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Sleep behaviours and associated habits and the progression of pre-diabetes to type 2 diabetes mellitus in adults: A systematic review and meta-analysis

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Abstract

Introduction: Certain sleep behaviours increase risk of type 2 diabetes mellitus (T2DM) in the general population, but whether they contribute to the progression from pre-diabetes to T2DM is uncertain. We conducted a systematic review to assess this.

Methods: Structured searches were performed on bibliographic databases (MEDLINE, EMBASE and CINAHL) from inception to 26/04/2021 for longitudinal studies/trials consisting of adults⩾18 years with pre-diabetes and sleep behaviours (short or long sleep duration (SD), late chronotype, insomnia, obstructive sleep apnoea, daytime napping and/or night shift employment) that reported on incident T2DM or glycaemic changes. The Newcastle-Ottawa Scale was used for quality assessment.

Results: Six studies were included. Meta-analysis of three studies ($n = 20{,}139$) demonstrated that short SD was associated with greater risk of progression to T2DM, hazard ratio (HR) 1.59 (95% CI 1.29–1.97), I^2 heterogeneity score 0%, $p < 0.0001$, but not for long SD, HR 1.50 (0.86–2.62), I^2 heterogeneity 77%, $p = 0.15$. The systematic review showed insomnia and night shift duty were associated with higher progression to T2DM. Studies were rated as moderate-to-high quality.

Conclusions: Progression from pre-diabetes to T2DM increases with short SD, but only limited data exists for insomnia and night shift duty. Whether manipulating sleep could reduce progression from pre-diabetes to T2DM needs to be examined.

Keywords

Pre-diabetes, type 2 diabetes mellitus, sleep disorders, systematic review

Introduction

Pre-diabetes (also known as non-diabetic hyperglycaemia) represents a state where glucose levels are above the normal defined range, but lower than the diagnostic thresholds for type 2 diabetes mellitus (T2DM).[1-5] People with pre-diabetes are at higher risk of progressing to T2DM than people with normoglycaemia. Thus, pre-diabetes is considered an important target for T2DM prevention strategies.[5, 6] As the prevalence of T2DM is increasing

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and is associated with a major economic and health burden, there is a need to identify new potential methods to prevent T2DM in high risk people, to complement existing lifestyle measures.[7–9]

Short and long sleep duration, changes to sleep-wake cycle (late chronotype, night shift work), daytime 'napping', insomnia, and obstructive sleep apnoea (OSA) are very prevalent and have been shown to be associated with increased risk of T2DM in general population.[10–19] However, whether they are associated with increased risk of progression to T2DM in people with pre-diabetes is largely unknown. For this systematic review, we use the term sleep behaviours to encompass changes to sleep duration, and sleep-wake cycle (later chronotype, night shift), insomnia and OSA.

The aim of this study was to systematically identify and evaluate the current published literature regarding the associations between sleep behaviours and T2DM in people with pre-diabetes. If sufficient information was available, a meta-analysis was performed.

Methods

This systematic review was registered on International Prospective Registry of Systematic Reviews (PROSPERO Identification number: CRD42021248758) database and meets the requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[20] The Participants, Interventions, Comparisons, Outcomes, and Study design framework were followed to identify key study concepts in the research question a priori, and to facilitate the search process.

Data sources, search strategy and study selection

The search strategy was developed by SM and AT, in collaboration with an experienced local hospital health sciences librarian, to identify relevant studies using MEDLINE, Embase and CINAHL bibliographic databases. Databases were searched using a combination of appropriate subject headings for indexed articles, tailored to individual bibliographic databases where required, and free-text terms relevant to the framed question of this review, which were combined using Boolean operators. The reference lists of review articles and of included original publications were also screened for potentially relevant studies. The full electronic search strategy used for one database is included in Appendix 1. Literature searches were performed from inception up to 26th April 2021.

After conducting the electronic database searches, duplicates were removed and two investigators (SM and SCM) independently screened and assessed titles and abstracts of identified studies for eligibility. The full text of these papers was retrieved and independently assessed for inclusion by the same two reviewers. Discrepancies were resolved through a third investigator (CA) where necessary until a consensus was reached. To attempt to identify any further papers not identified through electronic database searches, reference lists of included original and relevant review articles were examined and hand-searched.

We included longitudinal studies that were either cohort, prospective or retrospective or clinical trials of minimum six months' duration that considered the impact of sleep behaviours on adults ⩾18 years old with pre-diabetes (any international biochemical definition) at baseline, with at least one future blood test result (either fasting plasma glucose, FPG, two-hour plasma glucose, 2-hr PG, or glycated haemoglobin, HbA1c) or assessment for T2DM (e.g. through use of glucose lowering therapies).[1-4] We included studies of any language, as long they were available as full-text articles. Exposure was considered as a measurement of any of the following: (1) measurement of habitual sleep duration (objectively measured or self-reported), (2) chronotype (via questionnaire or objectively measured) and the presence/absence of (3) obstructive sleep apnoea (objectively measured), (4) insomnia (questionnaire or physician diagnosed) or (5) any daytime napping (self-reported or objectively measured) or (6) night shift employment/duty. No sample size restriction was applied to studies. If multiple published reports from the same study were available, we included only the one with the most detailed information for both exposure and outcome.

The exclusion criteria consisted of studies that were cross-sectional, of animal populations, focused on any type of diabetes as an outcome or gestational diabetes at baseline, or clinical trials without a control arm or less than six months' duration.

Data extraction and quality assessment

One investigator (SM) extracted the data and the second investigator (SCM) independently checked for consistency. Any discrepancies that existed were discussed in arbitration (SM, SCM and CA) until a consensus was reached. Data was extracted on the following: first author's surname, year of publication, country of origin of the population studied, type of study (e.g. cohort or clinical trial), sleep variable under analysis and its method of measurement, exact pre-diabetes diagnosis and its method of measurement (including diagnostic criteria), sample size, population demographic characteristics (*e.g.* age, sex, ethnicity, BMI) and recruitment, any baseline exclusions made, length of follow-up and method for assessment of final outcomes (blood tests or diabetes medications). In addition, for the results at final follow-up, where reported we extracted data on (1) number of incident T2DM cases; (2) incident T2DM density rate per 1000 person-years; (3) hazard ratios, HRs, or relative risks, RRs, for T2DM with corresponding 95% confidence intervals, 95% CI, according

to stratifications of the sleep exposure and (4) the covariates adjusted for in the original statistical analysis. When studies had several adjustment models, we extracted HRs/RRs that reflected the maximum extent of adjustment for potentially confounding variables. If data on glycaemic status was not available at final follow-up, we extracted data on glycaemic test results at baseline and final follow-up and their corresponding absolute changes.

Quality assessment/risk of bias was performed independently by two reviewers (SM and CA) according to the Newcastle-Ottawa Quality Assessment Scale.[21] This scale awards a maximum of nine points to each study: four for selection of participants and measurement of exposure, two for comparability of cohorts on the basis of the design or analysis, and three for assessment of outcomes and adequacy of follow-up. We assigned scores of 0–3, 4–6 and 7–9 for low, moderate and high quality of studies, respectively, following methods used in another systematic review.[15]

Statistical analysis

Meta-analysis was only attempted if sufficient data was available. This only occurred for sleep duration (see below); for other exposures, we proceeded with a narrative systematic review only due to the lack of enough studies to perform a meta-analysis. The HRs or RRs and 95% CIs were considered as the effect size for all studies.

We estimated the pooled HR (and 95% CI) using a random-effects model. By comparison with the reference category of sleep duration, we estimated the pooled risk and 95% CI of progressing to T2DM for the short and the long sleep categories.

Heterogeneity among studies was quantified by I^2 statistic. We considered low, moderate, and high I^2 values to be 25, 50 and 75%, respectively.[22]

All statistical analyses for the meta-analysis were performed with Review Manager (RevMan) software Version 5.4.1 (Copenhagen, Cochrane Collaboration) and all tests were two-sided with p-level of $p<0.05$ considered as statistically significant.

Results

Identification of studies

There were 332 abstracts derived from the search strategy, from which 30 met inclusion criteria for full-text analysis; of these six studies were included in the systematic review (Ref. 23–28; Figure 1).

Summary of included studies and study characteristics

Three studies measured sleep duration as the exposure and there was one for insomnia, OSA and night shift duties. Table 1 describes the baseline characteristics of these studies and Table 2 describes the findings. Of the six studies included, four were cohort studies and two were post hoc analyses of clinical trials. Two studies were from the USA, one study was from each of Finland, Japan and South Korea and a global study was conducted in four continents. The length of follow-up ranged from 22 months to seven years, with incident T2DM cases of 3.7–29.2% (Table 2).

Assessment of study quality

All six studies were considered to be of moderate or high quality for the purposes of this review, with a median score of 7 (interquartile range 6.25–7), Appendix 2.

Sleep duration

From 17,983 people with pre-diabetes (HbA1c 5.7–6.4%) followed up for 22 months, Kim et al. reported significant associations for progression to T2DM with <5 and 5 to 6 hours/night sleep duration, measured via self-reported questionnaires, compared to 6–8 hours as the reference point. The adjusted HRs were 1.68 (95% confidence intervals, 95% CI, 1.30–2.16) and 1.42 (1.16–1.74), respectively.

Nuyujukian et al. performed oral glucose tolerance tests (OGTTs) on 1899 people with pre-diabetes (impaired glucose tolerance, IGT, and/or impaired fasting glycaemia, IFG) over two years and reported a significant association between sleeping <6 hours/night, measured via self-reported questionnaires, and progression to T2DM, HR 1.55 (1.11–2.17) after adjustment for age and sex, compared to the reference category of 6–8 hours/night. This association was attenuated after adjustment for all covariates, HR 1.33 (0.85–2.08). In contrast, in Tuomilehto et al., 257 people with IGT undertook annual OGTTs in a longer-term follow-up of seven years. They reported a sleep duration of <6.5 hours/night, measured using a personal diary, was associated with a non-significant adjusted HR of 1.68 (0.79–3.59) compared to the reference category of 7–8.5 hours.

Considering long sleep durations, Kim et al. and Nuyujukian et al. reported no association between the progression of pre-diabetes to T2DM with sleep durations of ⩾8 hours/night. The adjusted HRs were 1.02 (0.61–1.71) and 1.23 (0.85–1.78), respectively. In contrast, Tuomilehto et al. reported a significant association for long sleep durations of 9–9.5 and ⩾10 hours, with adjusted HRs of 2.29 (1.38–3.80) and 2.74 (1.67–4.50), respectively.

Data from these three studies were used to conduct meta-analysis featuring 20,139 participants. Short sleep duration was associated with greater risk of progression to T2DM, HR 1.59 (1.29–1.97), I^2 for heterogeneity score = 0%, $p < 0.0001$ (Figure 2). The overall effect was not

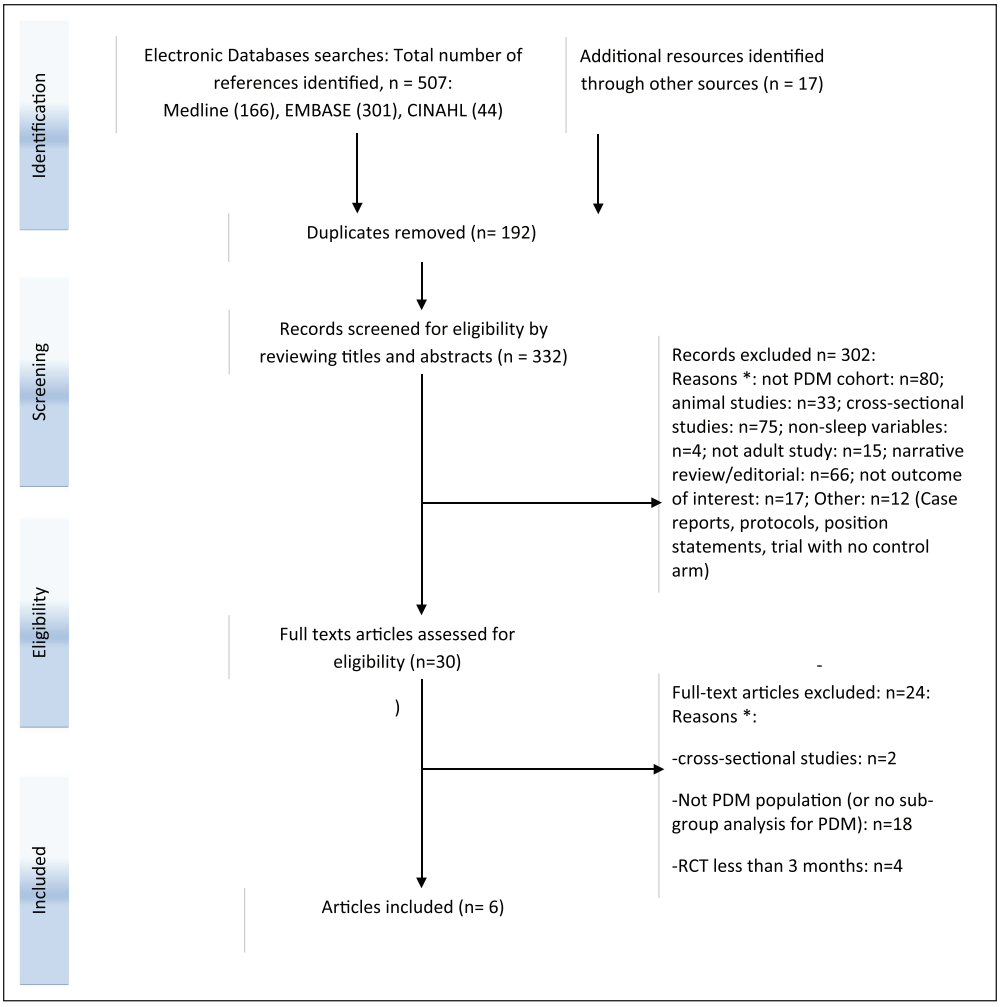

Figure 1. Flow chart to demonstrate the process of study selection. Key: n= number, PDM = pre-diabetes, RCT = randomised controlled trial. * For reasons excluded, there may have been more than 1 reason; however, the allocated category represents the first obvious reason for exclusion.

altered when a short sleep duration category was changed from <5 hours to 5 to 6 hours in Kim et al., HR 1.43 (1.19–1.71), I^2 for heterogeneity = 0%, $p = 0.0001$. There was no evidence of significant statistical heterogeneity.

Long sleep duration was not associated with greater risk of progression to T2DM, HR 1.50 (0.86–2.62), I^2 for heterogeneity = 77%, $p = 0.15$. There was evidence of statistical heterogeneity. The effect was not altered when a long sleep duration category was changed from ⩾10 hours to 9 to 9.5 hours in Tuomilehto et al., HR 1.41 (0.91–2.19), I^2 for heterogeneity = 77%, $p = 0.13$.

Using fixed effects models in place of random-effects models did not change the significance for associations for either short or long sleep duration.

Other sleep exposures

In LeBlanc et al., 81,233 people with pre-diabetes undertook serial HbA1c and FPG measurements; the presence of insomnia (n = 24,126; 29.7%) was associated with higher progression to T2DM than those without insomnia, adjusted HR 1.28 (1.24–1.33). This association remained even when FPG or HbA1c were added to the statistical models, HRs 1.28 (1.23–1.33) and 1.32 (1.25–1.40), respectively.

In Toshihiro et al., from 128 men with IGT and/or IFG undergoing annual OGTTs, 36 (28.1%) progressed to T2DM. Working night shift duties was associated with an increased risk of progression to T2DM, adjusted HR 5.48 (1.82–16.49).

Regarding the natural history of progression to T2DM in 230 people with pre-diabetes and moderate-to-severe OSA undertaking usual care (not on a continuous positive airway pressure intervention), Loffler et al. reported 38 (16.5%) people developed T2DM over 4.3 years. In comparison, 7.7% of people with moderate-to-severe OSA, but normal levels of glucose and HbA1c, developed incident T2DM. Finally, over the 4.3 years, in people with

Table 1. Baseline characteristics of studies included in the systemic review.

No	Study	Study type	Sleep variable measured or diagnosed	Pre-diabetes diagnosis ± criteria used	*N**	Population/ setting	Cohort baseline mean/ median characteristics: Age (years), % female, BMI or % obese	Baseline exclusions	Length of follow-up	Outcome analysed	Diabetes assessment at follow-up
1	Kim, 2017, South Korea	Cohort	Sleep duration (self-report via questionnaire)	HbA1c 39–46 mmol/mol (5.7–6.4%)	17,983	Attending annual health hospital visits	Age 41.9 years, 33% female, 40.8% obese	Narcolepsy, Malignancy, DM, or Anti-DM	22 months	Glycaemic status	HbA1c or use of GLTs
2	Tuomilehto, 2009, Finland	RCT, post hoc analysis	Sleep duration (self-report via activity diary)	IGT (WHO 1999 criteria)	522 (257 in control arm)	Undertaking lifestyle program	Age 55 years 67.4% female BMI 31.1	Severe Thyroid & liver disease, low life expectancy	7 years	Glycaemic status	OGTT
3	Nuyujukian, 2015, USA	Cohort	Sleep duration (self-report via Questionnaire)	IFG ± IGT (ADA 1997).	1899	Undertaking lifestyle program	Across Sleep duration categories: Age 46.7–48.1 years, females 76.7–72.4% BMI 35.0–36.5 All native Alaskans	Not completing the lifestyle intervention	2 years (range 0.5–3 years)	Glycaemic status	OGTT
4	LeBlanc, 2018, USA	Cohort	Insomnia (29.7%) vs. no Insomnia (70.3%), at baseline or during study	HbA1c 39–46 mmol/mol (5.7–6.4%) or IFG (ADA 1997)	81,233	Electronic medical records for medical care visits	Age 57.5 53.6% female 39.3% obese 81.0% white ethnicity	OSA, SDB, restless leg, periodic leg move disorder	4.3 years (standard deviation 2.8)	Glycaemic status	HbA1c, FPG or database for T2DM or GLTs
5	Loffler, 2020, Global trial	RCT, post hoc analysis	OSA (moderate-to-severe)	Sub-group with PDM: IFG or HbA1c (ADA 2019)	452 with PDM (230 in control arm)	Trial of CPAP (intervention) vs usual care (control arm)	Age 61.1, 14.8% female BMI 29.2	severe daytime sleepiness, severe nocturnal hypoxemia	4.3 years	Glycaemic status and change in glycaemia	FPG, HbA1c & use of GLTs
6	Toshihiro, 2008, Japan.	Cohort	Night duty work (self-report via questionnaire)	IGT ± IFG (ADA 1997)	128	Attending annual health visits	Men only; age 49.3 years	Hepatitis B or C	3.2 years (standard deviation 0.1)	Glycaemic status	OGTT

*N is presented as for the total study population, then followed by control arm (CA) where relevant.
Anti-DM meds = use of anti-diabetic medications, CA = control arm, CPAP = continuous positive airway pressure, DM = diabetes, GLT = glucose lowering therapy, *N* = number, OGTT = oral glucose tolerance test, RCT = randomised controlled trial, SD = sleep duration, SDB = sleep disordered breathing, TIB = time-in-bed, UC = usual care, WHO = World Health Organization.

Table 2. Incidence and risk of T2DM at final follow-up or change in glycaemic test results in the included studies.

No	Study	Total incident T2DM cases, n (%)*	Incidence density (ID) for T2DM (per 1000 person-years, 95% CI)	Baseline covariates adjusted for in calculating T2DM risk	Results for risk of progression to T2DM
1	Kim, 2017	664 (3.7%)	Total cohort: ID was 21. For SD of ⩽5.0, 5.0–6.0, 6.0–8.0 and ⩾8.0 hours, IDs were 25.4, 23.1, 16.9 and 16.9. No 95% CI available. SD was rounded up/down to nearest hour.	Age, sex, marital status, education level, depressive symptoms, antidepressant use, perceived health status, family history of diabetes, sleep apnoea, shiftwork, snoring, difficult breathing during sleep, use of sleeping pill, smoking status, alcohol intake, physical activity and baseline HbA1c level	For SD of ⩽5.0, 5.0–6.0 and ⩾ 8.0 hours, adjusted HRs were 1.68 (95% CI 1.30–2.16) and 1.44 (1.17–1.76) and 1.23 (0.85–1.78), compared to reference group of 6.0–8.0 hours. SD was rounded up/down to nearest hour.
2	Tuomilehto,2009	182 (29.2%); 107 (42.5%) in control)	In control arm: for SD of <6.5, 7.0–8.5, 9.0–9.5 and ⩾10.0 hours, IDs were 71 (95% CI 40–129), 48 (35–67), 92 (62–138) and 113 (81–156)	Age, sex, BMI, smoking, alcohol intake, hypertension medication, leisure-time physical activity, 1-year change in body weight.	In control arm: for SD of <6.5, 9.0–9.5 and ⩾10.0 hours, adjusted HRs were 1.68 (95% CI 0.79–3.59), 2.29 (1.38–3.80), 2.74 (1.67–4.50), compared to reference group of 7.0–8.5 hours.
3	Nuyujukian, 2015	184 (9.7%)	For SD of ⩽6.0, 6.0–8.0 and ⩾8.0 hours, IDs were 46 (95% CI 37–57), 32 (23–42) and 33 (24–44).	Age, sex, BMI, body weight, socioeconomic status, health behaviours and health status, % weight loss	For SD of ⩽6.0 and ⩾8.0 hours, adjusted HRs (for age and sex) were 1.55 (95% CI 1.11–2.17) and 1.01 (0.63–1.63), compared to reference of >6.0 to <8.0 hours. After adjustment for all risk factors, HRs were 1.33 (0.85–2.08) and 1.02 (0.61–1.71)
4	LeBlanc, 2018	4564 (18.9%) for insomnia; 10,062 (17.6%) without insomnia	n/a	Age, BMI, sex, race, ethnicity, and history of heart failure or myocardial infarction, hypertension, high triglycerides, low HDL, and smoking status	In Insomnia group, adjusted HR was 1.28 (95% CI 1.24–1.33), compared to non-insomnia group. HRs remained unchanged after adjustment for baseline HbA1c level (HR 1.32; 1.25–1.40) or FPG (HR 1.28; 1.23–1.33).
5	Loffler, 2020	72 (15.9%) (38 (16.5%) in usual care)	n/a	—	In the control arm, fasting plasma glucose increased from 5.65 to 5.91 mmol/l and HbA1c from 6.04 to 6.15%; both were non-significant changes.
6	Toshihiro, 2008	36 (28.1%)	n/a	Age, BMI, systolic blood pressure, ALT, GGT, total protein, creatinine, triglyceride, HDL-C, LDL-C, uric acid, amylase, ESR, WBC, Hb, FPG, urinary protein, blue collar job, administrative position, business bachelor, stress in daily life, satisfaction, fatigue, alcohol drinking, current smoking.	Night shit duty associated with progression to T2DM, adjusted HR 5.48 (95% CI 1.82–16.49), $p = 0.002$.

*incidence across all arm/groups.
HR = hazard ratio, ID = incidence density, n/a= not available, SD = sleep duration, T2DM = Type 2 diabetes mellitus, 95% CI = 95% confidence interval.

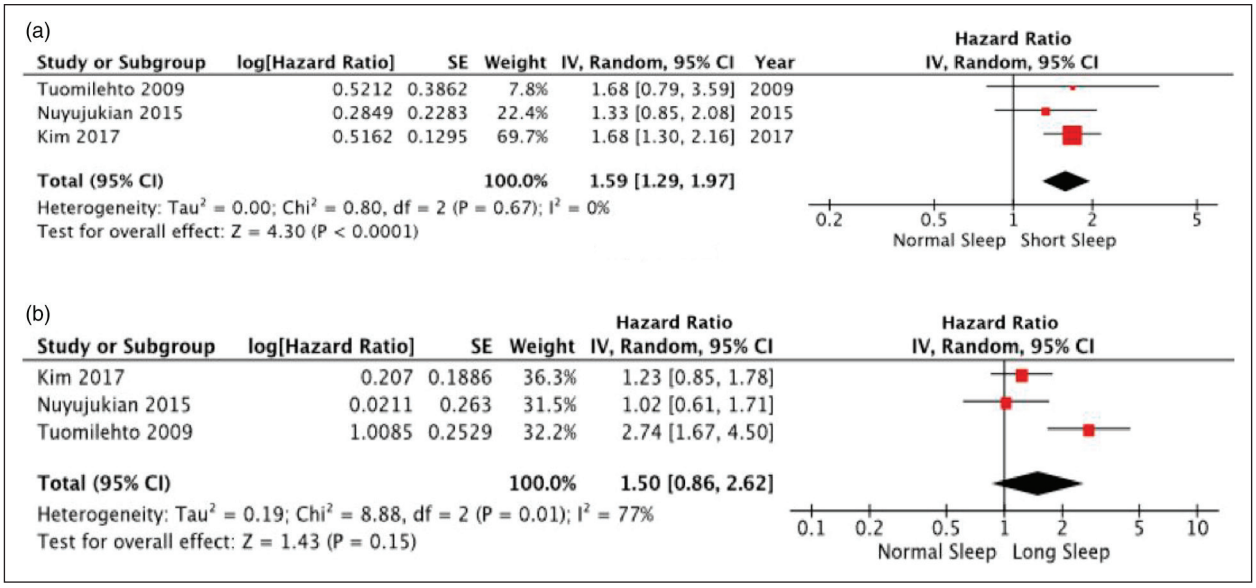

Figure 2. The association between progression of pre-diabetes to Type 2 diabetes mellitus with (a) short sleep duration and (b) long sleep duration. (a) Short sleep duration compared to normal sleep (reference categories). (b) Long sleep duration compared to normal sleep (reference categories).

pre-diabetes and OSA, levels of FPG increased from 5.65 to 5.91 mmol/l and HbA1c from 6.04 to 6.15%; both were considered non-significant changes.

Discussion

In this study, we found a significant association between short sleep duration and the risk of developing T2DM in people with pre-diabetes. We found no such significant association in people with long sleep duration. Insomnia and night shift work were also associated with increased risk of developing T2DM in pre-diabetes but we only found one study for each condition.

The six studies that contributed to the analysis all used well-defined and validated methods for the definitions for pre-diabetes and T2DM, allowing accuracy in the detection of prevalence and incidence rates. The statistical models used for calculating hazard ratios for risk of T2DM featured adjustments for an extensive number of baseline risk factor variables that could affect glycaemia.

In the three studies that used sleep duration as the exposure, this was measured using subjective methods of either self-report questionnaires or personal diaries to best estimate sleep duration. An alternative method would be to use objective measures of sleep duration, such as accelerometers or wearable technologies, for example, smart wristwatches, which can better differentiate between actual sleep time and time spent in bed. Studies generally suggest objectives methods produce lower estimates of sleep duration than self-report measures.[29–31] Using objectives measures, however, may be less feasible for implementation and analysis in large scale cohort studies.[32] The study investigating insomnia as the exposure found 30% of people with pre-diabetes had insomnia diagnostic codes on their electronic medical records or were using sleep medications. This prevalence may have differed if other methods were used, however the reported prevalence is similar to that from cross-sectional data of people with pre-diabetes reporting higher levels of insomnia symptoms in questionnaires and also a recent systematic review in people with T2DM, at 25.6% and 39%, respectively.[33, 34]

There are plausible mechanisms explaining the association of short sleep duration and increased risk of incident T2DM, including hormonal changes in levels of melatonin, cortisol and catecholamines impacting on glucose tolerance.[35–36] Habitual short sleep duration is associated with sympathetic predominance either to lower vagal tone or increase sympathetic activity, which can reduce response of β-pancreatic cells to glucose and lower insulin sensitivity.[37–39] Experimental sleep restriction can impact on insulin resistance and secretion by prolonging nocturnal growth hormone secretion and increasing early morning noradrenaline.[40] Additionally, sleep restriction is associated with increased levels of free fatty acids, increasing gluconeogenesis which can lead to insulin resistance.[40–42] In people without T2DM, sleep restriction is associated with reduced insulin sensitivity without a compensatory increase in insulin secretion, suggesting impaired β-cell function.[43] Short sleep duration/sleep restriction impacts on appetite regulating hormones, to increase ghrelin/leptin ratio, produce higher levels of endocannabinoids and may lower levels of glucagon-like peptide-1.[44–48] Subsequently this can lead to increased hunger, appetite, caloric intake and positive energy balances which induce weight gain,

especially as there is also an associated decrease in physical activity with sleep restriction.[44–49] Short sleep duration has been shown to be a risk factor for developing obesity and weight gain and might have an impact on weight loss intervention.[50] The impact of sleep manipulation on weight could also be one of the potential mechanisms of a favourable impact on T2DM risk.[50] However, the field of sleep manipulation and its impact on weight is still in its early stages with small number of short studies.[50]

Considering the global burden of T2DM, our study highlights the importance of examining sleep extension as a strategy to aid the prevention of T2DM in people with pre-diabetes, alongside existing lifestyle measures.[7–9] Sleep extension has demonstrated to be feasible in adults.[51] Secondly, our systematic review highlights the paucity of data regarding sleep behaviours/disorders and the progression to T2DM in pre-diabetes. This is despite cross-sectional studies and general population longitudinal studies showing associations between short sleep duration and T2DM.[14, 15,52] Hence, there is a need for more robust evidence to assess the associations between short sleep duration and T2DM in pre-diabetes.

Regarding limitations of the study, the lack of consensus on definitions for short and long sleep duration meant that reference groups in statistical models between studies may not have been defined using exactly the same cut-points. Secondly, diagnostic criteria for T2DM and pre-diabetes have changed over time, impacting on one study, which did not use of HbA1c for diagnosis.[1–4] Thirdly, the final number of studies included in the meta-analysis was small and thus some caution is required when interpreting the results, especially for the lack of association between long sleep duration and the risk of T2DM.

The strengths of this study are the systematic approach and robust methods used to obtain our results, ensuring they met accepted standards for meta-analyses. We considered a wide range of sleep behaviours and definitions of pre-diabetes, which were used in the comprehension list of search terms in the search strategy. We analysed full-text articles for studies featuring cohorts with people without T2DM at baseline for any possible sub-analyses of people with pre-diabetes, allowing us to detect as many eligible studies as possible. This is the first systematic review to detail the existing literature of the impact of sleep behaviours on the progression of pre-diabetes to T2DM.

In conclusion, short sleep duration was associated with increased risk of progressing from pre-diabetes to T2DM. Additionally, there was limited data suggesting that insomnia and night shift duty are associated with progression to T2DM but more studies are needed. Future research needs to explore the role of the variety of different sleep disorders and their interactions and mechanisms in the progression from pre-diabetes to T2DM. Manipulating specific sleep behaviours might serve as a potential target to aid current measures of T2DM prevention in people with pre-diabetes.

Key messages

- Certain sleep behaviours/habits are associated with incident T2DM in people from the general population. Less is known about this association for high risk people with pre-diabetes.
- Our meta-analysis demonstrates short sleep duration in people with pre-diabetes is associated with progression to T2DM.
- Limited data from the systematic review demonstrates insomnia and night shift duty work are also associated with T2DM.
- The potential benefits of sleep manipulation should be examined as a method to prevent progression from pre-diabetes to T2DM, alongside lifestyles measures.

Abbreviations

95% CI = 95% confidence intervals
2-hr PG = two-hour plasma glucose
FPG = fasting plasma glucose
HR = hazard ratio
IFG = impaired fasting glucose
IGT = impaired glucose tolerance
OGTT = oral glucose tolerance test
RCT = randomised clinical trials
RR = relative risks
SE = standard error
T2DM = type 2 diabetes mellitus.

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Author contributions

SAM – conceived the idea for the review, designed the study, developed the search strategy, conducted the literature searches, screened articles for inclusion, selected and retrieved relevant papers, determined inclusion/exclusion of papers, conducted data extraction, performed the analysis, performed the critical analysis and wrote the manuscript.
SCM – screened articles for inclusion, selected and retrieved relevant papers, determined inclusion/exclusion of papers, verified data extraction and drafted the manuscript.
CA – performed the critical analysis, was the third reviewer for any discrepancies and drafted the manuscript.
GB – drafted the manuscript.
KN – drafted the manuscript.
AAT – conceived the idea for the review, designed the study, developed the search strategy, supervised the meta-analyses and drafted the manuscript.

Data availability

Data used in this study (including an unpublished protocol) is retained by the research team.

Declaration of conflicting interests

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Appendix 1. Example of search terms used for Medline

1. ("Non-diabetic hyperglyc?emi*").ti,ab
2. (Prediabetes).ti,ab
3. (Pre-diabetes).ti,ab
4. *"PREDIABETIC STATE"/
5. ("Intermediate hyperglyc?emi*").ti,ab
6. (Impaired ADJ2 glucose).ti,ab
7. ("borderline diabetes").ti,ab
8. (IFG).ti,ab
9. *"GLUCOSE INTOLERANCE"/
10. ("Glucose intolerance").ti,ab
11. (1 OR two OR 3 OR four OR 5 OR 6 OR seven OR 8 OR 9 OR 10)
12. (Sleep ADJ1 (duration OR deprivation OR disorder* OR stage* OR length OR pattern* OR problem*)).ti,ab
13. (Chronotype).ti,ab
14. (Morning* ADJ2 Evening*).ti,ab
15. (Circadian ADJ1 (rhythm OR clock*)).ti,ab
16. ("Biological Clock*").ti,ab
17. ("Social jetlag").ti,ab
18. ("Sleep debt").ti,ab
19. ("Sleep Initiation and Maintenance Disorder").ti,ab
20. ("obstructive sleep apn?ea").ti,ab
21. *"SLEEP APNEA SYNDROMES"/OR *"SLEEP APNEA, OBSTRUCTIVE"/
22. (Napping).ti,ab
23. ("Sleep wake disorder*").ti,ab
24. (wakefulness).ti,ab
25. ("Shift work*").ti,ab
26. (Insomnia).ti,ab
27. ("sleep disordered breathing").ti,ab
28. (12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27)
29. (11 AND 28)
30. ("Type 2 diabetes").ti,ab
31. *"DIABETES MELLITUS, TYPE 2"/
32. (T2DM OR T2D).ti,ab
33. ("type two diabetes").ti,ab
34. (30 OR 31 OR 32 OR 33)
35. (29 AND 34)

Appendix 2. Quality assessment of the 6 research reports included in the analysis

Study – First author	Kim	Tuomilehto	Nuyujukian	LeBlanc	Loffler	Toshihiro
Question no						
1	1	1	1	1	1	0
2	1	1	1	1	1	0
3	0	0	0	1	1	0
4	0	0	0	0	0	0
5	1	1	1	1	0	1
6	1	1	1	1	0	1
7	1	1	1	1	1	1
8	1	1	1	1	1	1
9	1	1	1	1	1	1
Total Score	7	7	7	8	6	5

Brief outline of scoring criteria (see reference 21 for full details)

1. Representativeness of the exposed cohort: 1 mark: truly or somewhat representative; 0 marks: selected group/no description
2. Selection of the non-exposed cohort: 1 mark: same community; 0 marks: different source/no description
3. Ascertainment of exposure: 1 mark: secure record/structured interview; 0 marks: written self-report/no description
4. Demonstration that outcome of interest was not present at start of study: 1 mark: yes; 0 marks: no
5+6. Comparability of cohorts on the basis of the design or analysis: 1 mark: study controls for important risk factor; 1 mark: study controls for any additional important factor
7. Assessment of outcome: 1 mark independent blind assessment/record linkage; 0 marks self-report/no description
8. Was follow-up long for enough outcomes: 1 mark: yes; 0 marks: no.
9. Adequacy of follow-up of cohorts: 1 mark: complete follow-up/subjects lost to follow up unlikely to introduce bias. 0 marks: no description/high loss.