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The Epidemiology of Sleep and Diabetes

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Abstract

Purpose of review: To provide an overview of the mechanistic and epidemiologic evidence linking sleep-related exposures, such as short sleep duration, obstructive sleep apnea, shift work, and insomnia, with type 2 diabetes risk in adults.

Recent findings: Both poor sleep habits and sleep disorders are highly prevalent among adults with type 2 diabetes. In observational studies, short sleep duration, obstructive sleep apnea, shift work, and insomnia are all associated with higher risk of incident type 2 diabetes and may predict worse outcomes in those with existing diabetes. However, interventional studies addressing sleep abnormalities in populations with or at high risk for type 2 diabetes are scarce.

Summary: Although common sleep abnormalities are associated with risk of incident type 2 diabetes and worse prognosis in those with established diabetes, there are few randomized trials evaluating the impact of sleep-focused interventions on diabetes, making it difficult to determine whether the relationship is causal.

Keywords

sleep duration; obstructive sleep apnea; type 2 diabetes; epidemiology

Introduction

Although we spend a third of our lives sleeping, clinicians rarely consider sleep when caring for individuals with type 2 diabetes. Nevertheless, exposures that occur during sleep may affect insulin resistance, beta cell function and glycemic control. In this paper, we review the epidemiology of sleep-related exposures and type 2 diabetes in adults, including hypothesized mechanisms. We focus on chronic insufficient sleep, obstructive sleep apnea (OSA), shift work, and insomnia.

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Conflict of Interest

Rachel P. Ogilvie declares that she has no conflict of interest.

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Human and Animal Rights and Informed Consent

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What is sleep?

Sleep is a biologically important reversible state of inactivity associated with reduced responsiveness to the external environment. Sleep occurs in all multicellular animals, indicating its universal and fundamental functionality [1]. Like hunger or thirst, there exists a homeostatic drive for sleep. As an organism goes without sleep, it gets continuously sleepier and is more likely to fall asleep. In animal studies, complete sleep deprivation leads to death after a few weeks [2]. While sleep is tied to health, its exact function remains controversial [3]. Leading theories suggest that sleep allows brain energy stores to rebuild [4], facilitates synaptic plasticity thereby promoting memory and learning [5], and provides an opportunity for the clearance of neural waste [6].

Sleep/wake regulation is tied to circadian rhythms, the body's internal clock that regulates metabolic processes. The master circadian clock in the suprachiasmatic nucleus of the hypothalamus regulates the sleep drive that regularizes daily sleep patterns. Timing of sleep is a rough marker of circadian phase. Conversely, because light is the strongest stimulus for shifting circadian rhythms, and sleep terminates exposure to light, sleep and its timing impact circadian rhythms. Thus, sleep and circadian rhythms are intertwined.

Mechanisms

In recent years, there has been interest in the link between sleep and pathophysiologic changes predisposing to type 2 diabetes. One such pathway is the effect of poor sleep on insulin sensitivity. In laboratory studies, sleep restriction to 4-5 hours per night for about a week results in lower glucose tolerance and insulin sensitivity [7, 8]. At the cellular level, four days of 4.5 hour sleep restriction reduces insulin sensitivity in subcutaneous adipocytes as assessed by ability of exogenous insulin to increase levels of phosphorylated Akt *in vitro* [9]. Of note, a 3-week trial of 1.5 hour sleep restriction found worsening insulin sensitivity at one week that did not persist at two and three week assessments, suggesting compensatory mechanisms might reduce the long term impacts of sleep restriction [10]. Nevertheless, in a small uncontrolled six-week intervention study, sleep extension was correlated with improvements in insulin sensitivity as assessed by the quantitative insulin check index (QUICKI) [11]. Isolated suppression of slow wave sleep over 3 nights without changing total sleep time also results in lower insulin sensitivity, suggesting this sleep stage may play a role in glucose homeostasis [12, 13].

OSA-related exposures also produce impairments in insulin sensitivity. Experimental fragmentation of sleep for two nights while maintaining total sleep time constant reduced insulin sensitivity by 25% [12]. Similarly, intermittent hypoxia, another characteristic exposure of OSA, lowers insulin sensitivity in human and mouse models [14, 15]. These findings have been corroborated by observational studies, which have found cross-sectional associations between OSA and insulin resistance among people without type 2 diabetes [16-18].

Circadian misalignment, whereby sleep and feeding occur at abnormal circadian phase, also has adverse effects on insulin sensitivity. In a 10-day protocol where sleep and feeding were

misaligned relative to endogenous rhythms but total sleep time and food intake were held constant, insulin sensitivity was worsened [19].

The impact of sleep-related exposures on beta cell function has been less well studied. Sleep restriction studies have found, despite the reduction in insulin sensitivity, no change occurs in the acute insulin response to glucose leading to a reduced disposition index, suggesting an impairment in the ability of pancreatic beta cells to respond to the stress of sleep restriction [8]. A similar pattern of response was observed with selective slow wave sleep suppression [12]. However, in the Insulin Resistance and Atherosclerosis Study (IRAS), shorter self-reported habitual sleep duration was associated with a greater acute insulin response [20]. Regarding OSA-related exposures, pancreatic beta cells are exquisitely sensitive to hypoxia [21]. In humans, acute exposure to intermittent hypoxia does not lead to an increase in the acute insulin response to glucose, despite the reduction in insulin sensitivity leading to a reduction in the disposition index [14]. Moderate to severe OSA has also been associated with lower pancreatic β-cell function [22].

There are several mechanisms by which sleep abnormalities may impact pathways predisposing to type 2 diabetes. Elevations in sympathetic neural output is an important pathway. Normal sleep is associated with a substantial reduction in sympathetic neural output [23]. In-laboratory sleep restriction results in higher levels of nocturnal catecholamines [23, 24]. Further, markers of heart rate variability suggest alterations in sympathovagal balance during periods of wake following sleep restriction, isolated slow wave sleep restriction, sleep fragmentation, and exposure to intermittent hypoxia [7, 12-14]. In OSA, there is higher sympathetic neural output both during wake and sleep, which reduces rapidly with treatment [25].

Alterations in cortisol, which has a strong circadian rhythm, may represent another potential mechanism by which sleep impacts type 2 diabetes risk. In laboratory studies of sleep restriction, cortisol levels rise in the evening after deprivation [7, 26]. Shift workers also have greater chronic exposure to cortisol than day workers as assessed by hair cortisol [27].

Inflammation may represent another pathway linking sleep and type 2 diabetes risk. Both sleep disturbances and insomnia have been associated with higher circulating markers of inflammation [28]. Small studies have suggested elevations in circulating markers of inflammation in those with OSA fall with treatment [29, 30]. A moderate sized clinical trial also found treatment of OSA over 12 weeks was associated with a reduction in C-reactive protein (CRP) levels [31]. Short term circadian misalignment has also been associated with elevations in CRP levels [32].

Alterations in melatonin signaling may represent yet another mechanism. Urinary levels of 6-sulfatoxymelatonin, the primary metabolite of melatonin, were associated with incident type 2 diabetes risk in a nested case control study, such that lower levels of melatonin secretion was associated with higher risk [33]. Genome-wide association studies have identified a common variant in the melatonin receptor 1B (MTNR1B) gene as a type 2 diabetes risk allele [34, 35]. Individuals with the risk polymorphism have impaired beta cell function as evidenced by a reduced acute insulin response to glucose and reduced

disposition index. Further, melatonin administration appears to acutely worsen oral glucose tolerance, primarily in those with the MTNR1B risk variant [36]. These results suggest that susceptibility to the adverse glycemic effects of circadian misalignment and shift work may be modulated by MTNR1B genotype.

Sleep duration

Correlates and prevalence of sleep duration

Sleep duration, often defined as the total amount of time spent asleep over a 24-hour period, is one of the simplest sleep dimensions to measure. Because of the increasing evidence linking insufficient sleep with adverse health outcomes, multiple professional organizations as well as the Centers for Disease Control and Prevention recommend that adults sleep at least seven hours per night [37-40]. However, data from the Behavioral Risk Factor Surveillance System (BRFSS) demonstrate that roughly a third of American adults were not meeting these recommendations [41].

Several demographic groups are at higher risk for short sleep duration. Older adults are at higher risk, as sleep duration declines with age by approximately ten minutes per decade [42-44]. Sex differences in sleep duration also exist, with men sleeping approximately 25-45 minutes less per night than women [42, 43, 45-47]. There are also racial differences, with African Americans generally sleeping 45–65 minutes less compared to whites [45, 46, 48]. In addition, those with lower levels of education are often at higher risk of short sleep [43, 44, 49, 50]. Unemployment is also associated with longer, more irregular sleep durations. Among the employed, those doing low paying manual work and high-level managers have higher prevalences of short sleep than those doing high paying blue collar work, clerical workers, and low-level managers [44, 51, 52].

There is also extensive evidence suggesting that short sleep duration may be a risk factor for obesity [53-55]. Short sleep duration is associated with higher risk of subsequent weight gain and obesity [56]. Short term reductions in sleep duration lead to increased food intake and reduced physical activity [57, 58]. However, the benefits of extending sleep duration on obesity are not yet clear [59].

Most epidemiological studies on sleep and type 2 diabetes rely on self-reported measures of sleep duration. Self-report of habitual sleep practices is inaccurate with overestimation of time spent sleeping and only modest correlations ranging from 0.20 to 0.47 compared to objective measures of sleep such as actigraphy and polysomnography [60-62]. Further, the error in self-report varies strongly by factors such as sex, race, employment status, and depression [60, 62, 63]. Importantly, self-reported long sleep duration is associated with type 2 diabetes (and other comorbidity) risk but there is no association when objective measures are used [64, 65]. The prevalence of long sleep duration is much greater with self-report than objective measures, suggesting that some individuals are reporting time in bed rather than time asleep [66, 67]. As such, associations between long self-reported sleep and type 2 diabetes may be due to limited physical activity, significant comorbidities from type 2 diabetes or its complications, or may reflect confounding due to predictors of error in self-report [66, 68].

Sleep duration and diabetes

There is an extensive literature on the association between habitual sleep duration and type 2 diabetes. Several cross-sectional studies with self-reported measures of sleep duration have found associations between both short and long sleep duration and measures of insulin resistance among people without diabetes [69, 70] as well as associations between sleep duration and impaired glucose tolerance [71, 72]. Few cross-sectional studies have used objective sleep measures to investigate the sleep duration – diabetes relationship. In the Multi-Ethnic Study of Atherosclerosis (MESA), actigraphy-derived sleep duration ≤ 5 hours was associated with approximately a 1.3-fold higher odds of elevated fasting glucose or hypoglycemic medication use compared to those sleeping 5-8 hours, while no association was found for long-sleep [64]. In contrast, in a subset of 155 CARDIA participants, no association between actigraphic sleep duration and fasting glucose or insulin resistance assessed using the homeostatic model assessment (HOMA) method was found [73].

There are many prospective studies on the association between sleep duration and type 2 diabetes in large community-based samples. Meta-analyses of prospective cohort studies show a U-shaped association between sleep duration and incident type 2 diabetes, with those reporting 7-8 hours of sleep per night at the lowest risk [65, 74]. In the Whitehall II study, those who increased their sleep over a five year period as well as consistent short sleepers had a 1.3-1.7 times higher odds of incident diabetes compared to those who consistently slept 7 hours a night [75]. However, no prospective studies have assessed the relationship between objective measures of sleep duration and incident type 2 diabetes.

There are few interventional studies on the effect of sleep extension on type 2 diabetes risk or glycemic control. An unblinded single arm study of 16 healthy volunteers who increased nightly sleep time by 1 hour for six weeks reported no improvement in fasting glucose and insulin levels despite increased actigraphic sleep duration [11]. A small four-week randomized study of healthy habitual short sleepers found no differences between sleep extension and control groups in fasting glucose, insulin, and HOMA [76]. A randomized trial of sleep extension versus control in 125 obese individuals found no improvement in fasting glucose, insulin, or QUICKI with sleep extension, though the intervention did not improve actigraphic sleep duration [59].

Obstructive Sleep Apnea (OSA)

Prevalence of OSA

One of the most common sleep disorders is OSA, a form of sleep-disordered breathing characterized by repetitive collapse of the upper airway during sleep. Symptoms of OSA include loud snoring, frequent awakenings from sleep, and excessive daytime sleepiness. OSA has been associated with hypertension, stroke, heart failure, and atrial fibrillation [77]. Notably, 85% of people with OSA are asymptomatic [78]. The primary metric used to quantify OSA severity, the apnea hypopnea index (AHI), is calculated as the number of complete (apnea) and partial (hypopnea) stoppages in breathing per hour of sleep [79]. An AHI of 5 to 15 events/hour signifies mild OSA, an AHI of 15 to 30 events/hour signifies moderate OSA and an AHI > 30 events/hour signifies severe OSA. The prevalence of OSA

in middle aged Americans is 34% in men and 17% in women, while the prevalence of moderate to severe OSA is 13% in men and 6% in women [80]. This prevalence has risen over the past two decades, likely due to the increasing age and body mass index (BMI) of the population [80].

The prevalence of OSA is high among people with type 2 diabetes. In the Sleep Heart Health Study, 23.8% of participants with self-reported diabetes had moderate or severe OSA [81], while in a substudy of the Look AHEAD trial, the prevalence of OSA was 86% and the prevalence of moderate to severe OSA was 53% [82]. A study of consecutive type 2 diabetes patients referred to a diabetes clinic reported the prevalence of moderate to severe OSA was 36% [83].

OSA risk factors

The prevalence of OSA in adults increases with age [84-88] and is greater in men than women. Among US adults, the prevalence of OSA is 20% in 30-49-year-old men and 38.5% in 50-70-year-old men, while it is 6.6% in 30-49 year old women and 24.4% in 50-70 year old women [80]. Among younger adults, the prevalence of OSA is roughly twice as high in men than women, but this sex difference narrows in older age due to menopause [86, 89-91]. Obesity is one of the strongest risk factors for OSA with a roughly 3% higher AHI for every 1% higher BMI [92]. The impact of obesity on OSA is driven by central adiposity, with waist circumference more strongly associated with OSA risk than BMI in many studies [93], although neck circumference also contributes to risk [86, 90]. Weight change is associated with change in AHI and randomized trials of weight loss interventions have demonstrated improvements in OSA severity [94-96]. Excess weight has been estimated to be responsible for over 40% of OSA cases among US adults [97]. Individuals of East Asian descent are at higher risk for OSA at a given BMI compared to other races, which appears to be related to differences in craniofacial anatomy [46, 98, 99].

OSA and diabetes

Cross-sectional analyses have consistently found OSA and type 2 diabetes co-exist. OSA is associated with fasting glucose intolerance [16, 64]. In a population-based study of middle-aged adults from Lausanne, Switzerland, the odds of diabetes among those in the highest quartile of AHI was 4.9-fold greater than the lowest quartile; after accounting for obesity and body fat distribution, the odds ratio was attenuated but remained elevated [90]. Among those with type 2 diabetes, those with severe OSA have adjusted hemoglobin A1c (HbA1c) levels that are 0.72% higher than those with no OSA after controlling for demographics, behaviors, comorbidities, and medications [100, 101].

Prospective studies have demonstrated that OSA is also associated with incident type 2 diabetes. In large community-based prospective cohort studies, OSA severity is associated with risk of incident type 2 diabetes [102, 103]. Similar associations have been identified in retrospective analyses of clinical cohorts of patients undergoing sleep testing for OSA evaluation [104, 105]. In one large clinical cohort, the 5-year cumulative incidence of type 2 diabetes was 7.5% in those with mild OSA, 9.3% in those with moderate OSA, and 14.9% in those with severe OSA [105].

Despite strong cross-sectional and prospective relationships between OSA and type 2 diabetes, the evidence that OSA treatment can alter type 2 diabetes risk or glycemic control is limited. First line therapy for OSA is continuous positive airway pressure (CPAP), a device that delivers positive pressure to the upper airway via a mask, thereby preventing its collapse during sleep [106]. Trials evaluating the impact of CPAP in OSA patients without diabetes have been inconsistent on whether it improves insulin sensitivity; however, a meta-analysis of six trials suggested a positive association [107]. In a trial of patients with OSA and impaired glucose tolerance (IGT), CPAP did not reduce the prevalence of IGT overall; however, a greater improvement in insulin sensitivity was found in those with severe OSA, suggesting a clinical benefit may exist in this subgroup [108]. A subsequent trial of CPAP in severe OSA patients with morbid obesity found CPAP lowered the prevalence of IGT from 47% to 24% while no change in prevalence was observed in the control arm [109]. In another trial of patients with OSA and prediabetes, two weeks of CPAP therapy delivered in the hospital to ensure 8 hours adherence improved insulin sensitivity, suggesting suboptimal adherence to CPAP may explain the mixed results found in more “real world” trials [110].

Data regarding the effect of CPAP on incident diabetes risk is limited. In a retrospective cohort study, no association of regular CPAP use with risk of incident type 2 diabetes was observed in those with mild OSA, but among those with moderate to severe OSA, regular use of CPAP was associated with a 47% risk reduction [104]. A dose-response relationship has been reported where greater CPAP use is associated with greater reduction in risk [111]. In a large clinical trial assessing the effect of CPAP on cardiovascular events, the cumulative incidence of diabetes was 4.9% in the CPAP arm versus 5.7% in the control arm, suggesting a 14% risk reduction [112]. However, the number of cases was small as the trial was not designed to evaluate this secondary endpoint.

Among those with type 2 diabetes, several studies have assessed the impact of CPAP on glycemic control. Early case series suggested CPAP may have a large effect [113]; however, cohort studies have generally found no improvement in HbA1c levels with initiation of CPAP therapy [114, 115]. Despite no change in HbA1c, some evidence suggests glucose levels during sleep are reduced and more stable [116]. Randomized trial data also suggests no impact of CPAP therapy on glycemic control in those with established type 2 diabetes. A small double-blind randomized trial of CPAP found no effect on glycemic control or insulin sensitivity measured by euglycemic clamp at 3 months [117]. A subsequent trial of 50 patients reported CPAP was associated with a 0.1%-point increase in HbA1c levels at 3 months but a 0.4%-point decrease at 6 months [118]. This benefit was not confirmed in a larger trial of 416 patients where no difference in HbA1c levels between CPAP and control groups was found at 6 months [119]. This lack of effect may be related to suboptimal adherence, as a small single arm study of 12 patients with OSA and type 2 diabetes treated with 8 hours CPAP in the hospital reported reductions in 24-hour glucose profiles due primarily to overnight glucose levels [120].

OSA and type 2 diabetes complications

Among those with type 2 diabetes, there has been interest in whether OSA is associated with microvascular complications. Cross-sectional studies suggest no clear relationship between

OSA and diabetic retinopathy [121]. However, a prospective study of type 2 diabetes patients attending diabetes clinics found OSA was associated with progression to preproliferative/proliferative diabetic retinopathy and among those with OSA, CPAP had a protective effect [122]. In a small study of type 2 diabetes patients with macular edema and OSA, adherence to CPAP was associated with improvement in visual acuity at 6 months [123]. For renal disease, cross-sectional studies have found OSA is associated with reductions in estimated glomerular filtration rate (eGFR) and proteinuria [124, 125]. Greater OSA severity also is associated with steeper decline in eGFR [126]. Evidence for a cross-sectional association between OSA and diabetic neuropathy in type 2 diabetes is mixed with more consistent evidence for an association in type 1 diabetes [127]. Nevertheless, one study found OSA is associated with foot ulcers in type 2 diabetes [128]. No randomized trials have yet evaluated whether treating OSA can prevent or improve microvascular complications.

Shift work

Shift work is typically defined as a schedule outside the usual 9 am – 5 pm workday. It can refer to both a consistent evening or night work schedule as well as work on a rotating shift schedule. Approximately 15% of the U.S. full-time working population are shift workers, with 4.7% working evening shifts, 3.2% night shifts, 3.1% irregular schedule shifts, and 2.5% rotating shifts [129].

The prevalence of shift work declines with age, with 22.3% of adults aged 20-24 years reporting shift work but only 12.5% of adults aged 55 to 64 [129]. The prevalence of shift work is higher in men (16.7%) than in women (12.4%) [129]. Racial differences also exist with blacks having the highest prevalence of shift work (20.8%) [129].

The circadian misalignment and shorter sleep duration that result from shift work may act synergistically on metabolism to increase weight and reduce insulin sensitivity [130, 131]. Four days of a simulated night shift work schedule reduces insulin sensitivity by 25% [132].

Numerous cohort studies have identified shift work as a risk factor for obesity and metabolic syndrome [133, 134]. Cohort studies have also found that both rotating and night shift work are associated with incident type 2 diabetes [135]. These associations are present in both blue collar and white collar occupations [135, 136]. In a cohort of female nurses, duration of exposure to shift work was monotonically associated with the risk of incident type 2 diabetes, with women who had at least 20 years history of shift work having 1.5 times higher risk compared to women with no exposure [137].

Insomnia

Insomnia is a common sleep disorder characterized by difficulty initiating or maintaining sleep, resulting in daytime fatigue or dysfunction [138]. The prevalence of insomnia among US adults is roughly 15% [139]. However, the prevalence of insomnia in T2DM is higher and has been rising more rapidly over time [140].

Insomnia prevalence increases with age and is more common among women than men [141-144]. Other risk factors include lower socioeconomic status, unemployment, divorced

or widowed marital status, depression, anxiety and other chronic health conditions [141, 143, 144].

An analysis of administrative billing data found individuals with a diagnosis of insomnia are at higher risk for incident type 2 diabetes, and this risk rises with longer duration of insomnia [145]. A meta-analysis of prospective cohort studies found insomnia symptoms are associated with incident type 2 diabetes, with higher risk in both those reporting difficulty initiating sleep and difficulty maintaining sleep [74]. Cross-sectional studies suggest a more severe insomnia subtype defined by both insomnia symptoms and objectively measured short sleep may be most closely associated with type 2 diabetes. [146, 147].

Type 2 Diabetes as a cause of poor sleep

While sleep exposures may predispose to type 2 diabetes, there are also pathways by which diabetes may adversely impact sleep. Pain from common complications such as peripheral neuropathy or nocturia from poor glycemic control may lead to disturbances in sleep [148-150]. In addition, diabetes may predispose to sleep disorders. A periodic breathing pattern during sleep is more common among those with diabetes, although whether this contributes to sleep symptoms is unclear [81]. Restless legs syndrome (RLS) is also common among patients with type 2 diabetes with a prevalence of 17-27% [151-153]. The mechanism by which type 2 diabetes increases RLS risk is unclear but may be partially mediated by peripheral neuropathy [152, 153].

Conclusion

Chronic insufficient sleep, OSA, shift work, and insomnia are highly prevalent in patients with type 2 diabetes. Prospective studies suggest that these conditions may contribute to the development of diabetes or worsen prognosis in those with established diabetes. However, interventional studies addressing sleep abnormalities in populations with or at high risk for type 2 diabetes are scarce. Thus, the extent to which strategies aimed at improving sleep can prevent the development of type 2 diabetes or improve clinical outcomes in those with established diabetes is not well understood. Nevertheless, because over 90% of people with diabetes report at least one sleep problem [154], there is a rationale for clinicians to ask patients with type 2 diabetes about their sleep. Addressing these common co-morbidities could improve symptoms and quality of life in patients with diabetes.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1. Hobson JA. Sleep is of the brain, by the brain and for the brain. Nature. 2005;437(7063):1254–6. doi:10.1038/nature04283. [PubMed: 16251949]

2. Everson CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: III. Total sleep deprivation. Sleep. 1989;12(1):13–21. [PubMed: 2928622]

3. Krueger JM, Frank MG, Wisor JP, Roy S. Sleep function: Toward elucidating an enigma. Sleep Med Rev. 2016;28:46–54. doi:10.1016/j.smrv.2015.08.005. [PubMed: 26447948]
4. Benington JH, Heller HC. Restoration of brain energy metabolism as the function of sleep. Prog Neurobiol. 1995;45(4):347–60. [PubMed: 7624482]
5. Tononi G, Cirelli C. Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. Neuron 2014;81(1):12–34. doi:10.1016/j.neuron.2013.12.025. [PubMed: 24411729]
6. Xie L, Kang H, Xu Q, Chen MJ, Liao Y, Thiyagarajan M et al. Sleep drives metabolite clearance from the adult brain. Science. 2013;342(6156):373–7. doi:10.1126/science.1241224. [PubMed: 24136970]
7. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet. 1999;354(9188):1435–9. doi:10.1016/S0140-6736(99)01376-8. [PubMed: 10543671]
8. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. Diabetes. 2010;59(9):2126–33. doi:10.2337/db09-0699. [PubMed: 20585000]
9. Broussard JL, Ehrmann DA, Van Cauter E, Tasali E, Brady MJ. Impaired insulin signaling in human adipocytes after experimental sleep restriction: a randomized, crossover study. Ann Intern Med. 2012;157(8):549–57. doi:10.7326/0003-4819-157-8-201210160-00005. [PubMed: 23070488]
10. Robertson MD, Russell-Jones D, Umpleby AM, Dijk DJ. Effects of three weeks of mild sleep restriction implemented in the home environment on multiple metabolic and endocrine markers in healthy young men. Metabolism. 2013;62(2):204–11. doi:10.1016/j.metabol.2012.07.016. [PubMed: 22985906]
11. Leproult R, Deliens G, Gilson M, Peigneux P. Beneficial impact of sleep extension on fasting insulin sensitivity in adults with habitual sleep restriction. Sleep. 2015;38(5):707–15. doi:10.5665/sleep.4660. [PubMed: 25348128]
12. Tasali E, Leproult R, Ehrmann DA, Van Cauter E. Slow-wave sleep and the risk of type 2 diabetes in humans. Proc Natl Acad Sci U S A. 2008;105(3):1044–9. doi:10.1073/pnas.0706446105. [PubMed: 18172212]
13. Stamatakis KA, Punjabi NM. Effects of sleep fragmentation on glucose metabolism in normal subjects. Chest. 2010;137(1):95–101. doi:10.1378/chest.09-0791. [PubMed: 19542260]
14. Louis M, Punjabi NM. Effects of acute intermittent hypoxia on glucose metabolism in awake healthy volunteers. J Appl Physiol (1985). 2009;106(5):1538–44.doi:10.1152/japplphysiol.91523.2008. [PubMed: 19265062]
15. Iiyori N, Alonso LC, Li J, Sanders MH, Garcia-Ocana A, O'Doherty RM et al. Intermittent hypoxia causes insulin resistance in lean mice independent of autonomic activity. Am J Respir Crit Care Med. 2007;175(8):851–7. doi:10.1164/rccm.200610-1527OC. [PubMed: 17272786]
16. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE et al. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. American journal of epidemiology. 2004;160(6):521–30. doi:10.1093/aje/kwh261. [PubMed: 15353412]
17. Pamidi S, Wroblewski K, Broussard J, Day A, Hanlon EC, Abraham V et al. Obstructive sleep apnea in young lean men: impact on insulin sensitivity and secretion. Diabetes Care. 2012;35(11):2384–9. doi:10.2337/dc12-0841. [PubMed: 22912423]
18. Kent BD, Grote L, Bonsignore MR, Saaresranta T, Verbraecken J, Levy P et al. Sleep apnoea severity independently predicts glycaemic health in nondiabetic subjects: the ESADA study. The European respiratory journal. 2014;44(1):130–9. doi:10.1183/09031936.00162713. [PubMed: 24696120]
19. Scheer FA, Hilton MF, Mantzoros CS, Shea SA. Adverse metabolic and cardiovascular consequences of circadian misalignment. Proc Natl Acad Sci U S A. 2009;106(11):4453–8. doi:10.1073/pnas.0808180106. [PubMed: 19255424]
20. Beihl DA, Liese AD, Haffner SM. Sleep duration as a risk factor for incident type 2 diabetes in a multiethnic cohort. Ann Epidemiol. 2009;19(5):351–7. doi:10.1016/j.annepidem.2008.12.001. [PubMed: 19362278]
21. Dionne KE, Colton CK, Yarmush ML. Effect of hypoxia on insulin secretion by isolated rat and canine islets of Langerhans. Diabetes. 1993;42(1):12–21. [PubMed: 8420809]

22. Punjabi NM, Beamer BA. Alterations in Glucose Disposal in Sleep-disordered Breathing. Am J Respir Crit Care Med. 2009;179(3):235–40. doi:10.1164/rccm.200809-1392OC. [PubMed: 19011148]

23. Somers VK, Dyken ME, Mark AL, Abboud FM. Sympathetic-nerve activity during sleep in normal subjects. N Engl J Med. 1993;328(5):303–7. doi:10.1056/NEJM199302043280502. [PubMed: 8419815]

24. Irwin M, Thompson J, Miller C, Gillin JC, Ziegler M. Effects of sleep and sleep deprivation on catecholamine and interleukin-2 levels in humans: clinical implications. J Clin Endocrinol Metab. 1999;84(6):1979–85. doi:10.1210/jcem.84.6.5788. [PubMed: 10372697]

25. Somers VK, Dyken ME, Clary MP, Abboud FM. Sympathetic neural mechanisms in obstructive sleep apnea. J Clin Invest. 1995;96(4):1897–904. doi:10.1172/JCI118235. [PubMed: 7560081]

26. Leproult R, Copinschi G, Buxton O, Van Cauter E. Sleep loss results in an elevation of cortisol levels the next evening. Sleep. 1997;20(10):865–70. [PubMed: 9415946]

27. Manenschijn L, van Kruysbergen RG, de Jong FH, Koper JW, van Rossum EF. Shift work at young age is associated with elevated long-term cortisol levels and body mass index. J Clin Endocrinol Metab. 2011;96(11):E1862–5. doi:10.1210/jc.2011-1551. [PubMed: 21880805]

28. Irwin MR, Olmstead R, Carroll JE. Sleep Disturbance, Sleep Duration, and Inflammation: A Systematic Review and Meta-Analysis of Cohort Studies and Experimental Sleep Deprivation. Biol Psychiatry. 2016;80(1):40–52. doi:10.1016/j.biopsych.2015.05.014. [PubMed: 26140821]

29. Ryan S, Taylor CT, McNicholas WT. Predictors of elevated nuclear factor-kappaB-dependent genes in obstructive sleep apnea syndrome. Am J Respir Crit Care Med. 2006;174(7):824–30. doi: 10.1164/rccm.200601-066OC. [PubMed: 16840748]

30. Yokoe T, Minoguchi K, Matsuo H, Oda N, Minoguchi H, Yoshino G et al. Elevated levels of C-reactive protein and interleukin-6 in patients with obstructive sleep apnea syndrome are decreased by nasal continuous positive airway pressure. Circulation. 2003;107(8):1129–34. [PubMed: 12615790]

31. Gottlieb DJ, Punjabi NM, Mehra R, Patel SR, Quan SF, Babineau DC et al. CPAP versus oxygen in obstructive sleep apnea. N Engl J Med. 2014;370(24):2276–85. doi:10.1056/NEJMoa1306766. [PubMed: 24918372]

32. Leproult R, Holmback El, Van Cauter E. Circadian misalignment augments markers of insulin resistance and inflammation, independently of sleep loss. Diabetes. 2014;63(6):1860–9. doi: 10.2337/db13-1546. [PubMed: 24458353]

33. McMullan CJ, Schernhammer ES, Rimm EB, Hu FB, Forman JP. Melatonin secretion and the incidence of type 2 diabetes. JAMA. 2013;309(13):1388–96. doi:10.1001/jama.2013.2710. [PubMed: 23549584]

34. Bouatia-Naji N, Bonnefond A, Cavalcanti-Proenca C, Sparso T, Holmkvist J, Marchand M et al. A variant near MTNR1B is associated with increased fasting plasma glucose levels and type 2 diabetes risk. Nat Genet. 2009;41(1):89–94. doi:10.1038/ng.277. [PubMed: 19060909]

35. Lyssenko V, Nagorny CL, Erdos MR, Wierup N, Jonsson A, Spegel P et al. Common variant in MTNR1B associated with increased risk of type 2 diabetes and impaired early insulin secretion. Nat Genet. 2009;41(1):82–8. doi:10.1038/ng.288. [PubMed: 19060908]

36. Garaulet M, Gomez-Abellan P, Rubio-Sastre P, Madrid JA, Saxena R, Scheer FA. Common type 2 diabetes risk variant in MTNR1B worsens the deleterious effect of melatonin on glucose tolerance in humans. Metabolism. 2015;64(12):1650–7. doi:10.1016/j.metabol.2015.08.003. [PubMed: 26440713]

37. Consensus Conference Panel, Watson NF, Badr MS, Belenky G, Bliwise DL, Buxton OM et al. Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society on the Recommended Amount of Sleep for a Healthy Adult: Methodology and Discussion. Sleep. 2015;38(8): 1161–83. doi:10.5665/sleep.4886. [PubMed: 26194576]

38. Centers for Disease Control and Prevention. Sleep and sleep disorders. https://www.cdc.gov/features/sleep/. https://www.cdc.gov/features/sleep/.

39. Hirshkowitz MWK, Albert SM, Alessi C, Bruni O; DonCarlos L, Hazen N, Herman J, Katz ES, Kheirandish-Gozal L, Neubauer DN, O'Donnell AE, Ohayon M, Peever J, Rawding R, Sachdeva RC, Setters B, Vitiello MV, Ware JC, Adams Hillard PJ. National Sleep Foundation's sleep time

duration recommendations: methodology and results summary. Sleep Health. 1(1):40–3. [PubMed: 29073412]

40. Mukheijee S, Patel SR, Kales SN, Ayas NT, Strohl KP, Gozal D et al. An Official American Thoracic Society Statement: The Importance of Healthy Sleep. Recommendations and Future Priorities. Am J Respir Crit Care Med. 2015;191 (12):1450–8. doi:10.1164/rccm.201504-0767ST. [PubMed: 26075423]
41. Liu Y, Wheaton AG, Chapman DP, Cunningham TJ, Lu H, Croft JB. Prevalence of Healthy Sleep Duration among Adults--United States, 2014. MMWR Morb Mortal Wkly Rep. 2016;65(6):137–41. doi:10.15585/mmwr.mm6506a1. [PubMed: 26890214]
42. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep. 2004;27(7): 1255–73. [PubMed: 15586779]
43. Silva GE, Goodwin JL, Sherrill DL, Arnold JL, Bootzin RR, Smith T et al. Relationship between reported and measured sleep times: the sleep heart health study (SHHS). Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2007;3(6): 622–30. [PubMed: 17993045]
44. Krueger PM, Friedman EM. Sleep duration in the United States: a cross-sectional population-based study. American journal of epidemiology. 2009;169(9):1052–63. doi:10.1093/aje/kwp023. [PubMed: 19299406]
45. Lauderdale DS, Knutson KL, Yan LL, Rathouz PJ, Hulley SB, Sidney S et al. Objectively measured sleep characteristics among early-middle-aged adults: the CARDIA study. American journal of epidemiology. 2006;164(1):5–16. doi:10.1093/aje/kwj199. [PubMed: 16740591]
46. Chen X, Wang R, Zee P, Lutsey PL, Javaheri S, Alcantara C et al. Racial/Ethnic Differences in Sleep Disturbances: The Multi-Ethnic Study of Atherosclerosis (MESA). Sleep. 2015;38(6):877–88. doi:10.5665/sleep.4732. [PubMed: 25409106]
47. Hale L, Do DP. Racial differences in self-reports of sleep duration in a population-based study. Sleep. 2007;30(9):1096–103. [PubMed: 17910381]
48. Ertel KA, Berkman LF, Buxton OM. Socioeconomic status, occupational characteristics, and sleep duration in African/Caribbean immigrants and US White health care workers. Sleep. 2011;34(4): 509–18. [PubMed: 21461330]
49. Stamatakis KA, Kaplan GA, Roberts RE. Short sleep duration across income, education, and race/ethnic groups: population prevalence and growing disparities during 34 years of follow-up. Ann Epidemiol. 2007;17(12):948–55. doi:10.1016/j.annepidem.2007.07.096. [PubMed: 17855122]
50. Ryu SY, Kim KS, Han MA. Factors associated with sleep duration in Korean adults: results of a 2008 community health survey in Gwangju metropolitan city, Korea. J Korean Med Sci. 2011;26(9):1124–31. doi:10.3346/jkms.2011.26.9.1124. [PubMed: 21935265]
51. Patel SR, Sotres-Alvarez D, Castaneda SF, Dudley KA, Gallo LC, Hernandez R et al. Social and Health Correlates of Sleep Duration in a US Hispanic Population: Results from the Hispanic Community Health Study/Study of Latinos. Sleep. 2015;38(10):1515–22. doi:10.5665/sleep.5036. [PubMed: 26085298]
52. Basner M, Fomberstein KM, Razavi FM, Banks S, William JH, Rosa RR et al. American time use survey: sleep time and its relationship to waking activities. Sleep. 2007;30(9):1085–95. [PubMed: 17910380]
53. Ogilvie RP, Patel SR. The epidemiology of sleep and obesity. Sleep Health. 2017;3(5):383–8. doi: 10.1016/j.sleh.2017.07.013. [PubMed: 28923198]
54. Capers PL, Fobian AD, Kaiser KA, Borah R, Allison DB. A systemic review and meta-analysis of randomized controlled trials of the impact of sleep duration on adiposity and components of energy balance. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2015;16(9):771–82. doi:10.1111/obr.12296. [PubMed: 26098388]
55. Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity. 2008;16(3): 643–53. doi:10.1038/oby.2007.118. [PubMed: 18239586]
56. Patel SR, Malhotra A, White DP, Gottlieb DJ, Hu FB. Association between reduced sleep and weight gain in women. American journal of epidemiology. 2006;164(10):947–54. doi:10.1093/aje/kwj280. [PubMed: 16914506]

57. Spaeth AM, Dinges DF, Goel N. Effects of Experimental Sleep Restriction on Weight Gain, Caloric Intake, and Meal Timing in Healthy Adults. Sleep. 2013;36(7):981–90. doi:10.5665/sleep.2792. [PubMed: 23814334]
58. Bromley LE, Booth JN, 3rd, Kilkus JM, Imperial JG, Penev PD. Sleep restriction decreases the physical activity of adults at risk for type 2 diabetes. Sleep. 2012;35(7):977–84. doi:10.5665/sleep.1964. [PubMed: 22754044]
59. Cizza G, Piaggi P, Rother KI, Csako G, Sleep Extension Study G. Hawthorne effect with transient behavioral and biochemical changes in a randomized controlled sleep extension trial of chronically short-sleeping obese adults: implications for the design and interpretation of clinical studies. PloS one. 2014;9(8):e104176. doi:10.1371/journal.pone.0104176. [PubMed: 25141012]
60. Cespedes EM, Hu FB, Redline S, Rosner B, Alcantara C, Cai J et al. Comparison of Self-Reported Sleep Duration With Actigraphy: Results From the Hispanic Community Health Study/Study of Latinos Sueno Ancillary Study. American journal of epidemiology. 2016;183(6):561–73. doi:10.1093/aje/kwv251. [PubMed: 26940117]
61. Jackson CL, Patel SR, Jackson WB, 2nd, Lutsey PL, Redline S. Agreement between self-reported and objectively measured sleep duration among white, black, Hispanic, and Chinese adults in the United States: Multi-Ethnic Study of Atherosclerosis. Sleep. 2018. doi:10.1093/sleep/zsy057.
62. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? Epidemiology. 2008;19(6):838–45. doi:10.1097/EDE.0b013e318187a7b0. [PubMed: 18854708]
63. Matthews KA, Patel SR, Pantesco EJ, Buysse DJ, Kamarck TW, Lee L et al. Similarities and differences in estimates of sleep duration by polysomnography, actigraphy, diary, and self-reported habitual sleep in a community sample. Sleep Health. 2018;4(1):96–103. doi:10.1016/j.sleh.2017.10.011. [PubMed: 29332687]
64. Bakker JP, Weng J, Wang R, Redline S, Punjabi NM, Patel SR. Associations between Obstructive Sleep Apnea, Sleep Duration, and Abnormal Fasting Glucose. The Multi-Ethnic Study of Atherosclerosis. Am J Respir Crit Care Med. 2015;192(6):745–53. doi:10.1164/rccm.201502-0366OC. [PubMed: 26084035]
65. Shan Z, Ma H, Xie M, Yan P, Guo Y, Bao W et al. Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care. 2015;38(3):529–37. doi:10.2337/dc14-2073. [PubMed: 25715415]
66. Knutson KL. Does inadequate sleep play a role in vulnerability to obesity? Am J Hum Biol. 2012;24(3):361–71. doi:10.1002/ajhb.22219. [PubMed: 22275135]
67. Patel SR, Blackwell T, Ancoli-Israel S, Stone KL, Osteoporotic Fractures in Men-Mr OSRG. Sleep characteristics of self-reported long sleepers. Sleep. 2012;35(5):641–8. doi:10.5665/sleep.1822. [PubMed: 22547890]
68. Patel SR, Malhotra A, Gottlieb DJ, White DP, Hu FB. Correlates of long sleep duration. Sleep. 2006;29(7):881–9. [PubMed: 16895254]
69. Liu R, Zee PC, Chervin RD, Arguelles LM, Birne J, Zhang S et al. Short sleep duration is associated with insulin resistance independent of adiposity in Chinese adult twins. Sleep Med. 2011;12(9):914–9. doi:10.1016/j.sleep.2011.04.006. [PubMed: 21940204]
70. Pyykkonen AJ, Isomaa B, Pesonen AK, Eriksson JG, Groop L, Tuomi T et al. Sleep duration and insulin resistance in individuals without type 2 diabetes: the PPP-Botnia study. Ann Med. 2014;46(5):324–9. doi:10.3109/07853890.2014.902226. [PubMed: 24813456]
71. Chaput JP, Despres JP, Bouchard C, Astrup A, Tremblay A. Sleep duration as a risk factor for the development of type 2 diabetes or impaired glucose tolerance: analyses of the Quebec Family Study. Sleep Med. 2009;10(8):919–24. doi:10.1016/j.sleep.2008.09.016. [PubMed: 19332380]
72. Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med. 2005;165(8):863–7. doi:10.1001/archinte.165.8.863. [PubMed: 15851636]
73. Knutson KL, Van Cauter E, Zee P, Liu K, Lauderdale DS. Cross-sectional associations between measures of sleep and markers of glucose metabolism among subjects with and without diabetes: the Coronary Artery Risk Development in Young Adults (CARDIA) Sleep Study. Diabetes Care. 2011;34(5): 1171–6. doi:10.2337/dc10-1962. [PubMed: 21411507]

74. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2010;33(2):414–20. doi: 10.2337/dc09-1124. [PubMed: 19910503]

75•. Ferrie JE, Kivimaki M, Akbaraly TN, Tabak A, Abell J, Davey Smith G et al. Change in Sleep Duration and Type 2 Diabetes: The Whitehall II Study. Diabetes Care. 2015;38(8):1467–72. doi: 10.2337/dc15-0186. [PubMed: 26068863] This study showed that both persistent short sleepers and those who increased their sleep over five years had a higher risk of incident type 2 diabetes compared to those consistently sleeping seven hours a night.

76. Al Khatib HK, Hall WL, Creedon A, Ooi E, Masri T, McGowan L et al. 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. 2018;107(1):43–53. doi:10.1093/ajcn/nqx030. [PubMed: 29381788]

77. Dong JY, Zhang YH, Qin LQ. Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. Atherosclerosis. 2013;229(2):489–95. doi:10.1016/j.atherosclerosis. 2013.04.026. [PubMed: 23684511]

78. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proceedings of the American Thoracic Society. 2008;5(2): 136–43. doi:10.1513/pats.200709-155MG. [PubMed: 18250205]

79. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, Jr. et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005;28(4):499–521. [PubMed: 16171294]

80. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. American journal of epidemiology. 2013;177(9):1006–14. doi: 10.1093/aje/kws342. [PubMed: 23589584]

81. Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R et al. Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. Diabetes Care. 2003;26(3):702–9. [PubMed: 12610025]

82. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care. 2009;32(6):1017–9. doi: 10.2337/dc08-1776. [PubMed: 19279303]

83. Einhom D, Stewart DA, Erman MK, Gordon N, Philis-Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with type 2 diabetes mellitus. Endocr Pract. 2007;13(4):355–62. doi:10.4158/EP.13.4.355. [PubMed: 17669711]

84. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001;163(3 Pt 1): 608–13. doi:10.1164/ajrccm.163.3.9911064. [PubMed: 11254512]

85. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. Am J Respir Crit Care Med. 1998;157(1): 144–8. doi:10.1164/ajrccm. 157.1.9706079. [PubMed: 9445292]

86. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002;162(8):893–900. [PubMed: 11966340]

87. Ancoli-Israel S, Kripke DF, Klauber MR, Mason WJ, Fell R, Kaplan O. Sleep-disordered breathing in community-dwelling elderly. Sleep. 1991;14(6):486–95. [PubMed: 1798880]

88. Duran J, Esnaola S, Rubio R, Iztueta A. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. Am J Respir Crit Care Med. 2001;163(3 Pt 1):685–9. doi:10.1164/ajrccm.163.3.2005065. [PubMed: 11254524]

89. Tishler PV, Larkin EK, Schluchter MD, Redline S. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA. 2003;289(17):2230–7. doi:10.1001/jama.289.17.2230. [PubMed: 12734134]

90. Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. The Lancet Respiratory medicine. 2015;3(4):310–8. doi:10.1016/S2213-2600(15)00043-0. [PubMed: 25682233]

91. Mirer AG, Young T, Palta M, Benca RM, Rasmuson A, Peppard PE. Sleep-disordered breathing and the menopausal transition among participants in the Sleep in Midlife Women Study. Menopause. 2017;24(2):157–62. doi:10.1097/GME.0000000000000744. [PubMed: 27760083]
92. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015–21. [PubMed: 11122588]
93. Grunstein R, Wilcox I, Yang TS, Gould Y, Hedner J. Snoring and sleep apnoea in men: association with central obesity and hypertension. Int J Obes Relat Metab Disord. 1993;17(9):533–40. [PubMed: 8220656]
94. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med. 2005;165(20):2408–13. doi:10.1001/archinte.165.20.2408. [PubMed: 16287771]
95. Araghi MH, Chen YF, Jagielski A, Choudhury S, Banerjee D, Hussain S et al. Effectiveness of lifestyle interventions on obstructive sleep apnea (OSA): systematic review and meta-analysis. Sleep. 2013;36(10):1553–62, 62A-62E. doi:10.5665/sleep.3056. [PubMed: 24082315]
96. Greenburg DL, Lettieri CJ, Eliasson AH. Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. Am J Med. 2009;122(6):535–42. doi:10.1016/j.amjmed.2008.10.037. [PubMed: 19486716]
97. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. J Appl Physiol (1985). 2005;99(4):1592–9. doi:10.1152/japplphysiol.00587.2005. [PubMed: 16160020]
98. Mehra R, Stone KL, Blackwell T, Ancoli Israel S, Dam TT, Stefanick ML et al. Prevalence and correlates of sleep-disordered breathing in older men: osteoporotic fractures in men sleep study. Journal of the American Geriatrics Society. 2007;55(9):1356–64. doi:10.1111/j.1532-5415.2007.01290.x. [PubMed: 17767677]
99. Lee RW, Vasudavan S, Hui DS, Prvan T, Petocz P, Darendeliler MA et al. Differences in craniofacial structures and obesity in Caucasian and Chinese patients with obstructive sleep apnea. Sleep. 2010;33(8):1075–80. [PubMed: 20815189]
100. Aronsohn RS, Whitmore H, Van Cauter E, Tasali E. Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. Am J Respir Crit Care Med. 2010;181(5):507–13. doi:10.1164/rccm.200909-1423OC. [PubMed: 20019340]
101. Kent BD, Grote L, Ryan S, Pepin JL, Bonsignore MR, Tkacova R et al. Diabetes mellitus prevalence and control in sleep-disordered breathing: the European Sleep Apnea Cohort (ESADA) study. Chest. 2014;146(4):982–90. doi:10.1378/chest.13-2403. [PubMed: 24831859]
102. Muraki I, Tanigawa T, Yamagishi K, Sakurai S, Ohira T, Imano H et al. Nocturnal intermittent hypoxia and the development of type 2 diabetes: the Circulatory Risk in Communities Study (CIRCS). Diabetologia. 2010;53(3):481–8. doi:10.1007/s00125-009-1616-0. [PubMed: 19946661]
103. Nagayoshi M, Punjabi NM, Selvin E, Pankow JS, Shahar E, Iso H et al. Obstructive sleep apnea and incident type 2 diabetes. Sleep Med. 2016;25:156–61. doi:10.1016/j.sleep.2016.05.009. [PubMed: 27810258]
104. Botros N, Concato J, Mohsenin V, Selim B, Doctor K, Yaggi HK. Obstructive sleep apnea as a risk factor for type 2 diabetes. Am J Med. 2009;122(12):1122–7. doi:10.1016/j.amjmed.2009.04.026. [PubMed: 19958890]
105. Kendzerska T, Gershon AS, Hawker G, Tomlinson G, Leung RS. Obstructive sleep apnea and incident diabetes. A historical cohort study. Am J Respir Crit Care Med. 2014;190(2):218–25. doi:10.1164/rccm.201312-2209OC. [PubMed: 24897551]
106. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet. 1981;1(8225):862–5. [PubMed: 6112294]
107. Iftikhar IH, Hoyos CM, Phillips CL, Magalang UJ. Meta-analyses of the Association of Sleep Apnea with Insulin Resistance, and the Effects of CPAP on HOMA-IR, Adiponectin, and Visceral Adipose Fat. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2015;11(4):475–85. doi:10.5664/jcsm.4610. [PubMed: 25700870]

108. Weinstock TG, Wang X, Rueschman M, Ismail-Beigi F, Aylor J, Babineau DC et al. A controlled trial of CPAP therapy on metabolic control in individuals with impaired glucose tolerance and sleep apnea. Sleep. 2012;35(5):617–25B. doi:10.5665/sleep.1816. [PubMed: 22547887]

109. Salord N, Fortuna AM, Monasterio C, Gasa M, Perez A, Bonsignore MR et al. A Randomized Controlled Trial of Continuous Positive Airway Pressure on Glucose Tolerance in Obese Patients with Obstructive Sleep Apnea. Sleep. 2016;39(1):35–41. doi:10.5665/sleep.5312. [PubMed: 26350474]

110. Pamidi S, Wroblewski K, Stepien M, Sharif-Sidi K, Kilkus J, Whitmore H et al. Eight Hours of Nightly Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea Improves Glucose Metabolism in Patients with Prediabetes. A Randomized Controlled Trial. Am J Respir Crit Care Med. 2015;192(1):96–105. doi:10.1164/rccm.201408-1564OC. [PubMed: 25897569]

111. Ioachimescu OC, Anthony J, Jr., Constantin T, Ciavatta MM, McCarver K, Sweeney ME. VAMONOS (Veterans Affairs' Metabolism, Obstructed and Non-Obstructed Sleep) Study: Effects of CPAP Therapy on Glucose Metabolism in Patients with Obstructive Sleep Apnea. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2017;13(3):455–66. doi:10.5664/jcsm.6502. [PubMed: 28095965]

112. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X et al. CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea. N Engl J Med. 2016;375(10):919–31. doi: 10.1056/NEJMoa1606599. [PubMed: 27571048]

113. Babu AR, Herdegen J, Fogelfeld L, Shott S, Mazzone T. Type 2 diabetes, glycemic control, and continuous positive airway pressure in obstructive sleep apnea. Arch Intern Med. 2005;165(4): 447–52. doi:10.1001/archinte.165.4.447. [PubMed: 15738376]

114. Myhill PC, Davis WA, Peters KE, Chubb SA, Hillman D, Davis TM. Effect of continuous positive airway pressure therapy on cardiovascular risk factors in patients with type 2 diabetes and obstructive sleep apnea. J Clin Endocrinol Metab. 2012;97(11):4212–8. doi:10.1210/jc. 2012-2107. [PubMed: 22962427]

115. Donovan LM, Rueschman M, Weng J, Basu N, Dudley KA, Bakker JP et al. The effectiveness of an obstructive sleep apnea screening and treatment program in patients with type 2 diabetes. Diabetes Res Clin Pract. 2017;134:145–52. doi:10.1016/j.diabres.2017.10.013. [PubMed: 29054482]

116. Dawson A, Abel SL, Loving RT, Dailey G, Shadan FF, Cronin JW et al. CPAP therapy of obstructive sleep apnea in type 2 diabetics improves glycemic control during sleep. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2008;4(6):538–42. [PubMed: 19110882]

117. West SD, Nicoll DJ, Wallace TM, Matthews DR, Stradling JR. Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. Thorax. 2007;62(11):969–74. doi:10.1136/thx.2006.074351. [PubMed: 17557769]

118. Martinez-Ceron E, Barquiel B, Bezos AM, Casitas R, Galera R, Garcia-Benito C et al. Effect of Continuous Positive Airway Pressure on Glycemic Control in Patients with Obstructive Sleep Apnea and Type 2 Diabetes. A Randomized Clinical Trial. Am J Respir Crit Care Med. 2016;194(4):476–85. doi:10.1164/rccm.201510-1942OC. [PubMed: 26910598]

119••. Shaw JE, Punjabi NM, Naughton MT, Willes L, Bergenstal RM, Cistulli PA et al. The Effect of Treatment of Obstructive Sleep Apnea on Glycemic Control in Type 2 Diabetes. Am J Respir Crit Care Med. 2016;194(4):486–92. doi:10.1164/rccm.201511-2260OC. [PubMed: 26926656] This multicenter randomized trial showed that among patients with relatively well-controlled type 2 diabetes and obstructive sleep apnea., there was no effect of treating obstructive sleep apnea with CPAP on glycemic control.

120. Mokhlesi B, Grimaldi D, Beccuti G, Van Cauter E. Effect of one week of CPAP treatment of obstructive sleep apnoea on 24-hour profiles of glucose, insulin and counter-regulatory hormones in type 2 diabetes. Diabetes Obes Metab. 2017;19(3):452–6. doi:10.1111/dom.12823. [PubMed: 27860160]

121. Leong WB, Jadhakhan F, Taheri S, Chen YF, Adab P, Thomas GN. Effect of obstructive sleep apnoea on diabetic retinopathy and maculopathy: a systematic review and meta-analysis. Diabet Med. 2016;33(2): 158–68. doi:10.1111/dme.12817. [PubMed: 26031931]

122•. Altaf QA, Dodson P, Ali A, Raymond NT, Wharton H, Fellows H et al. Obstructive Sleep Apnea and Retinopathy in Patients with Type 2 Diabetes. A Longitudinal Study. Am J Respir Crit Care Med. 2017;196(7):892–900. doi:10.1164/rccm.201701-0175OC. [PubMed: 28594570] In a clinic-based study, OSA was associated with sight threatening diabetic retinopathy cross-sectionally and progression to preproliferative/proliferative diabetic retinopathy longitudinally.

123. Mason RH, Kiire CA, Groves DC, Lipinski HJ, Jaycock A, Winter BC et al. Visual improvement following continuous positive airway pressure therapy in diabetic subjects with clinically significant macular oedema and obstructive sleep apnoea: proof of principle study. Respiration. 2012;84(4):275–82. doi:10.1159/000334090. [PubMed: 22189259]

124. Furukawa S, Saito I, Yamamoto S, Miyake T, Ueda T, Niiya T et al. Nocturnal intermittent hypoxia as an associated risk factor for microalbuminuria in Japanese patients with type 2 diabetes mellitus. Eur J Endocrinol. 2013;169(2):239–46. doi:10.1530/EJE-13-0086. [PubMed: 23704715]

125. Stadler S, Zimmermann T, Franke F, Rheinberger M, Heid IM, Boger CA et al. Association of sleep-disordered breathing with diabetes-associated kidney disease. Ann Med. 2017;49(6):487–95. doi:10.1080/07853890.2017.1306100. [PubMed: 28281834]

126. Tahrani AA, Ali A, Raymond NT, Begum S, Dubb K, Altaf QA et al. Obstructive sleep apnea and diabetic nephropathy: a cohort study. Diabetes Care. 2013;36(11):3718–25. doi:10.2337/dc13-0450. [PubMed: 24062320]

127. Gu X, Luo X, Wang X, Tang J, Yang W, Cai Z. The correlation between obstructive sleep apnea and diabetic neuropathy: A meta-analysis. Prim Care Diabetes. 2018. doi:10.1016/j.pcd.2018.03.005.

128. Altaf QA, Ali A, Piya MK, Raymond NT, Tahrani AA. The relationship between obstructive sleep apnea and intra-epidermal nerve fiber density, PARP activation and foot ulceration in patients with type 2 diabetes. J Diabetes Complications. 2016;30(7): 1315–20. doi:10.1016/j.jdiacomp.2016.05.025. [PubMed: 27324704]

129. Bureau of Labor Statistics U.S. Department of Labor. Workers on Flexible and Shift Schedules in May 2004. 2005 https://www.bls.gov/news.release/pdf/flex.pdf.

130. McHill AW, Melanson EL, Higgins J, Connick E, Moehlman TM, Stothard ER et al. Impact of circadian misalignment on energy metabolism during simulated nightshift work. Proc Natl Acad Sci U S A. 2014;111(48):17302–7. doi:10.1073/pnas.1412021111. [PubMed: 25404342]

131. Buxton OM, Cain SW, O'Connor SP, Porter JH, Duffy JF, Wang W et al. Adverse metabolic consequences in humans of prolonged sleep restriction combined with circadian disruption. Sci Transl Med. 2012;4(129):129ra43. doi:10.1126/scitranslmed.3003200.

132. Bescos R, Boden MJ, Jackson ML, Trewin AJ, Marin EC, Levinger I et al. Four days of simulated shift work reduces insulin sensitivity in humans. Acta Physiol (Oxf). 2018;223(2):e13039. doi:10.1111/apha.13039. [PubMed: 29356345]

133. Wang F, Zhang L, Zhang Y, Zhang B, He Y, Xie S et al. Meta-analysis on night shift work and risk of metabolic syndrome. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2014;15(9):709–20. doi:10.1111/obr.12194. [PubMed: 24888416]

134. Liu Q, Shi J, Duan P, Liu B, Li T, Wang C et al. Is shift work associated with a higher risk of overweight or obesity? A systematic review of observational studies with meta-analysis. Int J Epidemiol. 2018. doi:10.1093/ije/dyy079.

135. Gan Y, Yang C, Tong X, Sun H, Cong Y, Yin X et al. Shift work and diabetes mellitus: a meta-analysis of observational studies. Occup Environ Med. 2015;72(1):72–8. doi:10.1136/oemed-2014-102150. [PubMed: 25030030]

136. Knutsson A, Kempe A. Shift work and diabetes--a systematic review. Chronobiol Int. 2014;31(10):1146–51. doi:10.3109/07420528.2014.957308. [PubMed: 25290038]

137. Pan A, Schernhammer ES, Sun Q, Hu FB. Rotating night shift work and risk of type 2 diabetes: two prospective cohort studies in women. PLoS Med. 2011;8(12):e1001141. doi:10.1371/journal.pmed.1001141. [PubMed: 22162955]

138. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd edition. Darien, IL: American Academy of Sleep Medicine; 2014.

139. Roth T, Coulouvrat C, Hajak G, Lakoma MD, Sampson NA, Shahly V et al. Prevalence and perceived health associated with insomnia based on DSM-IV-TR; International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; and Research Diagnostic Criteria/International Classification of Sleep Disorders, Second Edition criteria: results from the America Insomnia Survey. Biol Psychiatry. 2011;69(6):592–600. doi:10.1016/j.biopsych.2010.10.023. [PubMed: 21195389]
140. Ford ES, Cunningham TJ, Giles WH, Croft JB. Trends in insomnia and excessive daytime sleepiness among U.S. adults from 2002 to 2012. Sleep Med. 2015;16(3):372–8. doi:10.1016/j.sleep.2014.12.008. [PubMed: 25747141]
141. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA. 1989;262(11):1479–84. [PubMed: 2769898]
142. Buysse DJ, Angst J, Gamma A, Ajdacic V, Eich D, Rossler W. Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep. 2008;31(4):473–80. [PubMed: 18457234]
143. Morphy H, Dunn KM, Lewis M, Boardman HF, Croft PR. Epidemiology of insomnia: a longitudinal study in a UK population. Sleep. 2007;30(3):274–80. [PubMed: 17425223]
144. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep medicine reviews. 2002;6(2):97–111. [PubMed: 12531146]
145. Lin CL, Chien WC, Chung CH, Wu FL. Risk of type 2 diabetes in patients with insomnia:A population-based historical cohort study. Diabetes Metab Res Rev. 2018;34(1). doi:10.1002/dmrr.2930.
146. Vgontzas AN, Liao D, Pejovic S, Calhoun S, Karataraki M, Bixler EO. Insomnia with objective short sleep duration is associated with type 2 diabetes: A population-based study. Diabetes Care. 2009;32(11):1980–5. doi:10.2337/dc09-0284. [PubMed: 19641160]
147. Cespedes EM, Dudley KA, Sotres-Alvarez D, Zee PC, Daviglus ML, Shah NA et al. Joint associations of insomnia and sleep duration with prevalent diabetes: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL). J Diabetes. 2016;8(3):387–97. doi:10.1111/1753-0407.12308. [PubMed: 25952169]
148. Gore M, Brandenburg NA, Dukes E, Hoffman DL, Tai KS, Stacey B. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. J Pain Symptom Manage. 2005;30(4):374–85. doi:10.1016/j.jpainsymman.2005.04.009. [PubMed: 16256902]
149. Galer BS, Gianas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description, and quality of life. Diabetes Res Clin Pract. 2000;47(2):123–8. [PubMed: 10670912]
150. Chiu AF, Huang MH, Wang CC, Kuo HC. Higher glycosylated hemoglobin levels increase the risk of overactive bladder syndrome in patients with type 2 diabetes mellitus. Int J Urol. 2012;19(11):995–1001. doi:10.1111/j.1442-2042.2012.03095.x. [PubMed: 22774846]
151. Skomro RP, Ludwig S, Salamon E, Kryger MH. Sleep complaints and restless legs syndrome in adult type 2 diabetics. Sleep Med. 2001;2(5):417–22. [PubMed: 14592391]
152. Lopes LA, Lins Cde M, Adeodato VG, Quental DP, de Bruin PF, Montenegro RM, Jr., et al. Restless legs syndrome and quality of sleep in type 2 diabetes. Diabetes Care. 2005;28(11):2633–6. [PubMed: 16249531]
153. Merlino G, Fratticci L, Valente M, Del Giudice A, Noacco C, Dolso P et al. Association of restless legs syndrome in type 2 diabetes: a case-control study. Sleep. 2007;30(7):866–71. [PubMed: 17682657]
154. Plantinga L, Rao MN, Schillinger D. Prevalence of self-reported sleep problems among people with diabetes in the United States, 2005-2008. Prev Chronic Dis. 2012;9:E76. [PubMed: 22440550]