Furthermore, an independent relationship between insulin resistance, as determined by LAR, and sleep duration in a population at risk of but without overt T2DM is demonstrated. This suggests that disruptions to sleep duration, particularly more than 9 hours/24-hours, are a potential driver of metabolic dysfunction. Sleep

duration represents a potentially modifiable risk factor that could be considered in prevention strategies for T2DM. The emerging complex physiological interaction between sleep, metabolic processes and adverse health outcomes requires further research. Future studies should be designed to address the direction of causality, employ validated objective measures of sleep to include napping and physical activity. The potential public health impact of addressing sleep behaviours in the prevention or management of chronic diseases such as diabetes corroborates this call for further research.

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Table 1: Descriptive characteristics by average sleep in a 24 hour period

		Average sleep in a 24 hour period (hours)					
Variable	**All**	**≤5.5**	**6-6.5**	**7-7.5**	**8-8.5**	**≥9**	**P-value[a]**
Age (years)	63.1 (8.2)	63.0 (8.4)	62.2 (8.4)	62.6 (8.1)	63.7 (8.0)	64.4 (8.2)	<0.001
Female (%)	37.6	41.2	38.2	38.3	36.6	36.5	0.813
Ethnicity (%)							
White European	87.9	86.3	86.7	88.4	87.9	88.7	
South Asian	9.3	10.7	10.3	9.6	9.5	6.1	
Other	2.8	3.1	3.0	2.0	2.7	5.1	0.149
Self-reported MVPA (MET-hours /week)	40.5 (54.5)	39.4 (53.4)	43.4 (59.8)	38.6 (48.1)	40.9 (54.7)	40.6 (63.3)	0.673
Total	**2848**	**131**	**476**	**900**	**1048**	**293**	

Data are presented as mean (standard deviation) or percentage.

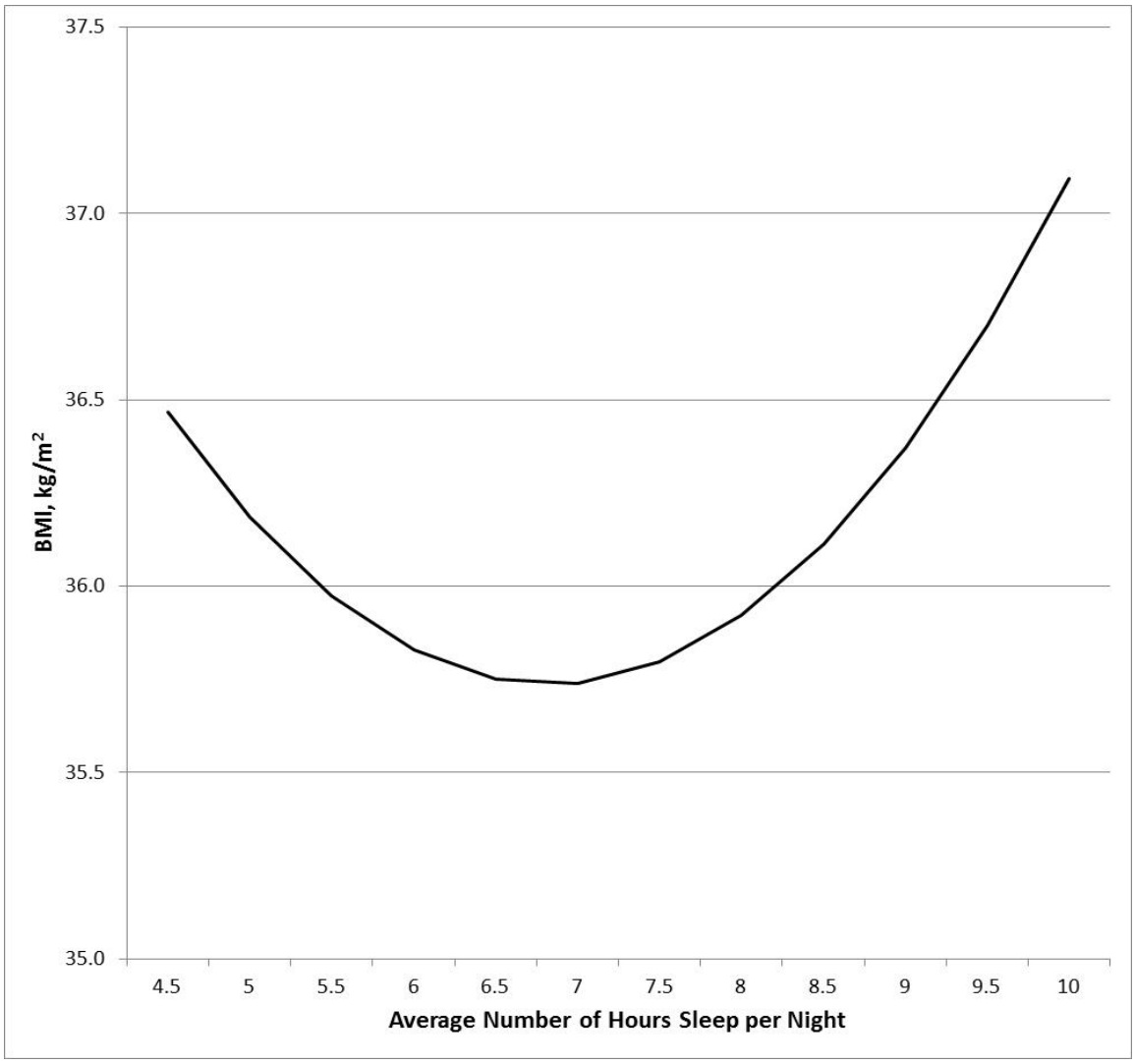
Abbreviations: MVPA, Moderate to vigorous physical activity.

[a] P-values test for a difference between the sleep categories and were estimated using ANOVA tests for continuous variables and using chi-squared tests for categorical variables

	Mean (SD) by average number of hours slept in a 24 hour period					Coefficient (95% CI)			
						Unadjusted model		Adjusted model[a]	
Variable	**≤5.5**	**6-6.5**	**7-7.5**	**8-8.5**	**≥9**	**Linear term**	**Quadratic term**	**Linear term**	**Quadratic term**
Obesity measures									
BMI (kg/m^2)	33.1	32.9	32.5	32.5	33.5	-0.03 (-0.22, 0.16)	0.13 (0.06, 0.21)**	0.05 (-0.13, 0.22)	0.13 (0.06, 0.22)***
	(5.5)	(6.0)	(5.8)	(5.5)	(6.5)				
Weight (kg)	92.8	94.1	92.7	93.1	95.4	0.36 (-0.21, 0.93)		0.41 (-0.14, 0.96)	0.33 (0.09, 0.56)**
	(18.0)	(18.7)	(18.0)	(17.3)	(19.9)				
Waist circumference (cm)	107.4	107.6	106.4	107.3	109.4	0.13 (-0.31, 0.56)	0.28 (0.10, 0.46)**	0.10 (-0.34, 0.54)	0.26 (0.08, 0.45)**
	(13.4)	(13.3)	(13.1)	(13.1)	(14.0)				
Glycaemic factors									
Fasting glucose (mmol/l)	5.3	5.3	5.4	5.3	5.3	0.01 (-0.01, 0.04)		0.01 (-0.02, 0.04)	0.01 (0.00, 0.02)*
	(0.7)	(0.8)	(1.0)	(0.7)	(0.9)				
2-hour glucose (mmol/l)	6.6	6.5	6.6	6.5	6.8	0.06 (-0.02, 0.13)		-0.01 (-0.10, 0.08)	0.04 (0.00, 0.08)*
	(2.5)	(2.3)	(2.8)	(2.3)	(2.5)				
HbA1c (%)	5.9	5.9	6.0	5.9	5.9	0.00 (-0.01, 0.02)		0.01 (-0.01, 0.02)	
	(0.5)	(0.5)	(0.6)	(0.5)	(0.5)				
% IGT[a]	28.2	28.8	29.1	29.3	33.8	1.04 (0.98, 1.12)		0.98 (0.91, 1.06)	1.04 (1.00, 1.07)*
Fasting insulin (μIU/ml)	11.0	10.9	9.5	10.8	14.3	0.50 (0.00, 0.99)*		0.53 (0.07, 1.00)*	
	(6.6)	(6.6)	(6.2)	(7.5)	(9.6)				
2-hour insulin (μIU/ml)	73.3	70.0	56.5	66.5	77.7	1.43 (-2.46, 5.33)		2.89 (-1.10, 6.88)	
	(68.6)	(56.1)	(48.6)	(56.2)	(65.8)				
Adipokines									
Adiponectin (μg/ml)	12.9	13.4	13.3	12.9	10.7	-0.49 (-0.96, -0.01)*		-0.53 (-1.00, -0.06)*	
	(6.6)	(7.7)	(6.3)	(7.1)	(5.4)				
Leptin (mg/ml)	11.5	9.9	10.7	11.6	12.8	0.47 (-0.10, 1.03)		0.36 (-0.04, 0.76)	
	(6.9)	(7.0)	(8.2)	(8.3)	(9.5)				
Leptin:Adiponectin ratio	1.05	1.00	0.94	1.16	1.34	0.08 (0.02, 0.15)**		0.07 (0.02, 0.12)*	
	(0.70)	(0.89)	(0.75)	(0.97)	(1.06)				
Physical activity									
Average steps per day[b]	6752	6764	6651	6640	5819	-117.3 (-233.0, -1.69)*	-50.2 (-99.2, -1.2)*	-104.1 (-207.0, -1.2)*	
	(3532)	(3141)	(3168)	(3166)	(2561)				

* P < 0.05, ** P < 0.01, *** P < 0.001.
Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; IGT, Impaired Glucose Regulation; SD, Standard Deviation.
a Adjusted for age, sex, ethnicity, BMI, waist circumference and physical activity, except that the obesity measures were not adjusted for BMI or waist circumference.
b Measured using pedometers in Let's Prevent Diabetes and using accelerometers in Walking Away from Diabetes (735 missing values). Additionally adjusted for wear time.

Figure 1: Adjusted model showing the relationship between sleep duration and body mass index.



Abbreviations: BMI, Body Mass Index.

Figure 2: Adjusted model showing the relationship between sleep duration and weight.

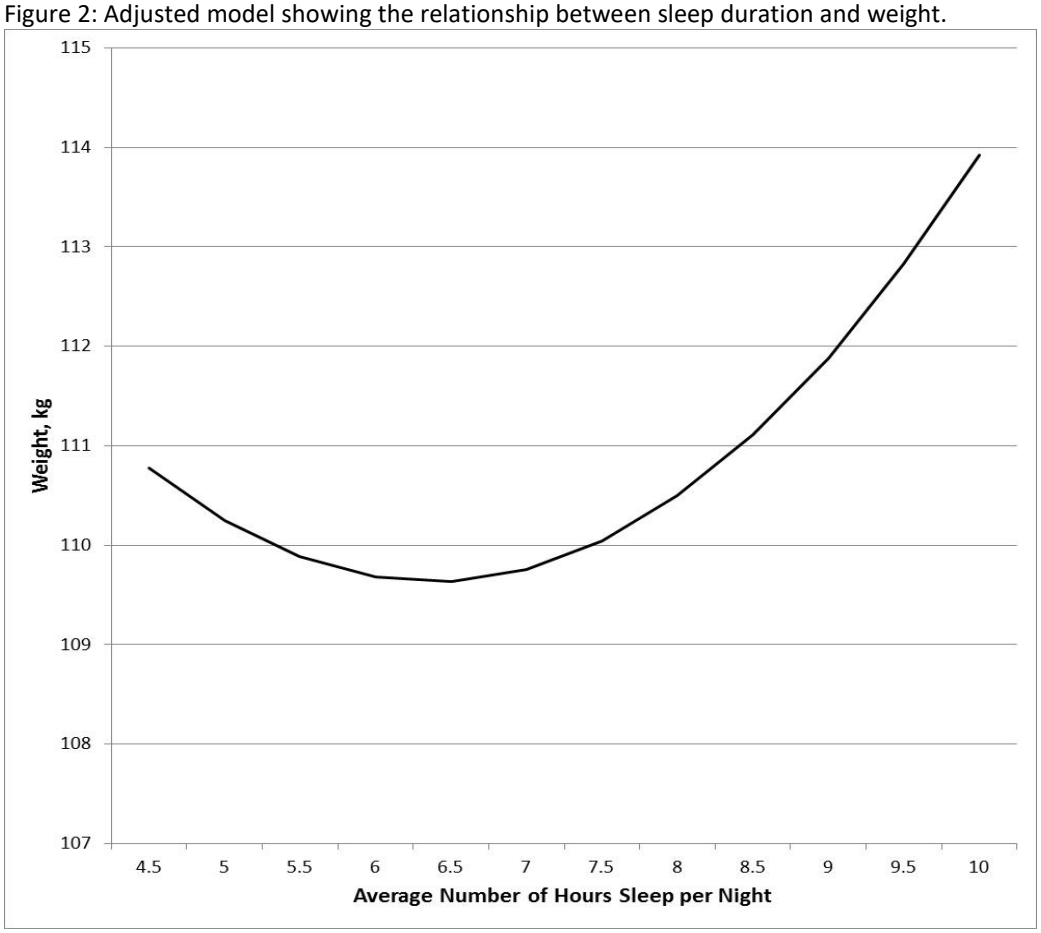


Figure 3: Adjusted model showing the relationship between sleep duration and waist circumference.

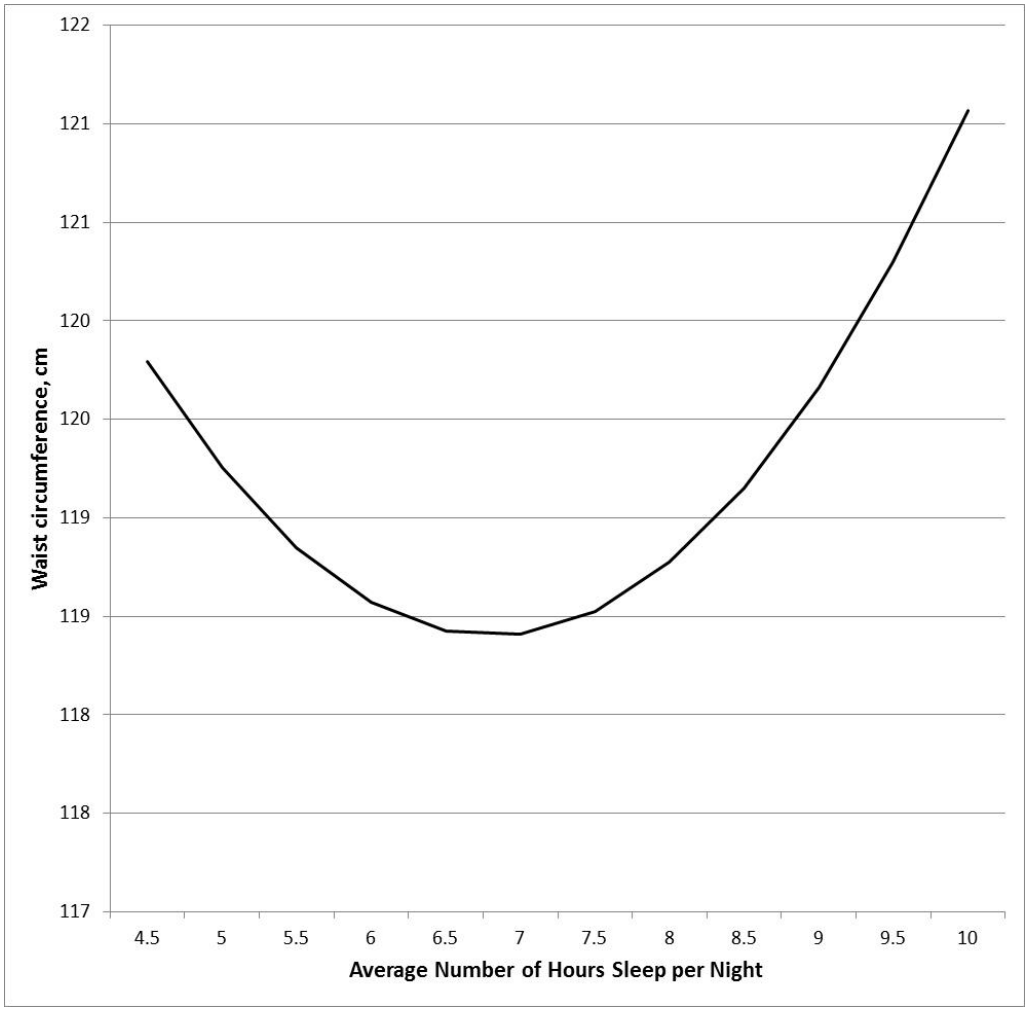


Figure 4: Adjusted model showing the relationship between sleep duration and fasting glucose