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Sweet dreams or bitter nightmare: a narrative review of 25 years of research on the role of sleep in diabetes and the contributions of behavioural science

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Abstract

The aim of this review was to provide an overview of developments, clinical implications and gaps in knowledge regarding the relationship between diabetes and sleep over the past 25 years, with special focus on contributions from the behavioural sciences. Multiple prospective observational and experimental studies have shown a link between suboptimal sleep and impaired glucose tolerance, decreased insulin sensitivity and the development of type 2 diabetes. While prevalence rates of suboptimal sleep vary widely according to definition, assessment and sample, suboptimal subjective sleep quality appears to be a common reality for one-third of people with type 1 diabetes and over half of people with type 2 diabetes. Both physiological and psychosocial factors may impair sleep in these groups. In turn, suboptimal sleep can negatively affect glycaemic outcomes directly or indirectly via suboptimal daytime functioning (energy, mood, cognition) and self-care behaviours. Technological devices supporting diabetes self-care may have both negative and positive effects. Diabetes and its treatment also affect the sleep of significant others. Research on the merits of interventions aimed at improving sleep for people with diabetes is in its infancy. Diabetes and sleep appear to be reciprocally related. Discussion of sleep deserves a central place in regular diabetes care. Multi-day, multi-method studies may shed more light on the complex relationship between sleep and diabetes at an individual level. Intervention studies are warranted to examine the potential of sleep interventions in improving outcomes for people with diabetes.

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Introduction

Sleep serves multiple functions, with varying levels of evidence for theories focusing on the immune system, energy conservation and replenishment, removal of brain waste products, restoration of cognitive and behavioural performance, and brain connectivity [1]. There is no single measure of sleep, as the construct spans multiple dimensions and levels of analysis [1,2]. Sleep medicine has mainly studied sleep disorders and deficiencies, with more recent perspectives focusing on more general sleep characteristics important for health, including sleep duration, efficiency (i.e. the ease of falling asleep and returning to sleep), timing (the placement of sleep within the 24-h day), and satisfaction [1,2]. From a biological perspective, sleep timing depends on two physiological processes: sleep debt (i.e. increased sleep pressure with longer prior wakefulness) and an internal circadian clock that synchronizes biological sleep/wake rhythms to our 24-h day by environmental light signals and neurohormonal pathways (including melatonin) [3]. Human behaviours related to 24-h light access and work/social obligations may override these physiological processes, and lead to a condition called 'circadian misalignment', in which the behavioural sleep–wake schedule is not in synchrony with endogenous circadian rhythms [3]. The last two decades have seen an explosion in the number of studies highlighting the important role of sleep in physical and mental health [2], and public health approaches are starting to incorporate the message that sleep is as central to health as physical activity and diet.

Diabetes is a growing health problem of global dimensions. Only recently has it been acknowledged that suboptimal sleep can impact on the development and overall regulation of diabetes, whereas several components of diabetes and its management may affect sleep [4,5]. As of

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What's new?

- In 1994, studying suboptimal sleep in people with diabetes was highlighted as a promising new research area.
- Since then, a large evidence base has illustrated the myriad of ways in which sleep and diabetes are linked.
- Suboptimal sleep is a common reality for many people with diabetes, which may negatively impact glycaemic and psychosocial outcomes.
- In turn, physiological and psychosocial factors may impair sleep.
- Sleep deserves a more central place in regular diabetes care.
- Future studies may focus on clarifying the interactions of sleep and diabetes on the individual level, as well as on evaluating the merits of sleep interventions in this group.

2017, the American Diabetes Association's Standards of Medical Care have recommended assessment of sleep pattern and duration as part of the comprehensive medical evaluation, given their links to glycaemic outcomes. The present narrative review will provide an overview of developments, clinical implications and gaps in knowledge regarding the relationship between diabetes and sleep over the past 25 years, with a special focus on contributions from the behavioural sciences.

Evidence base 25 years ago

In the discussion of their 1994 pioneering article about sleep disturbances in diabetes, Sridhar and Madhu [6] specified a set of hypotheses which, in the years that followed, have come to dominate the research agenda in this field: (1) sleep disturbances are common in people with diabetes; (2) antecedents of these problems are often physiological in nature, although psychosocial factors should not be overlooked; and (3) sleep disturbances affect the quality of life, mood and coping abilities of people with diabetes [6]. Their recommendation that 'further studies must be done to understand the exact relationship between sleep complaints and diabetes' [6] has not remained unheard. The past 25 years have generated an impressive evidence base highlighting the myriad of ways sleep and diabetes are linked.

Overview of findings in the past 25 years

Sleep and the development of diabetes

Experimental studies in healthy adults have long shown that sleep is a key process in metabolic functioning. Sleep restriction to 4 h per night over 6 consecutive nights decreased glucose tolerance by 40% [7]. Even a single night of sleep restriction to 4 h was enough to decrease hepatic and peripheral insulin sensitivity by 19–25% [8]. Sleep timing appears to play a role as well, with a 53% reduction in insulin sensitivity when bedtimes are misaligned with endogenous circadian rhythms as compared to 39% with circadian alignment, while keeping the amount of sleep loss across both conditions identical [9].

Suboptimal sleep has also been implicated in the development of diabetes, in particular type 2 diabetes. Prospective studies have found an association between shift work and increased risk of type 2 diabetes, most likely attributable to irregular sleep schedules resulting in circadian misalignment (an overview can be found in Leproult *et al.* [9]). Furthermore, a systematic review and meta-analysis from 2010 based on 10 prospective studies (n=107 756; follow-up range 4–32 years) concluded that several measures of sleep quantity and quality predicted the risk of developing type 2 diabetes [10]. These included short duration of sleep (≤5–6 h/night: relative risk 1.28, 95% CI 1.03–1.60), long duration of sleep (>8–9 h/night: relative risk 1.48, 95% CI 1.13–1.96), difficulty initiating sleep (relative risk 1.57, 95% CI 1.25–1.97), and difficulty maintaining sleep (relative risk 1.84, 95% CI 1.39–2.43) [10]. A later meta-analysis of 10 prospective studies (n=482 502; follow-up range 2–16 years) confirmed the U-shaped association between sleep duration and risk of type 2 diabetes, with the lowest risk observed at a sleep duration of 7–8 h/day [11]. The authors calculated that the risk of developing diabetes increased by 9% for each hour shorter than 7 h of sleep/day and by 14% for each hour longer sleep [11]. These findings are limited by the use of self-reported and single time-point assessments of sleep, an overrepresentation of people from Europe, the USA and Japan, and the possibility of confounding by suboptimal physical activity or diet [10,11]. Suggested mechanisms relating suboptimal sleep to decreases in glucose tolerance and insulin sensitivity include changes in appetite-regulating hormones, increased activity of the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis, alterations in melatonin secretion and growth hormone metabolism, and low-grade inflammation [10,11]. Confounding by undiagnosed medical conditions such as obstructive sleep apnoea syndrome is also possible. Obstructive sleep apnoea syndrome (sleep-disordered breathing characterized by repetitive collapse of the upper airway) has been found to be related to insulin resistance and incident type 2 diabetes [12]. Obesity (in particular central adiposity) is an important risk factor for both obstructive sleep apnoea syndrome and type 2 diabetes [12].

A prospective study based on data from the Norwegian HUNT Study (n=53 394) suggested that sleep disturbances (i.e. self-reported problems with initiating sleep and/or maintaining sleep often or almost every night during the last month) were associated with 50% greater risk of adult-onset autoimmune diabetes [defined as age ≥35 years and anti-

glutamic acid decarboxylase (GAD)-positivity: hazard ratio 95% CI 1.01–2.22; *n*=121) [13]; however, these findings should be interpreted with caution, as there were only 30 people classified as having 'classic' type 1 diabetes, i.e. insulin treatment at time of diagnosis, anti-GAD positivity, or anti-GAD negativity with C-peptide levels <150 pmol/l.

Prevalence of suboptimal sleep in diabetes and comparison with people without diabetes

In a sample of almost 10 000 adults with self-reported diabetes participating in the US National Health and Nutrition Examination Survey, 93% reported at least one sleep problem, i.e. inadequate sleep, severe sleep deprivation, frequent daytime sleepiness, frequent sleeping pill use, apnoea (defined as frequent self-reported stops in breathing, snorting or gasping, or self-reported diagnosis of sleep apnoea by a health professional), nocturia, and leg symptoms including frequent jerks or cramps and diagnosed restless legs syndrome [14]. The rate of suboptimal subjective sleep quality generally ranges between 30% and 35% in adults with type 1 diabetes and between 40% and 70% in adults with type 2 diabetes, compared with a range of 10–30% in the general population and elderly people without diabetes [15]. When directly comparing subjective sleep variables across both diabetes types, those with type 2 diabetes reported a slightly shorter sleep duration, less optimal sleep quality and efficiency, and more sleep disturbance [15].

Obstructive sleep apnoea syndrome is a common comorbidity in type 1 and type 2 diabetes, in which autonomic neuropathy may play a role by compromising upper airway reflexes and pharyngeal muscle control [16]. The prevalence of obstructive sleep apnoea syndrome in adults with type 2 diabetes has been found to be as high as 8b6%, with 24–53% having moderate to severe symptoms [12]. In adults with type 1 diabetes, these numbers have been estimated at 52% and 17%, respectively [16]. By comparison, rates in middle-aged adults from the general population range from 6% to 34%, depending on symptom severity and time period [12]. Restless legs syndrome is a sleep-related movement disorder characterized by complex leg movements to alleviate unpleasant sensations in the legs [12]. It may affect one in four adults with type 2 diabetes as opposed to 5–15% in the general population, with a potential role for peripheral neuropathy [12].

With respect to direct comparisons of sleep characteristics with people without diabetes, most studies have focused on type 1 diabetes. As to sleep architecture (i.e. the structural organization of sleep in terms of types and stages), a decreased amount of slow wave ('deep') sleep has been found in people with type 1 diabetes compared to matched controls without diabetes [17]. Furthermore, this group may experience more impact from 'social jetlag' (i.e. the difference in sleep timing between week and weekend days). Young adults with type 1 diabetes slept an average of 2 h longer on weekend days as compared to week days, while this was just under 1 h in their peers without diabetes [18]. A small meta-analysis comparing sleep in people with and without type 1 diabetes found that children/adolescents with type 1 diabetes had a significantly shorter polysomnography-based sleep duration than healthy controls [16]. With respect to adults, there was no difference in self-reported sleep duration between those with and without type 1 diabetes [16]. As to sleep quality, scores did not differ between adults with and without type 1 diabetes when based on polysomnography or dichotomized self-reported sleep quality scores [16]. Self-reported continuous sleep quality scores were significantly worse in adults with type 1 diabetes compared to healthy controls [16]; however, it should be noted that this meta-analysis only included three studies per comparison. Furthermore, even though self-report measures are often used and offer a good perspective on subjective experience, they often overestimate time spent asleep and show moderate correlations with objective measures [12]. Potential explanations for any differences between people with and without diabetes include nocturnal glucose levels, diabetes treatment, diabetes complications, and associated conditions (Table 1).

Sleep and short-term glycaemic outcomes

Restricting sleep to 4 h in a single night has been shown to induce peripheral insulin resistance in adults with type 1 diabetes, as evidenced by decreased glucose disposal rate during a hyperinsulinaemic euglycaemic clamp study [19], very similar to findings in people without diabetes [8].

Table 1 Potential causes of suboptimal sleep in people with diabetes*

Category	Factor
Related to nocturnal glucose levels	Hypoglycaemia, absolute level
	Hyperglycaemia, absolute level†
	Rapid changes/high variability
Related to diabetes treatment (in particular technological devices)	Pump/continuous glucose monitoring alarms
	Pump/continuous glucose monitoring discomforts
Related to diabetes complications	Neuropathy/neuropathic pain
	Heart failure†
Related to associated conditions	Depressive symptoms
	Anxiety symptoms
Related to general conditions	Substance abuse (e.g. alcohol)
	Medication use (e.g. anti-hypertensives)
	Leg cramps
	Heartburn

*List of factors is not exhaustive, but aims to illustrate the different categories of causes using common examples from literature and clinical experience.
†This may cause nocturia, which also disturbs sleep.

Furthermore, the risk of hypoglycaemia is increased during the night, through a combination of factors including the long fast, hyperinsulinaemia and increased glucose consumption during rapid eye movement (REM) sleep. Sleep also suppresses counter-regulatory hormone responses to and symptomatic awareness of hypoglycaemia [20]. Compared to those without diabetes of comparable gender, age and BMI, people with type 1 diabetes showed a defective awakening response to induced nocturnal hypoglycaemia [20]. As to recovery from hypoglycaemia, sleep deprivation did not exacerbate hypoglycaemia-induced cognitive impairment, but was associated with persistence of both cognitive dysfunction and hypoglycaemia symptoms during the post-hypoglycaemia recovery period in adults with type 1 diabetes [21].

Sleep and HbA_{1c}

A systematic review of 20 prospective studies (n=69 329; 15 studies included in meta-analysis) among adults with type 2 diabetes found a U-shaped association between sleep duration and HbA_{1c}, where short and long sleep duration were associated with 0.23% (95% CI 0.10–0.36) and 0.13% (95% CI 0.02–0.25) higher HbA_{1c}, respectively, compared with normal sleep [22]. Suboptimal subjective sleep quality showed a similar relation, but only for continuous HbA_{1c} levels (0.35%, 95% CI 0.12–0.58) [22]. A few cross-sectional studies using more objective measures of sleep (electroencephalogram, actigraphy) found associations between HbA_{1c} and sleep quality measures (including sleep efficiency, fragmentation and latency, i.e. the time needed to fall asleep), but not sleep duration [23].

A small meta-analysis explored the associations between sleep and HbA_{1c} in type 1 diabetes, pooling two to six studies per subtopic [16]. In adults, there was a significant association between sleep duration and HbA_{1c}, but only when sleep measurements were based on self-report [16]. Those who reported sleeping >6 h had a significantly lower HbA_{1c} level compared to those reporting ≤6 h of sleep (–0.24%, 95% CI –0.47 to –0.02) [16]. Similarly, those with HbA_{1c} <53 mmol/mol (7%) reported sleeping an average of 17 min (95% CI 4–30) more than those with HbA_{1c} ≥53 mmol/mol (7%) [16]. Studies using objective sleep measurements did not find a significant difference in HbA_{1c} between those sleeping >6 h and ≤6 h, nor did objective sleep duration differ according to HbA_{1c} status [16]. In children, no significant associations were found between sleep duration and HbA_{1c}, but the analysis was based on only two studies [16]. As to sleep quality, adults with optimal scores had significantly lower HbA_{1c} levels compared to those with suboptimal scores, when based on self-report (–0.19%, 95% CI –0.30 to –0.08), but not when based on objective measurements [16]. Higher sleep variability (day-to-day changes in timing and duration) also appears to negatively affect glycaemic outcomes [24].

Proposed mechanisms include direct effects of suboptimal sleep on glucose metabolism (e.g. insulin resistance), as well as indirect effects on diabetes self-care behaviours through impairments in energy, mood and cognition, which will be described below.

Sleep and self-care behaviours

The impact of sleep on glucose levels may be partially attributable to its effects on diabetes self-care behaviours. Most studies report an association between sleep duration and frequency of self-monitoring of blood glucose (SMBG). In a study among adolescents with type 1 diabetes, objective SMBG frequency mediated the association between actigraphy-measured sleep duration and HbA_{1c} [25]. Every additional hour of sleep was associated with almost one extra glucose measurement and an HbA_{1c} reduction of 0.33%. Another study among adolescents and young adults with type 1 diabetes also reported an association between self-reported longer sleep duration (but not sleep disturbances or sleep quality) and more frequent SMBG, particularly in boys/men [26]. Furthermore, diary-based sleep duration was associated with next day's SMBG and total daily insulin bolus frequency (derived from pump/glucometer downloads) among adolescents with type 1 diabetes, in that a 15- and 20-min increase in sleep was associated with, respectively, one additional SMBG measurement and one additional bolus [27].

A common theoretical model posits that suboptimal sleep may directly interfere with self-care through impairment of cognition [28]. Sleep deficits are known to hamper cognitive processes central to self-care, including decision-making, planning, problem-solving, interpretation and manipulation of information, task accuracy, and maintaining attention [28]. In line with this model, higher subjective sleep quality in older adolescents with type 1 diabetes was associated with fewer self-regulatory difficulties surrounding glucose measurement, including being easily distracted and putting off measuring [29]. In contrast, sleep quality was not associated with self-reported frequency of SMBG, potentially as a result of mealtimes serving as a structured marker for glucose checking as well as compensatory efforts by parents. In another study among adults with type 1 diabetes, 12% reported that awaking during the night negatively affected their ability to calculate a bolus insulin dose, illustrated by comments such as 'feels like your brain isn't working properly' [30]. Furthermore, 33% of participants indicated their ability to make optimal diabetes-related decisions was affected, as 'exhaustion impedes all decisions'. In a qualitative study among adolescents aged 13–17 years with type 1 diabetes, several teens described becoming more 'forgetful' or 'lazy' about diabetes management and making unhealthy food choices in case of suboptimal sleep the night before [31]. Emotional problems (including symptoms of depression, anxiety and stress) are likely to play a role as well in the relationship between suboptimal sleep and self-care [5]. Suboptimal sleep has been associated with worse emotional

well-being, which, in turn, may negatively affect self-management behaviours and glucose levels [5].

Among adults with type 2 diabetes and self-reported daytime sleepiness, suboptimal subjective sleep quality was associated with less uptake of treatment recommendations [32]. Another study found suboptimal sleep quality to be related to a higher subjective self-care burden among adults with type 1 or type 2 diabetes, although this did not translate into less optimal self-care or self-reported HbA_{1c} [15]. The authors posited that sleep impairment might specifically augment the burden of self-care, with prolonged struggles to meet recommendations translating to higher HbA_{1c} later on [15].

Sleep and daytime functioning

Sleep characteristics have been related to multiple areas of psychosocial functioning. Suboptimal subjective sleep quality was associated with lower health status and diabetes-related quality of life in adults with type 2 diabetes [33]. Similarly, almost 80% of adults with type 1 diabetes believed waking in the night had a negative impact on their usual daily functioning, including mood and happiness, family relationships, work and the ability to exercise regularly and eat healthily [30]. Suboptimal subjective sleep quality has been related to higher levels of daytime sleepiness, fatigue, symptoms of depression and anxiety, and diabetes-specific distress in adults with type 1 or type 2 diabetes [15] and higher worries about hypoglycaemia in adults with type 1 diabetes [34]. Furthermore, increases in sleep quality have been associated with fewer next-day diabetes-specific and general stressors in adults with type 1 diabetes [35]. In paediatrics, sleepiness and suboptimal sleep habits have been related to reduced quality of life, depressed mood, and lower academic achievements [17] and sleep disturbances have even been shown to mediate the association between diabetes and neurocognitive and behavioural deficits [36]. Nocturnal hypoglycaemia may play an important role in determining next-day functioning, as the day after hypoglycaemia-disrupted sleep, two-thirds of adults with diabetes wanted to nap and/or rest and approximately half wanted to go to bed earlier [37]. They also reported tiredness and/or fatigue (77%), feeling less alert (52%), feeling down (56%), and fear of future nocturnal hypoglycaemic events (50%).

Potential causes of sleep disturbances in people with diabetes

Table 1 lists five categories of causes of suboptimal sleep in people with diabetes, using common examples from the literature and clinical experience. The role of nocturnal glucose levels and a selection of somatic/psychological comorbidities is further illustrated below.

Nocturnal glucose levels

From clinical practice, it is well known that abnormal glucose levels may interfere with sleep. Most research to date has focused on the role of nocturnal hypoglycaemia. In an international study in 300 people with type 1 or type 2 diabetes, 44% of participants indicated that nocturnal non-severe hypoglycaemia had a high impact on subjective sleep quality, and 40% reported that it was difficult to get back to sleep [37]. Hypoglycaemia may impact sleep irrespective of whether people wake up or continue sleeping. Nocturnal hypoglycaemia in type 1 diabetes has been associated with a deepening of sleep, as evidenced by increased slow-wave sleep and delta electroencephalogram power [38]. As to nocturnal hyperglycaemia, higher glucose levels have been related to lower subjective sleep quality and duration [39]. Higher night-time glucose level often results in the need to urinate more frequently, which may disrupt sleep [40]. Furthermore, higher glucose levels were associated with lower overnight excretion of melatonin in adults with type 1 diabetes [41], a hormone implicated in the proper regulation of sleep–wake patterns. In adolescents with type 1 diabetes, parent-reported longer sleep duration and trouble sleeping were related to longer time spent in hyperglycaemia (glucose >10 mmol/l), using continuous glucose monitoring (CGM) data [42]. Rather than absolute glucose levels, awakenings from sleep may be more dependent on the speed of change, e.g. rapid declines [38]. Also, higher glycaemic variability (represented by the standard deviation of measured levels) has been related to higher sleep latency and lower subjective sleep quality and duration [18,34,39].

Somatic and psychological comorbidities

Neuropathic pain, often nocturnal, has been related to suboptimal sleep in diabetes [12]. Depressive symptoms have also been shown to be an important correlate of suboptimal subjective sleep quality in diabetes [15], although the cross-sectional nature of most studies precludes final conclusions regarding the temporal order of both constructs. The association is likely to be reciprocal [15], in that depressive symptoms may have a direct effect on sleep, and sleep problems may impair mood. It should also be taken into account that major depression may include symptoms of insomnia and hypersomnia. Anxiety symptoms (either general or diabetes-specific worries) have also been cross-sectionally related to suboptimal subjective sleep quality [15,34].

Technological developments in diabetes management and sleep

The past decades have seen rapid developments in the availability of technological devices to aid in insulin administration and glucose measurement; however, their use may be hampered when asleep. For example, in a group of children and adolescents spending the night in a clinical research centre with real-time CGM, 29% awoke to individual alarms and 66% to alarm events, i.e. one or more alarms separated from previous alarms by > 30 min [43]. The

chance of responding to an alarm decreased with child age (53% in adolescents, 20% in 7–11 year olds, 17% in 4–6 year olds) and number of overnight alarms (40% for first alarm, 28% for subsequent alarm).

As to its impact on sleep, unfortunately, the introduction of technology does not coincide with positive effects by definition. For example, parent-reported sleep quality of children aged 2–12 years was not related to the use of diabetes-related technology, including insulin pumps and CGM [44]. Common downsides of technology relate to interruptions of sleep due to device-wearing discomfort and overnight alarms [45]. This may prompt switching off alarms overnight, in order to improve sleep for people with diabetes (and their significant others).

The newest generations of technological systems offer new hope in improving sleep for people with diabetes. For example, two studies randomized children and adults with type 1 diabetes to 12 weeks of automated closed-loop glucose control and then 12 weeks of open-loop sensor-augmented insulin pump therapy (or vice versa) in their home setting [45]. The introduction of closed-loop technology was associated with improved sleep, less worry about nocturnal hypoglycaemia, and improved general well-being, especially on waking. In another study among adults with type 1 diabetes using self-built hybrid closed-loop systems ('OpenAPS'), 94% reported some improvement in sleep quality and 56% reported a large improvement [46]. In comparison, sensor-augmented pump therapy did not reduce worries about hypoglycaemia and only modestly improved sleeping [45].

Sleep in significant others of people with diabetes

Sleep in people with diabetes and their relatives are closely linked. Both actigraphy-based and self-reported measures of sleep in children with type 1 diabetes have been associated with the same measures in parents [44,47]. Similarly, greater self-reported sleep quality in adults with type 1 diabetes was related to greater sleep quality in their spouses [35]. Interestingly, increased spousal daily sleep quality was associated with fewer general stressors for both partners [35]. Diabetes and its treatment may directly impact sleep in significant others. For example, among people with type 1 and type 2 diabetes who had a bed partner present during a non-severe nocturnal hypoglycaemic event, 51% unintentionally woke them up and 20% woke them up on purpose for assistance or support [37]. In addition, sleep disruptions due to technology were reported by 73% of parents/caregivers and 59% of partners [48]. This was as frequent as at least four times/week for 54% and 12% of these, respectively, with the main reason being CGM alarms [48]. Sleep in family members may also be interrupted due to regular night-time checks and worries about nocturnal hypoglycaemia [24,48]. Conversely, improvements in parental sleep have also been reported after introduction of diabetes devices [45].

Translation/implementation: management of suboptimal sleep in diabetes care

At its core, the take-home-message for clinicians of the 1994 Sridhar and Madhu article has not changed based on the research findings of the previous 25 years: 'physicians caring for persons with diabetes must be able to recognise, diagnose and manage sleep disturbances in their patients when they occur' [6]. While the Standards of Care of the American Diabetes Association as of 2017 include recommendations to include assessment of sleep in regular care, research showing a causal relationship between interventions aimed at improving sleep and improvements in physiological and psychosocial functioning among people with diabetes is still in its infancy.

In a 2018 review of therapeutic considerations aiding sleep in type 2 diabetes, cognitive behavioural therapy and pharmaceutical sleep aids for insomnia, continuous airway pressure for obstructive sleep apnoea syndrome, and lifestyle interventions including physical activity were highlighted to improve sleep without detrimentally affecting glucose levels [49]. In a randomized pilot study among 31 adults with type 2 diabetes who did not sleep before midnight, a combination of conventional diabetes education and sleep education reduced HbA_{1c}, fasting glucose and insulin resistance more than diabetes education alone [50]. Sleep modification interventions in the context of type 1 diabetes are scarce. In a randomized controlled trial, young people aged 10–16 years either followed a sleep extension intervention including instructions to increase bedtime up to 10 h or 1 h more than their naturalistic sleep, or a fixed sleep duration condition in which duration was anchored to their average naturalistic sleep [51]. Feasibility analyses suggested that sleep modification in natural settings was possible, with an average increase in total sleep time of 41 min in the intervention group and 6 min in the control group. In total, 80% of intervention participants followed the sleep extension instructions for 1 week, despite the fact that most found the schedule somewhat or very difficult; however, only 46% was at least somewhat likely to continue with the recommendations [51]. In a quasi-experiment with control group and pre-test/post-test design, young people aged 6–18 years were assigned to an intervention condition with videotaped sleep hygiene education and practice tips over 3 days, and a control condition [52]. When comparing subjective sleep quality score at baseline and on the fourth day, there was a significant improvement in the intervention but not the control group, with more optimal post-test scores for the former [52].

Future research directions

While the importance of attention to sleep in people with diabetes has been illustrated by the studies discussed in this review, a new wave of research is needed to better understand the complex interrelations between sleep, glucose levels, and

other variables [24]. Recommendations to move the field forward include a call for longitudinal multi-day studies with both between- and within-person designs that dynamically combine self-reports of sleep with objective measures of both sleep and glucose levels [5,16,24]. These may also shed more light on the longitudinal relationship between sleep quality and glycaemic variables. Future studies also need to address potentially confounding factors, such as socio-economic status, shift work, physical activity and diet, that affect both diabetes and sleep [10]. In addition, important steps still need to be made in translating research findings into appropriate awareness among people with diabetes and clinicians alike, as well as feasible intervention tools [24]. More intervention studies are needed to examine the potential of sleep interventions in improving physiological and psychosocial outcomes for people with diabetes. Input about suitable behavioural targets for intervention may come from multiple sources. First, case studies may illustrate successful approaches in clinical practice, including cognitive behavioural therapy and relaxation therapy. Second, qualitative studies may shed more light on barriers to and facilitators of obtaining sufficient sleep. These include the use of electronic devices before bed and sleep disturbances related to diabetes (e.g. having to delay bedtime due to diabetes management, awakenings as a result of hypo- or

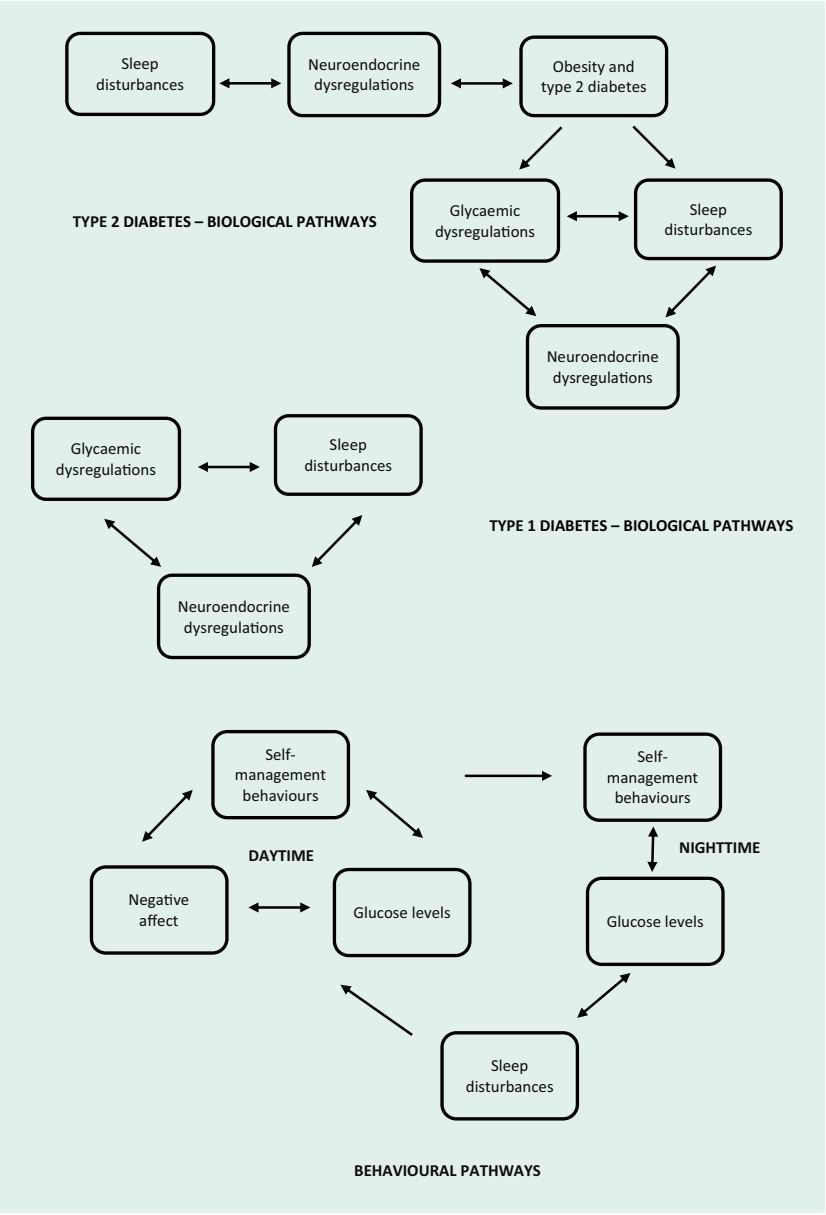

FIGURE 1 Summary of biological and behavioural pathways relating sleep and diabetes, based on the models of Barone and Menna-Barreto [4] and Monzon *et al.* [5].

hyperglycaemia symptoms), as well as consistently setting bedtimes, limiting distractions around bedtime, and using relaxation techniques [31]. Third, interventions that have proven potential to improve sleep in other populations may provide useful insights, including moving bedtimes and targeting distractors of sleep, such as emotions and environmental factors [24]. Furthermore, it is important to follow the continuing advancements in diabetes technology [24], as higher rates of time in target, coupled with reduced burden of device use, hold great promise to improve sleep for people with diabetes.

Conclusion

Over the last 25 years, it has become well established that sleep deserves a central place in regular diabetes care, on a par with traditional factors such as diet and exercise. Suboptimal sleep increases the risk of developing type 2 diabetes. Furthermore, sleep impairments are a common reality for children and adults living with type 1 or type 2 diabetes, disrupting and being disrupted by both physiological and psychosocial/behavioral factors. As to biological pathways (Fig. 1), there appears to be a reciprocal relationship for type 2 diabetes, in which sleep characteristics negatively impact neurological and endocrine systems, promoting obesity and type 2 diabetes, as well as exacerbate glycaemic outcomes, while diabetes itself often leads to sleeping difficulties [4]. For type 1 diabetes, suboptimal glycaemic outcomes may negatively affect sleep in terms of quality and/or length, which in turn can exacerbate glycaemic outcomes by inducing insulin resistance and glucose intolerance [4]. As to behavioural pathways (Fig. 1), negative affect may impact daytime self-management behaviours and glucose levels; these subsequently impact night-time behaviours and glucose levels, which influence sleep, followed by a deterioration in negative affect, behaviours and glucose levels the next day [5]. The time has come to incorporate sleep more integrally into the diabetes education and self-care routine. This process can be supported by new research efforts to better understand the interaction between sleep and diabetes on a more individual level and by broadening awareness and tools available in clinical practice to support people improving sleep, diabetes outcomes and quality of life.

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References

1 Krueger JM, Frank MG, Wisor JP, Roy S. Sleep function: Toward elucidating an enigma. *Sleep Med Rev* 2016; **28**: 46–54.
2 Buysse DJ. Sleep health: can we define it? Does it matter? *Sleep* 2014; **37**: 9–17.
3 Reutrakul S, Van Cauter E. Interactions between sleep, circadian function, and glucose metabolism: implications for risk and severity of diabetes. *Ann N Y Acad Sci* 2014; **1311**: 151–173.
4 Barone MT, Menna-Barreto L. Diabetes and sleep: a complex cause-and-effect relationship. *Diabetes Res Clin Pract* 2011; **91**: 129–137.
5 Monzon A, McDonough R, Meltzer LJ, Patton SR. Sleep and type 1 diabetes in children and adolescents: Proposed theoretical model and clinical implications. *Pediatr Diabetes* 2019; **20**: 78–85.
6 Sridhar GR, Madhu K. Prevalence of sleep disturbances in diabetes mellitus. *Diabetes Res Clin Pract* 1994; **23**: 183–186.
7 Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999; **354**: 1435–1439.
8 Donga E, van Dijk M, van Dijk JG, Biermasz NR, Lammers GJ, van Kralingen KW *et al*. A single night of partial sleep deprivation induces insulin resistance in multiple metabolic pathways in healthy subjects. *J Clin Endocrinol Metab* 2010; **95**: 2963–2968.
9 Leproult R, Holmback U, Van Cauter E. Circadian misalignment augments markers of insulin resistance and inflammation, independently of sleep loss. *Diabetes* 2014; **63**: 1860–1869.
10 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**: 414–420.
11 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**: 529–537.
12 Ogilvie RP, Patel SR. The Epidemiology of Sleep and Diabetes. *Curr Diab Rep* 2018; **18**: 82.
13 Olsson L, Ahlbom A, Grill V, Midthjell K, Carlsson S. Sleep disturbances and low psychological well-being are associated with an increased risk of autoimmune diabetes in adults. Results from the Nord-Trondelag Health Study. *Diabetes Res Clin Pract* 2012; **98**: 302–311.
14 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.
15 Nefs G, Donga E, van Someren E, Bot M, Speight J, Pouwer F. Subjective sleep impairment in adults with type 1 or type 2 diabetes: Results from Diabetes MILES–The Netherlands. *Diabetes Res Clin Pract* 2015; **109**: 466–475.
16 Reutrakul S, Thakkinstian A, Anothaisintawee T, Chontong S, Borel AL, Perfect MM *et al*. Sleep characteristics in type 1 diabetes and associations with glycemic control: systematic review and meta-analysis. *Sleep Med* 2016; **23**: 26–45.
17 Perfect MM, Patel PG, Scott RE, Wheeler MD, Patel C, Griffin K *et al*. Sleep, glucose, and daytime functioning in youth with type 1 diabetes. *Sleep* 2012; **35**: 81–88.
18 Barone MT, Wey D, Schorr F, Franco DR, Carra MK, Lorenzi Filho G *et al*. Sleep and glycemic control in type 1 diabetes. *Arch Endocrinol Metab* 2015; **59**: 71–78.
19 Donga E, van Dijk M, van Dijk JG, Biermasz NR, Lammers GJ, van Kralingen K *et al*. Partial sleep restriction decreases insulin sensitivity in type 1 diabetes. *Diabetes Care* 2010; **33**: 1573–1577.
20 Schultes B, Jauch-Chara K, Gais S, Hallschmid M, Reiprich E, Kern W *et al*. Defective awakening response to nocturnal hypoglycemia in patients with type 1 diabetes mellitus. *PLoS Med* 2007; **4**: e69.
21 Inkster BE, Zammitt NN, Ritchie SJ, Deary IJ, Morrison I, Frier BM. Effects of Sleep Deprivation on Hypoglycemia-Induced Cognitive Impairment and Recovery in Adults With Type 1 Diabetes. *Diabetes Care* 2016; **39**: 750–756.
22 Lee SWH, Ng KY, Chin WK. The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: A systematic review and meta-analysis. *Sleep Med Rev* 2017; **31**: 91–101.

23 Zhu B, Hershberger PE, Kapella MC, Fritschi C. The relationship between sleep disturbance and glycaemic control in adults with type 2 diabetes: An integrative review. *J Clin Nurs* 2017; **26**: 4053–4064.

24 Perez KM, Hamburger ER, Lyttle M, Williams R, Bergner E, Kahanda S *et al*. Sleep in Type 1 Diabetes: Implications for Glycemic Control and Diabetes Management. *Curr Diab Rep* 2018; **18**: 5.

25 Frye SS, Perfect MM, Silva GE. Diabetes management mediates the association between sleep duration and glycemic control in youth with type 1 diabetes mellitus. *Sleep Med* 2019; **60**: 132–138.

26 Jaser SS, Ellis D. Sleep in Adolescents and Young Adults with Type 1 Diabetes: Associations with Diabetes Management and Glycemic Control. *Health Psychol Behav Med* 2016; **4**: 49–55.

27 McDonough RJ, Clements MA, DeLurgio SA, Patton SR. Sleep duration and its impact on adherence in adolescents with type 1 diabetes mellitus. *Pediatr Diabetes* 2017; **18**: 262–270.

28 Riegel B, Weaver TE. Poor sleep and impaired self-care: towards a comprehensive model linking sleep, cognition, and heart failure outcomes. *Eur J Cardiovasc Nurs* 2009; **8**: 337–344.

29 Turner SL, Queen TL, Butner J, Wiebe D, Berg CA. Variations in Daily Sleep Quality and Type 1 Diabetes Management in Late Adolescents. *J Pediatr Psychol* 2016; **41**: 661–669.

30 Barnard K, James J, Kerr D, Adolfsson P, Runion A, Serbedzija G. Impact of Chronic Sleep Disturbance for People Living With T1 Diabetes. *J Diabetes Sci Technol* 2016; **10**: 762–767.

31 Bergner EM, Williams R, Hamburger ER, Lyttle M, Davis AC, Malow B *et al*. Sleep in Teens With Type 1 Diabetes: Perspectives From Adolescents and Their Caregivers. *Diabetes Educ* 2018; **44**: 541–548.

32 Chasens ER, Korytkowski M, Sereika SM, Burke LE. Effect of poor sleep quality and excessive daytime sleepiness on factors associated with diabetes self-management. *Diabetes Educ* 2013; **39**: 74–82.

33 Luyster FS, Dunbar-Jacob J. Sleep quality and quality of life in adults with type 2 diabetes. *Diabetes Educ* 2011; **37**: 347–355.

34 Martyn-Nemeth P, Phillips SA, Mihailescu D, Farabi SS, Park C, Lipton R *et al*. Poor sleep quality is associated with nocturnal glycaemic variability and fear of hypoglycaemia in adults with type 1 diabetes. *J Adv Nurs* 2018; **74**: 2373–2380.

35 Tracy EL, Berg CA, Baucom KJW, Turner SL, Kelly CS, Van Vleet M *et al*. Daily sleep quality and daily stressors in couples coping with type 1 diabetes. *Health Psychol* 2019; **38**: 75–83.

36 Caruso NC, Radovanovic B, Kennedy JD, Couper J, Kohler M, Kavanagh PS *et al*. Sleep, executive functioning and behaviour in children and adolescents with type 1 diabetes. *Sleep Med* 2014; **15**: 1490–1499.

37 Fulcher G, Singer J, Castaneda R, Fraige Filho F, Maffei L, Snyman J *et al*. The psychosocial and financial impact of non-severe hypoglycemic events on people with diabetes: two international surveys. *J Med Econ* 2014; **17**: 751–761.

38 Pillar G, Schuscheim G, Weiss R, Malhotra A, McCowen KC, Shlitner A *et al*. Interactions between hypoglycemia and sleep architecture in children with type 1 diabetes mellitus. *J Pediatr* 2003; **142**: 163–168.

39 Farabi SS, Quinn L, Phillips S, Mihailescu D, Park C, Ali M *et al*. Endothelial Dysfunction is Related to Glycemic Variability and Quality and Duration of Sleep in Adults With Type 1 Diabetes. *J Cardiovasc Nurs* 2018; **33**: E21–E25.

40 Zhu B, Vincent C, Kapella MC, Quinn L, Collins EG, Ruggiero L *et al*. Sleep disturbance in people with diabetes: A concept analysis. *J Clin Nurs* 2018; **27**: e50–e60.

41 Amaral FG, Turati AO, Barone M, Scialfa JH, do Carmo Buonfiglio D, Peres R *et al*. Melatonin synthesis impairment as a new deleterious outcome of diabetes-derived hyperglycemia. *J Pineal Res* 2014; **57**: 67–79.

42 Hazen R, Fehr K, Fidler A, Cousino M, MacLeish S, Gubitosi-Klug R. Sleep disruption in adolescents with Type 1 diabetes mellitus: Relationships with adherence and diabetes control. *Diabetes Manage* 2015; **5**: 257–265.

43 Buckingham B, Block J, Burdick J, Kalajian A, Kollman C, Choy M *et al*. Response to nocturnal alarms using a real-time glucose sensor. *Diabetes Technol Ther* 2005; **7**: 440–447.

44 Jaser SS, Foster NC, Nelson BA, Kittelsrud JM, DiMeglio LA, Quinn M *et al*. Sleep in children with type 1 diabetes and their parents in the T1D Exchange. *Sleep Med* 2017; **39**: 108–115.

45 Barnard KD, Wysocki T, Ully V, Mader JK, Pieber TR, Thabit H *et al*. Closing the Loop in Adults, Children and Adolescents With Suboptimally Controlled Type 1 Diabetes Under Free Living Conditions: A Psychosocial Substudy. *J Diabetes Sci Technol* 2017; **11**: 1080–1088.

46 Lewis D, Leibrand S, Open APSC. Real-World Use of Open Source Artificial Pancreas Systems. *J Diabetes Sci Technol* 2016; **10**: 1411.

47 Feeley CA, Sereika SM, Chasens ER, Siminerio L, Charron-Prochownik D, Muzumdar RH *et al*. Sleep in Parental Caregivers and Children With Type 1 Diabetes. *J Sch Nurs* 2019: 1059840519865942.

48 Barnard K, Crabtree V, Adolfsson P, Davies M, Kerr D, Kraus A *et al*. Impact of Type 1 Diabetes Technology on Family Members/Significant Others of People With Diabetes. *J Diabetes Sci Technol* 2016; **10**: 824–830.

49 Tan X, van Egmond L, Chapman CD, Cedernaes J, Benedict C. Aiding sleep in type 2 diabetes: therapeutic considerations. *Lancet Diabetes Endocrinol* 2018; **6**: 60–68.

50 Li M, Li D, Tang Y, Meng L, Mao C, Sun L *et al*. Effect of Diabetes Sleep Education for T2DM Who Sleep After Midnight: A Pilot Study from China. *Metab Syndr Relat Disord* 2018; **16**: 13–19.

51 Perfect MM, Beebe D, Levine-Donnerstein D, Frye SS, Bluez GP, Quan SF. The Development of a Clinically Relevant Sleep Modification Protocol for Youth with Type 1 Diabetes. *Clin Pract Pediatr Psychol* 2016; **4**: 227–240.

52 Tumakaka GYS, Agustini N, Nurhaeni N, Rustina Y. The Effect of Sleep Hygiene Education on Sleep Quality in Children with Type 1 Diabetes Mellitus: A Preliminary Study. *Compr Child Adolesc Nurs* 2019; **42**: 189–196.