The role of sleep duration in diabetes and glucose control

Abstract

Sleep curtailment is common in the westernised world and coincides with an increase in the prevalence of Type 2 diabetes (T2DM). This review considers the recently published evidence for whether sleep duration is involved in the development of T2DM in humans and whether sleep has a role to play in glucose control in people who have diabetes. Data from large, prospective studies indicates a U-shaped relationship between sleep duration and the development of T2DM. Smaller, cross-sectional studies also support a relationship between short sleep duration and the development of both insulin resistance and T2DM. Intervention studies show that sleep restriction leads to insulin resistance, with recent sleep extension studies offering tantalising data showing a potential benefit of sleep extension on glucose control and insulin sensitivity. In people with established diabetes the published literature shows an association between poor glucose control and both short and long sleep duration. However, there are currently no studies that determine the causal direction of this relationship, nor whether sleep interventions are likely to offer benefit for people with diabetes to help them achieve tighter glucose control.

Introduction

Life on earth is governed by the 24-hour cycle of light and darkness associated with the rotation of the earth. Normally metabolic and physiological pathways are coordinated to this 24-hour cycle by an endogenous clock enabling our bodies to coordinate appropriate physiological processes to the time of day. Research in animals and humans suggests that the advent of a 24/7 lifestyle that disrupts our natural sleep cycles and their alignment to the external light/dark cycle is important in the regulation of energy balance and glucose metabolism [1; 2; 3]. Sleep curtailment has become a prevalent behaviour in the Western and developing world where it is estimated that average sleep duration has declined by almost 2 hours in the past 50 years [4]. In the USA and UK, a third of the population report getting less than 7 hours sleep per night[5; 6]. Coinciding with this there has been an explosion in the prevalence of type 2 diabetes (T2DM), raising the important question of whether there is a causal link between the two. This review will specifically consider the recently published evidence for whether sleep duration is involved in the development of T2DM in humans. It will not appraise the considerable number of studies looking predominantly at the role of sleep in the development of obesity. Nor will it address the separate, but related, literature linking sleep related breathing disorders to obesity and T2DM. Having considered the role of sleep duration per se in the development of diabetes, the evidence for whether sleep duration has a role to play in glucose control in people who have diabetes is reviewed.

Association between sleep duration and the risk of T2DM

Evidence from prospective studies

Several large cohort studies have investigated the association between sleep duration and the risk of subsequently developing T2DM, studied over varying lengths of follow-up[7; 8; 9; 10; 11; 12; 13; 14; 15; 16]. Details of their study design and outcomes are shown in Table 1a. Several big studies in the USA and Germany have shown a U-shaped association between sleep duration and increased risk of T2DM[7; 8; 9]. The studies relied on subjective measures, with sleep duration self-reported at baseline, and T2DM incidence was mainly by self-report of physician's diagnosis. Using 7 hours of sleep duration per night as a reference category, those with shorter and longer sleep duration were significantly more likely to develop T2DM over the follow-up period of 5-15 years (risk estimates ranging between 1.47-1.95 for short sleep duration, and between 1.40-3.12 for long sleep duration) . Regression models employed in the analysis were adjusted for many potential confounders, mainly; age, physical activity, BMI, alcohol consumption, ethnicity, education, marital status, depression and history of hypertension. Not all studies have shown this U-shaped relationship however. A large Australian study of >192,000 adults, used information recorded in medical insurance records [10] and reported a positive association between short (but not long) sleep duration and subsequent incidence of T2DM. However, T2DM incidence was determined from hospital admission records and so those who were not admitted to hospital during the follow-up period could not be identified as T2DM which might have led to underestimation of the actual diabetes incidence. In addition, the follow up period was relatively short (mean duration 2.3 years). Another prospective study examined the association of sleep duration with development of impaired fasting glucose (IFG) over six years of follow-up [11], with 6-8 hour sleep duration as a reference category, short (but not long) sleepers had higher odds of developing IFG (OR 3.0, 95% CI 1.05-8.59; OR 1.6, 95% CI 0.45-5.42: for short and long sleep duration respectively). Whereas a Finnish study in overweight individuals with impaired glucose tolerance found an increased risk of T2DM only in participants with long sleep duration $\geq$ 9 hours(HR 2.29, 95% CI 1.38–3.80)[14]. Finally two recent meta-analyses of nine[17] and fourteen[18] prospective cohort studies have also confirmed the U-shaped relationship (Figure 1).A couple of other studies have investigated the association between short compared to normal sleep duration and the risk of T2DM without examining for a U-shaped relationship. The first showed that sleeping $\leq$7 hours per night was associated with higher odds of developing T2DM after 6 years follow- (OR 1.96, 95% CI 1.10-3.50)[12]. Models were adjusted for age, sex, physical activity, smoking habit, weight gain, and abnormal glucose regulation at baseline. The study also found that the odds of becoming obese were significantly higher in subjects who slept ≤7 hours per night (OR 1.99, 95% CI 1.12-3.55). There was a lack of association between sleep duration and TD2M at 11 years follow-up that could be related to the attrition in study population over time and to the mediation effect exhibited by adjusting for weight gain in the model. The second study found a higher odds of T2DM after 2 years follow-up, sleeping ≤5 hours compared to >7 hours sleep duration (OR 5.37, 95% CI 1.38-20.91)[13]. But the logistic regression models were adjusted for fasting plasma glucose, an integral feature of the outcome measure - T2DM. This leads to a statistical phenomenon known as mathematical coupling thus rendering the result spurious [19; 20].

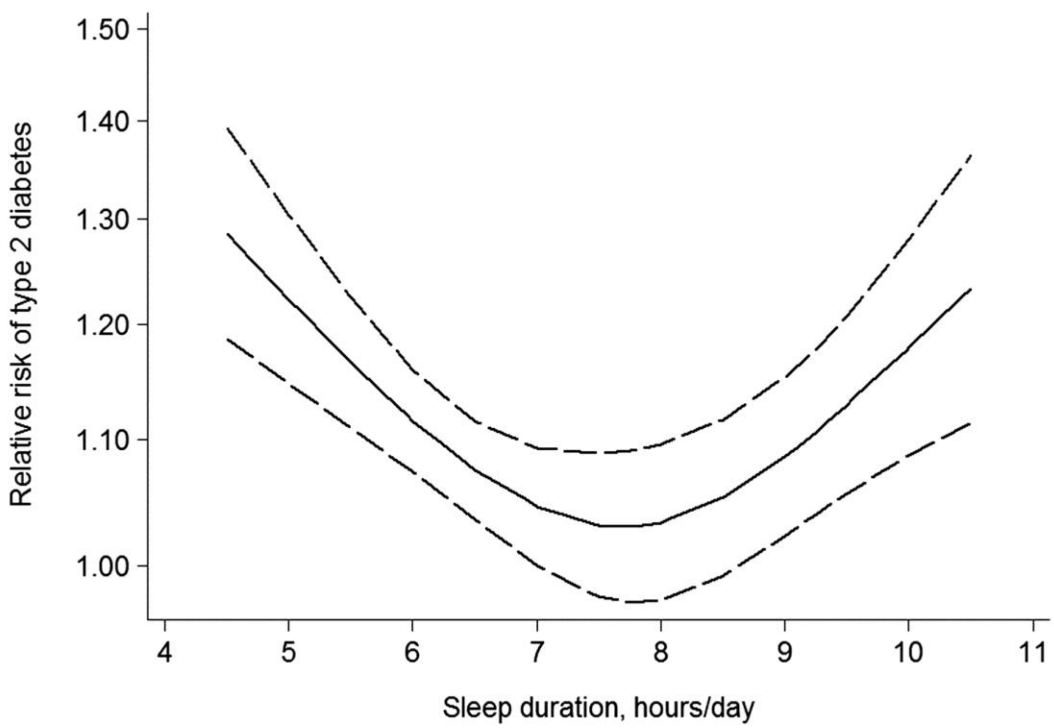

Figure 1. U-shaped relationship between sleep duration and risk of T2DM (adapted from Shan, Ma et al. 2015[17])

Extending the understanding of the relationship between sleep duration and risk of T2DM the impact of a change in sleep duration over time has also been investigated. In the Whitehall II study in the UK, change in sleep duration was calculated for participants without diabetes at the beginning and end of four 5-year cycles and T2DM incidence was observed at the end of the subsequent cycle[15].Another, rather convoluted, prospective study (the Nurses' Health Study) examined whether historic changes in women's sleep duration over the preceding 14 years was associated with developing T2DM over the subsequent 12 year follow up [(16)]. In both studies logistic regression models showed higher risk of developing T2DM in participants with chronic short sleep duration (≤5.5-6 hours) (Whitehall II study: OR 1.35, 95% CI 1.04- 1.76; Nurses' Health Study: HR 1.10, 95%CI 1.001, 1.21) and in those with an increase of ≥2 hours sleep duration (Whitehall II study: OR 1.65 , 95% CI 1.15- 2.37; Nurses' Health Study: HR 1.15, 95% CI 1.01- 1.30) compared to those who maintained a 7-8 hour sleep duration. After adjusting for body mass index (BMI) both associations were attenuated, suggesting that BMI is a mediator in the association. These studies suggest that the adverse metabolic influence of short sleep duration may not be ameliorated by increasing sleep duration later in life.

Taken together, these large, prospective studies which include both men and women, and a wide range of ages, show that a U-shaped relationship exists between self-reported sleep duration and the development of T2DM. Given the increasing societal pressures to sleep less this data is very persuasive of short sleep duration being implicated in the co-existent T2DM epidemic.

Evidence from cross- sectional studies

Whilst they do not carry the same weight as prospective studies, there have been several recent cross-sectional studies that suggest there may be some key sociodemographic factors that influence the relationship between sleep duration and T2DM, and these are summarised in Table 1-b. Again a U-shaped association between sleep duration (over a 24 hour period) and T2DM was observed in 130,943 adults, aged 18-85 years, using data from the National Health Interview Survey (NHIS) from 2004 to 2011 [(21)]. However, short and long sleep durations were more strongly associated with T2DM in white participants than in black. Adjustment for socioeconomic status and other health behavioural factors attenuated the associations in both groups and remained significant only in white participants. An additional cross-sectional study using the NHIS data, from years 2004-2005, also reported a U-shaped association between sleep duration and T2DM [(22)]. A Chinese study showed that longer sleep duration over a 24 hour period was positively associated with having the metabolic syndrome and T2DM, but only in women. [(23)]. Objectively measured sleep duration (using wrist actigraphy) showed a significant association between shorter sleep duration and having IFG and diabetes, but did not find any ethnic differences in a multi ethnic study [(24)].

Association between sleep duration and the risk of insulin resistance

One of the key features of T2DM is impaired insulin mediated glucose uptake, otherwise known as insulin resistance. This precedes the glucose abnormalities and clinical manifestation of T2DM, often by many years. A selection of both observational and intervention studies have recently explored the relationship between sleep duration and measures of insulin resistance and these are summarised in Table 2.

Evidence from cross sectional studies

A small study compared self-reported sleep duration in insulin-resistant individuals (n= 35) with that seen in insulin-sensitive individuals (n=21). Those with insulin resistance slept 43 minutes less/night (p-value = 0.018). The study also found that 60% of insulin-resistant participants slept less than 7 hours in comparison to only 24% only of insulin-sensitive participants (p-value 0.013), though no adjustment for potential confounders was performed [25].

Whilst observational studies are of interest, it is well designed interventional studies that really help us to understand the role of sleep duration in the development of insulin resistance and glucose tolerance. There have been a cluster of these published recently looking at the metabolic effects of both sleep restriction and sleep extension.

Evidence from sleep restriction clinical studies

Multiple small lab-based crossover studies on healthy young participants have looked at the effect of sleep restriction on insulin sensitivity and glucose tolerance [26; 27; 28; 29; 30]. Sleep restriction was associated with reduced insulin sensitivity in all the studies (except one[30]), with reduced glucose tolerance in one of them [27]. The study that found no effect on glucose or insulin aimed to determine the hormonal effects of restricting sleep duration under controlled feeding conditions [30]. A controlled diet was provided and the participants lost weight in both the habitual and short sleep phases. It is possible that in the context of negative energy balance, acute short sleep duration does not lead to a state of increased insulin resistance. These studies were all performed in controlled laboratory based environments and explored acute and often severe sleep restriction. One recent study has examined participants in their home environment to determine if milder and more chronic sleep restriction, akin to daily life, has a role to play [31]. Nineteen healthy, young, normal-weight men with habitual sleep durations of 7.0–7.5 hours and no sleep disturbances were randomised to either study arm (1.5 hours reduction in habitual bedtime) or control arm (habitual bedtime) for three weeks. Sleep restriction led to a decrease in insulin sensitivity at the end of first week but then recovered to baseline levels.

In summary these intervention studies are showing that sleep restriction is associated with the development of insulin resistance and impairment of glucose tolerance. Whether these effects are short lived adaptive responses to an acute stress, or whether they persist longer term and contribute to the risk of T2DM remains unclear.

Evidence from sleep extension clinical studies

Given that short sleep duration and sleep restriction are linked to the development of insulin resistance it is timely that a couple of studies are starting to address whether sleep extension has beneficial effects on insulin and glucose metabolism.

The first, a crossover study [(32)] showed that whilst insulin sensitivity deteriorates after acute sleep restriction it recovers after two days of catch-up sleep. Under lab-controlled conditions participants had up to 8.5 hours of sleep per night for 4 consecutive nights and up to 4.5 hours of sleep for another 4 consecutive nights in a randomised order. After the nights of restricted sleep participants had 2 'catch-up' nights of 10-12 hours of sleep. Participants had a 23% decrease in insulin sensitivity after 4 days of sleep curtailment compared to normal sleep. However, insulin sensitivity was restored after 2 days of catch-up sleep. Although the study showed that catch-up sleep may reverse the negative impact of short-term sleep deprivation, the long-term impact of a repeated sleep deprivation and catch-up sleep cycles on diabetes risk is not known.

The second study investigated whether sleep extension in the home environment has a positive impact on glucose metabolism in healthy adults with chronic sleep curtailment [(33)]. Sixteen young healthy non-obese adults, mostly females, had two weeks of habitual time in bed followed by 6 weeks of one hour per day extension time in bed. Glucose and insulin were assayed at the end of the two periods. During the intervention phase; participants mostly went to bed an hour earlier and had higher sleep duration during weekdays but maintained the same sleep duration during weekends. The study indicated no significant difference between pre- and post-intervention fasting glucose and insulin levels, though no statistics were shown [(34)]. A moderate linear relationship was reported between the relative change in sleep duration and the relative change in fasting glucose ($r = +0.65$, $P = 0.017$) and insulin levels ($r = -0.57$, $P = 0.053$), however we cannot quantify these relationships nor state if they were statistically significant, without a reported estimate measure of associations.

In conclusion, these sleep extension studies, offer tantalising data supporting a potential benefit of sleep extension on glucose control and insulin sensitivity. Much more work is clearly needed in this area.

Association between sleep duration and glycaemic control in patients with diabetes

Given the mounting evidence supporting a relationship between sleep duration and the development of insulin resistance and T2DM, it is relevant to consider whether sleep duration has an impact on glycaemic control in people with established diabetes. Most studies to date are cross sectional with sample size ranging from as low as 18 participants to as high as 8543 participants, and these are summarised in Table 3. Most of these studies assessed glycaemic control using HbA1c except one that used capillary glucose levels [35]. Sleep parameters were mainly self-reported except for three studies that measured sleep objectively using wrist actigraphy [35; 36; 37].

Evidence from cross-sectional studies using subjectively reported sleep duration

Okhuma et al showed that shorter and longer sleep durations were associated with a higher HbA1c level compared with a sleep duration of 6.5–7.4 hours in T2DM patients (Figure 2)[38]. Sleep duration including naps was self–reported. This U-shaped association was not attenuated after adjusting for BMI, total energy intake and depressive symptoms. A similar U-shaped relation was reported in a large Korean study which included participants with both T1DM and T2DM [39]. The association between short sleep duration and poor glycaemic control was strongest for females and participants below the age of 65 years. However, these associations was attenuated after adjusting for BMI and waist circumference and no association was observed after further adjustment for treatment status, duration of diabetes, and daily caloric intake. On the other hand, only longer sleep duration was associated with poor glycaemic control in T2DM patients in a large Chinese [40] and a smaller Taiwanese study [41]. Perceived sleep debt but not sleep duration was positively associated with HbA1c in African Americans with T2DM without diabetes complications and not using insulin[42].

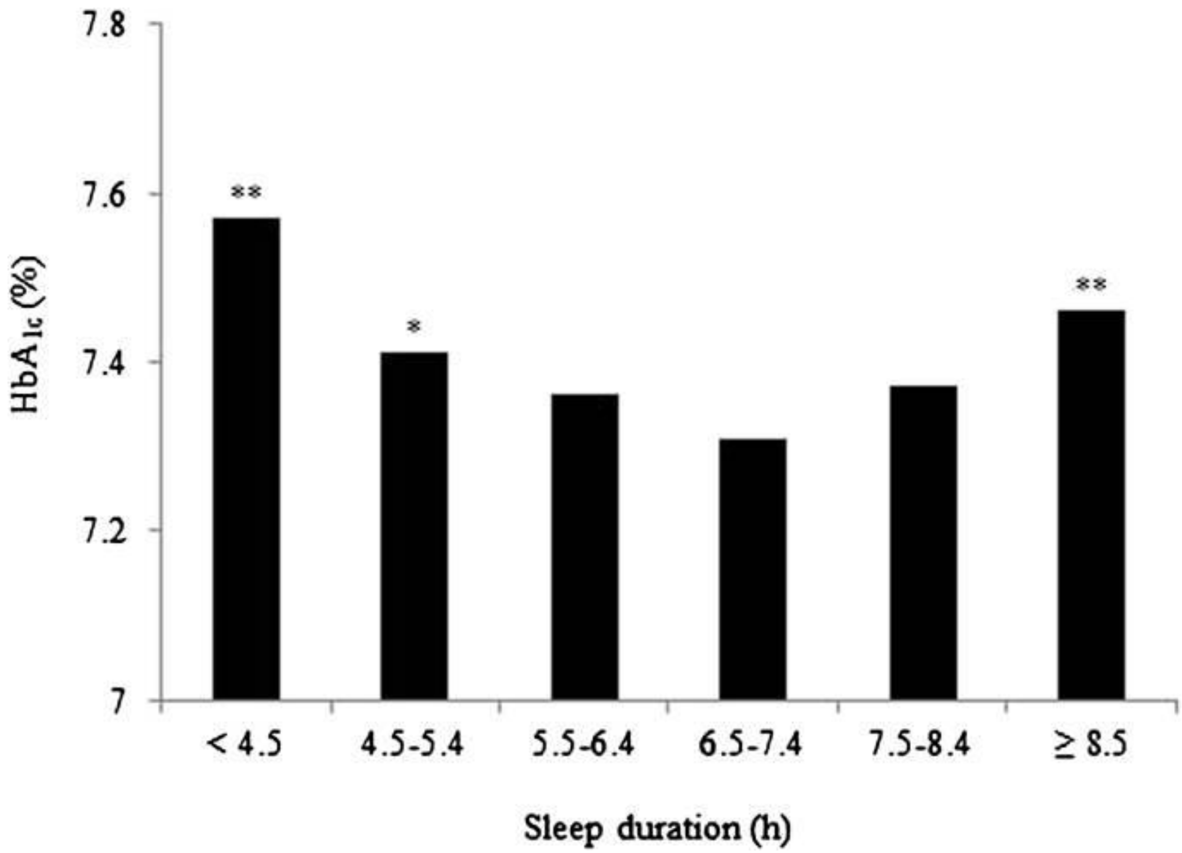

Figure 2. Higher HbA1c observed in shorter and longer sleep duration in Japanese T2DM compared to 6.5–7.4 hour sleep duration(*P < 0.05; **P < 0.01), adapted from Okhuma, T et al. 2013 [38]

Evidence from cross-sectional studies using objectively measured sleep duration

Using wrist actigraphy to objectively measure sleep parameters for three consecutive days in the home environment Trento et al. found no difference in sleep duration between T2DM and control subjects [36]. T2DM sleep quality was found to correlate slightly with glycaemic control, while no correlation with sleep duration was reported. On the other hand, Borel et al. shown that T1DM patients with shorter sleep duration (< 6.5 hours) had a higher HbA1c than those with longer sleep duration (> 6.5 hours), (mean 8.5% vs. mean 7.7%; p-value = 0.001) [37]. In an adjusted regression model shorter sleep duration was associated with 0.64% increase in mean HbA1c level compared to longer sleep duration but no 95% CI or p-value were reported. Participants with short sleep duration were also more likely to have obstructive sleep apnoea and as this was not considered in the analysis, part of the difference reported could be attributed to it.

Lastly Barone et al. assessed the association between objectively measured sleep parameters using wrist actigraphy and glycemic control using capillary glucose levels from glucometer in a group of 18 young adults with T1DM [35]. They showed a positive correlation between the average amount of rest at night and both average glucose levels (r = 0.5404; p-value = 0.0697) and glycemic variability (r = 0.5706; p-value = 0.0527). No estimate measure of the association nor adjustment for any potential confounders were made. Moreover, the average night rest duration was calculated from 10 days actigraphy which may have included two weekends for some participants and only one weekend for others, and thus it will be inevitably incomparable between participants.

In summary, in people with diabetes there also appears to be evidence of an association between both short and long sleep duration and worse glucose control. However, these studies are cross-sectional and so evidence of causality cannot be inferred. A complicating factor when interpreting the relationship between glucose and sleep in people with diabetes is that extremely poor glucose control is well recognised to cause polyuria, polydypsia and nocturia meaning they are awake during the night. Reverse causality cannot be excluded in these studies as they do not distinguish the severity of glucose control and are likely to include participants experiencing some of these osmotic symptoms. Randomised clinical trials with exposure to sleep duration modification (restriction or extending) and robust methods of assessing temporal glucose across the 24 hour day and night [43] are needed to yield more definitive answers.

Conclusions

The recently published literature of both observational and interventional studies strongly supports a role for both short and long sleep duration in the development of insulin resistance and T2DM. There are insufficient sleep intervention studies to determine whether this risk is modifiable long term. In people with established diabetes the published literature supports an association between poor glucose control and both short and long sleep duration. However, there are no studies that determine the causal direction of this relationship in people with diabetes nor whether sleep interventions may offer benefit in achieving glucose control. This is a fertile field for future research.

Table 1-a: Prospective studies on sleep duration and the risk of developing T2DM.

Author, year	country	participant	Study design	exposure	outcome	result	comment
Gangwisch et al., 2007[8]	USA	8992 adult aged 32-68 years from the NHANES I	Prospective cohort	Subjective nighttime sleep duration	T2DM incidence over 8-10 year follow-up period	U-shaped associations	
Yaggi et al., 2006[7]	USA	1564 men aged 40-70 years from the Massachusetts Male Aging Study	Prospective cohort study	Subjective nighttime sleep duration	T2DM incidence over 15 year follow-up period	U-shaped associations	
Kowall et al., 2016[9]	Germany	4814 adults aged 45-75 years from the Heinz Nixdorf Recall study	Prospective cohort study	Subjective nighttime sleep duration	T2DM incidence over 5 year follow-up period	U-shaped associations	
Holliday et al., 2013[10]	Australia	192728 adults aged ≥ 45 selected from medical insurance database	Prospective cohort study	Subjective sleep duration	T2DM incidence over a mean follow up period of 2.3 years	Positive association, only short sleep duration	Diabetes incidents extracted from hospital admission or mortality electronic records, short follow up period
Rafalson et al., 2010[11]	USA	363 participants; 91 cases, 272 controls, aged 35-79 years	nested case-control	Subjective sleep duration (weekdays only)	Impaired fasting glucose	Positive association, only short sleep duration	
Tuomilehto et al., 2009[14]	Finland	522 participants aged 40–64 years without diabetes randomly allocated either to a study arm or to a control arm.	Two Prospective cohorts based on arms of a randomised controlled trial	Subjective sleep duration	T2DM incidence over 7 year follow up period	Positive association, only long sleep duration	Only in the control arm cohort
Gutiérrez-Repiso et al., 2014[12]	Spain	1145 randomly selected participants aged 16-65 years from the Pizzara study	Prospective cohort	Subjective nighttime sleep duration	T2DM incidence at 6 and 11 years follow up	Positive association only at 6 year follow up	Change in sleep duration over the 11 year follow up
Kita et al., 2012[13]	Japan	3570 adults aged 35-55 years	Prospective cohort	Subjective sleep duration and sleep quality	T2DM incidence after 2 year follow up)	Positive spurious association	Statistical issues

Ferrie et al., 2015[15]	UK	5613 adults aged 35-55 years from the Whitehall II study	Prospective cohort, four 5-year cycles	Change in nighttime sleep duration in the following cycle	T2DM incidence at the end of subsequent cycle	Positive association, increase ≥ 2 hours	Association could be mediated by weight gain
Cespedes et al., 2016[16]	USA	59031 middle aged to old women without diabetes	Prospective cohort study	Change in sleep duration over 14 years	T2DM incidence over 12 year follow up period	Positive association, increase ≥ 2 hours	Association only with increase in sleep duration ≥ 2 h/day, Change in sleep duration from a historic baseline to time of enrolment

Table 1-b: Cross-sectional studies on sleep duration and the risk of developing T2DM.

Author, year	country	participant	Study design	exposure	outcome	result	comment
Jackson et al., 2013[21]	USA	130,943 adults aged 18-85 years from the NHIS (years 2004 to 2011)	Cross sectional	Subjective sleep duration in a 24 hours period	self-reported T2DM status	U-shaped associations	Stronger association in white population
Buxton and Marcelli, 2010[22]	USA	56507 adults from the NHIS (years 2004 to 2005)	Cross sectional	Subjective sleep duration in a 24 hours period	self-reported chronic diseases including T2DM	U-shaped associations	multilevel logistic regression
Wu et al., 2015[23]	China	25184 adults mean age 63 years from the Dongfeng-Tongji Cohort study	Cross sectional	Subjective sleep duration	Risk of metabolic syndrome including T2DM	No association with nighttime sleep duration	Positive association with daytime napping duration
Bakker et al., 2015[24]	USA	2151 participant aged 45-84 years from the Multi-Ethnic Study of Atherosclerosis	Cross sectional	Objective sleep duration	Diabetes	No association	Model adjusted for OSA

Table 2: Studies on sleep duration and development of insulin resistance

Author, year	country	participant	Study design	exposure	outcome	result	comment
Liu et al., 2013[25]	USA	56 non-diabetic overweight-obese participants	Cross sectional	Subjective sleep duration	Insulin sensitivity	Positive association	Only P-values reported.
Broussard et al., 2012[26]	USA	7 young healthy participants	Crossover clinical study	Sleep restriction	Insulin sensitivity	Positive association	
Nedeltcheva et al., 2009[27]	USA	11 young-middle aged healthy participants	Crossover clinical study	Sleep restriction	Insulin sensitivity and glucose tolerance	positive association	
Wang et al., online 2016[28]	USA	15 young healthy non-obese participants	Crossover clinical study	time-in-bed restriction by 1 to 3 hours for 3 nights	Insulin sensitivity and glucose tolerance	Positive association with insulin sensitivity	No association with glucose tolerance
Donga et al., 2010(1)[29]	The Netherlands	9 healthy participants, mean age 44.6 years	Crossover clinical study	Sleep restriction	Insulin sensitivity	Positive association	
St-Onge et al., 2012[30]	USA	27 healthy young non-obese adults	Crossover clinical study	Time in bed restricted to 4 hours	insulin sensitivity	No association	Participants had controlled diet and lost weight during the study
Robertson et al., 2013[31]	UK	19 healthy young lean men	Randomised controlled trial	Around 1.5 hours sleep restriction per night for 3 weeks	insulin sensitivity	Positive association only at the end of first week	absence of an overall effect of sleep restriction on insulin sensitivity
Broussard et al., 2016[32]	USA	19 healthy young lean men	Crossover clinical study	two days of catch-up sleep	Recovery of insulin sensitivity	Positive association	
Leproult et al., 2015[33]	Belgium	16 healthy young non-obese adults with chronic sleep restriction	Crossover clinical study	Around one hour sleep extension per night for 6 weeks	Fasting glucose and insulin levels	No difference in pre- and post-intervention levels	Moderate correlation between relative change in sleep duration and relative change in fasting glucose and insulin levels

Table 3: Studies on sleep and glycemic control in patients with diabetes

Author, year	country	participant	Study design	exposure	outcome	result	comment
Ohkuma et al., 2013[38]	Japan	4870 adults, aged ≥20 years with T2DM	Cross-sectional	Subjective sleep duration including naps	Glycemic control (HbA1c)	U-shaped associations	
Kim et al., 2013[39]	Korea	2134 adults, aged > 20 years with T1DM or T2DM	Cross-sectional	Subjective daily sleep duration	Glycemic control (HbA1c)	positive associations	J-shaped trend with HbA1c; stronger in females and in the younger age group (<65 years). Association disappear after adjusting for more covariate in the logistic regression model.
Zheng et al., 2015[40]	China	8543 adults, aged ≥40 years with T2DM or impaired glucose tolerance	Cross-sectional	Subjective nighttime sleep duration	Glycemic control (HbA1c, FPG, PPG)	Positive association with long sleep duration	Only adjusted means and p-values reported but no estimate of association
Tsai et al., 2012[41]	Taiwan	46 adults, aged 43-83 years with T2DM	Cross-sectional	Subjective sleep duration and quality (PSQI)	Glycemic control, HbA1c	Positive association	Participants with diabetic complication or major co-morbidities were excluded. association only with sleep efficiency and PSQI score of 8 or more but not sleep duration
Knutson et al., 2006[42]	USA	161 African Americans, mean age 57 years with T2DM	Cross sectional	Subjective sleep duration and sleep quality, modified PSQI, and perceived sleep debt	Glycemic control (HbA1c)	Positive association	Sleep debt association only in participants without diabetic complication or not using insulin. sleep quality only in participants with diabetic complication or using insulin association
Trento et al., 2008[36]	Italy	47 middle aged adults with T2DM and 23 healthy controls	Cross sectional study	Objective sleep parameters; duration and quality using wrist actigraphy	glycemic control (HbA1c) in T2DM group	Positive association	Weak negative correlation with sleep efficiency and mild positive correlation with moving time while asleep. No estimate measures of association reported
Borel et al., 2013[37]	France	79 adults, median age 40 years with T1DM	Cross sectional study	Objective sleep parameters using wrist actigraphy	glycemic control (HbA1c)	Positive association	
Barone et	Brazil	18 young adult,	Cross	Objective sleep	Glycemic control	No	Methodological issues

al., 2015[35]		aged 20-38 years with T1DM	sectional	measures using wrist actigraphy	(average glucose from glucometer reading)	association	

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