Sleep Optimization to Improve Glycemic Control in Adults with Type 1 Diabetes

Study Protocol

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Abstract

Despite improvements in treatment regimens and technology, less than 20% of adults with type 1 diabetes (T1D) achieve glycemic targets. Sleep is increasingly recognized as a potentially modifiable target for improving glycemic control. Diabetes distress, poor self-management behaviors, and reduced quality of life (QoL) have also been linked to sleep variability and insufficient sleep duration. The American Diabetes Association Standards of Medical Care in Diabetes incorporated sleep as an important component of the medical evaluation in persons with diabetes. However, no specific recommendation was given as to how to improve sleep. A significant gap of knowledge exists regarding the effects of sleep optimization on glycemic control in T1D. The purpose of this study is to determine the efficacy of a T1D-specific sleep optimization intervention (Sleep-Opt) on the primary outcomes of sleep variability, sleep duration and glycemic control (A1C); other glycemic parameters (glycemic variability, time in range), diabetes distress, self-management behavior, QoL, and other patient reported outcomes in working-age adults with T1D and habitual increased sleep variability or short sleep duration. To achieve these aims, we propose a randomized controlled trial in 120 working age adults (18 to 65 years) with T1D. Participants will be screened for habitual sleep variability (> 1 hour/week) or insufficient sleep duration (< 6.5 hours per night). Eligible subjects will be randomized to the Sleep-Opt group or healthy living attention control group for twelve weeks. A one-week run-in period is planned, with baseline measures of sleep by actigraphy (sleep variability and duration), glycemia (A1C and related glycemic measures: glycemic variability and time in range using continuous glucose monitoring), and other secondary outcomes: diabetes distress, self-management behaviors, quality of life and additional patient-reported outcomes. Sleep-Opt is a technology-assisted behavioral sleep intervention that we recently developed that leverages the rapidly increasing public interest in sleep tracking by consumers (+500% in 3 years). Our behavioral intervention employs four elements: a wearable sleep tracker, didactic content, an interactive smartphone application, and brief telephone counseling. The attention control group will participate in a healthy living information program. At midpoint (Week 6) completion (Week 12) and post-program (Week 24), baseline measures will be repeated to determine differences between the two groups and sustainability of the intervention.

Specific Aims

Despite improvements in treatment regimens and technology, less than 20% of adults with type 1 diabetes (T1D) achieve glycemic targets.[1] Sleep is increasingly recognized as a potentially modifiable target for improving glycemic control. Specifically, sleep variability (variability in sleep duration)[2] and insufficient sleep duration (insufficient total sleep time) may adversely affect glycemic control[3] via circadian misalignment,[4] diabetes distress, poor self-management behaviors, and reduced quality of life (QoL).[5-9] The American Diabetes Association has added sleep as an important component of medical evaluation in persons with diabetes.[10] However, research is limited as to how to optimize sleep among patients with T1D and whether such interventions improve important outcomes including glycemic control, diabetes distress and quality of life. The proposed study will determine the efficacy of a **T1D-specific sleep optimization intervention** (**Sleep-Opt)** targeted to reduce sleep variability, insufficient sleep duration and improve glycemic control (A1C; primary outcomes); other glucose parameters (glucose variability, time-in-range [TIR]), diabetes distress, self-management behavior, quality of life and other patient-reported outcomes in working-age adults with T1D and habitual increased sleep variability or insufficient sleep duration.

Our preliminary data demonstrated: **(1)** Sleep variability in T1D was associated with poor glycemic control, increased glycemic variability, and greater distress in cross-sectional studies of 71 working-age adults.[2,11] **(2)** A pilot study of a 2-week behavioral sleep optimization in adults without diabetes with habitual short sleep duration led to improved fasting insulin resistance; sleep gain significantly correlated with reduction in insulin resistance.[12] **(3)** Our team's pilot study of **Sleep-Opt** in T1D working-age adults demonstrated reduced sleep variability, A1C, glycemic variability, and improvement in self-reported fatigue, mood, sleep and distress.

The goal of this study is to examine whether the Sleep-Opt intervention, a novel intervention to reduce sleep variability and insufficient sleep duration, improves objective sleep and glucose parameters, diabetes distress, self-management behavior, QoL, and other patient-reported outcomes. Responding to *PA-18-330, Investigator Initiated Clinical Trials Targeting Diseases with the Mission of NIDDK, w*e will randomize 120 individuals with T1D and habitual increased sleep variability or insufficient sleep duration to a 12-week **Sleep-Opt** intervention or healthy living control group equal in time and attention. Our novel sleep optimization is based on behavior change principles (self-monitoring, goal setting, motivational enhancement) and employs a wearable sleep tracker, didactic content, and brief telephone counseling tailored to T1D.[13]

Specific aims: In 120 working-age adults (18-65 years) with T1D:

Aim 1: Determine the effect of the **Sleep-Opt** intervention, compared to an attention control group, on sleep variability, sleep duration and glycemic control (primary outcomes). Rationale: Sleep variability and insufficient sleep duration in T1D adults was associated with higher A1C, possibly related to circadian misalignment and reduced insulin sensitivity. Hypothesis: **Sleep-Opt** will result in improved sleep and glycemic control. Approach Assess sleep variability, sleep duration, and glycemic control as measured by actigraphy and A1C at Week 0 (baseline), Week 6 (mid-treatment), Week 12 (end of treatment) and post treatment Week 24, of **Sleep-Opt** compared to a 12-week healthy living attention control. Secondary outcomes include glycemic variability, time in range and other objectively measured sleep parameters.

Aim 2: Determine if **Sleep-Opt** will result in improved psychological and behavioral outcomes, including diabetes distress, diabetes self-management behavior, QoL, fatigue, mood, subjective sleep quality compared to the healthy living attention control group. Rationale: Sleep variability and insufficient sleep duration was associated with diabetes distress, poor self-management behavior and reduced QoL. Hypothesis: **Sleep-Opt** will lower diabetes distress, improve self-management behavior and QoL. Approach Assess diabetes distress, self-management behavior, QoL and other patient-reported outcomes (fatigue, mood, sleep quality) at Week 0 (baseline), Week 6 (mid-treatment), Week 12 (end of treatment), post treatment at Week 24 in **Sleep-Opt** compared to a 12-week healthy living attention control. .

Aim 3: Determine the contribution of changes in sleep variability and sleep duration during the intervention to changes in glycemic parameters (A1C, glycemic variability, time in range) Rationale: Sleep variability was associated with poor glycemic control and greater glycemic variability in T1D adults. Short sleep was associated with reduced insulin sensitivity in T1D. Hypothesis: Reduction in variability and improved sleep duration will correlate with improvement in glycemic parameters. Approach Analyze the relationship between changes in sleep variability, sleep duration, and glycemic parameters (outlined in Aim 1) after a 12-week **Sleep-Opt** and 12-week healthy living attention control at Week 0 (baseline), week 6 (mid-treatment), Week 12 (end of treatment) and week 24 (post-treatment).

Our long-term goal is to advance the understanding of the potential for sleep optimization as an important component of diabetes care to improve glycemic control and QOL. This goal aligns with and enables the NIDDK strategic plan to support research on the prevention, treatment, and cure of T1D and its complications.

Research Strategy

A. Significance

A.1 Importance of sleep to health

Sleep variability and insufficient sleep duration have negative health consequences in the general population. These include: changes in appetite and eating patterns,[14-16] obesity,[17] insulin resistance,[18], increased systemic inflammation,[19], metabolic syndrome, [20] dysglycemia,[21] risk for incident diabetes,[16] depression,[22] and a higher prevalence of cardiovascular disease (CVD).[23] Sleep times of less than 300 minutes have been associated with up to four times the mortality risk of those with greater than 300 minutes.[24,25] Each hour of increased sleep variability, as measured by standard deviation (SD) of sleep duration, was associated with a 27% higher odds of metabolic syndrome in a multi-ethnic population. [20] Work commitments, family and social obligations, and general stress have also been linked with poor sleep.[26,27] Negative health consequences of insufficient and irregular sleep may be amplified for persons with T1D, who must also cope with the added burden of managing a chronic condition.[28]

A.2 Insufficient and irregular sleep affects glycemic control in T1D

Up to 40% of adults with T1D had insufficient sleep (sleep duration < 6-6.5 h/night) either by self-report or objectively assessed.[2,29-36] Insufficient sleep is a predictor of poor glycemic control in T1D.[29,37] Increased insulin resistance likely plays a central role; one night of experimental sleep restriction (4 hours) in 7 patients with T1D was associated with decreased peripheral insulin sensitivity, compared to normal sleep duration (7.8 hours).[38] In our recent meta-analysis, adults with T1D who reported sleeping > 6 hours had 0.24% lower A1C levels than those sleeping ≤ 6 hours.[3]

In addition to insufficient sleep, sleep variability, a potential marker of circadian misalignment, can impact glycemic control. Up to 73% of adults with T1D have sleep variability (> 1 hour).[2,11] The circadian system plays an important role in glucose metabolism, and experimental circadian misalignment results in impaired glucose tolerance.[4,39] Thus, sleep variability could be detrimental to glycemic control. Supporting this hypothesis, recent studies have reported that sleep variability is an independent predictor of glycemic control in T1D. .[2,40,41] Sleep variability, SD of sleep duration as objectively measured by actigraphy, explained 8.2% to 15.8% of the variance in glycemic control.[2,40] In our study of 41 working-age adults with T1D, those with SD of sleep duration >1 hour had significantly higher A1C than those with SD sleep duration ≤1 hour (median 7.2% vs. 7.8%, $p = 0.008$). Sleep variability was also associated with increased daily insulin requirement, suggesting more insulin resistance in these individuals.[2] These findings were reproducible: another study in 65 adolescents with T1D also found that greater SD of sleep duration was significantly associated with higher A1C,[42] and in a study of 191 German T1D adolescents, greater variability of sleep timing between work and free days was associated with higher insulin requirements.[43] T1D patients lack endogenous insulin secretion; varying degrees of insulin resistance could lead to increased glycemic variability (within-day glucose fluctuations), a factor reported to be associated with increased microvascular complications and cardiovascular events in T1D.[44,45] Indeed, our pilot data in 30 T1D adults revealed that greater SD of sleep duration was associated with greater glycemic variability as measured by continuous glucose monitoring.[11]

These data strongly suggest that sleep variability and insufficient sleep duration affects glycemic control and glycemic variability, with the effect size similar to some standard treatments for T1D.[46,47] **Despite recognition from the American Diabetes Association that sleep patterns should be assessed in individuals with diabetes,[10] no published studies to date have explored the effects of sleep optimization (strategies to improve sleep duration and variability) on glycemic control in adults with T1D.** These data are needed and could have a large clinical impact, given the current state of suboptimal glycemic control and increasing incidence of T1D.

A.3 Sleep is related to diabetes distress, self-management behavior, and quality of life in T1D

Sleep is increasingly recognized as an important contributor to diabetes distress.[8,28] Diabetes distress pertains to the emotional burdens and worries associated with the complexities of managing diabetes.[48] Moderate to high distress levels are experienced by up to 54% of those with T1D.[48] Concern over blood glucose levels (particularly fear of hypoglycemia) is a major source of distress at night that impacts sleep.[49] Individuals with T1D report delaying sleep, waking during the night to monitor blood glucose levels, or maintaining blood glucose levels higher to avoid hypoglycemia. These self-management behaviors result in reports of less restful sleep and diminished well-being the subsequent day.[6] In a study of 267 adults with T1D, diabetes distress was found to be significantly higher in those adults who reported poor sleep quality. Those with poor sleep quality also experienced greater daytime sleepiness and diabetes regimen burdens.[28] Our

team conducted focus groups with T1D adults to examine contemporary challenges of diabetes self-management. Qualitative reports indicated that sleep was a major source of distress.[6]

Diabetes distress is associated with higher A1C, greater glycemic variability in T1D,[7,8,50] and poorer self-management behaviors (such as dietary/medication compliance,[51,52] prevention and management of hypoglycemia,[53] and physical inactivity).[54,55] Thus, diabetes distress can be a barrier to improving glycemic control and self-management behavior.[56] Interventions using diabetes-self management education alone or in combination with psychological components produced reported reductions in diabetes distress and improved glycemic control in some[8,57-60] but not all studies.[8,61] Despite these relationships, no studies to date explored the effects of sleep interventions specifically designed to address T1D distress and its effects on glycemic control.

Poor sleep has also been linked directly to self-management behavior. In a cross-sectional study of 45 adolescents, a significant relationship was found between sleep duration and self-management behavior.[62] Specifically, a 15- and 20-min increase in sleep was associated with one additional blood glucose check and one additional insulin bolus, respectively.[62] In addition, sleep variability (SD of sleep duration) was found to be a significant predictor of self-management behavior, explaining 6.1% of the variance in the frequency of blood glucose monitoring.[40] Thus improving sleep variability and duration could potentially improve self-management behavior.

Self-reported sleepiness and/or poor sleep habits have been correlated with reduced QoL, depressed mood, and reduced academic performance.[63] In addition, time spent in stage N2 (lighter sleep) as assessed by polysomnography has been significantly correlated with lower QoL.[63] Thus, improving sleep could potentially improve self-care behavior and QoL, but this has yet to be explored.

A.4 Why a sleep optimization intervention could improve glucose control in highly variable or short sleepers

The goal of this study is to improve glycemic control (A1C) by reducing sleep variability and improving insufficient sleep duration in T1D using a randomized controlled design. The secondary outcomes of glycemic variability, time in range (TIR), diabetes distress, diabetes self-management behavior, QoL and other patient-reported outcomes (e.g. fatigue, sleep quality, mood) will also be examined. We conceptualize that sleep duration variability > 1 hour across one week or insufficient sleep < 6.5 hours directly influence glycemic control, increase diabetes distress, and influence self-management behavior. Improving these sleep parameters will improve glycemic control, reduce glycemic variability and improve TIR, reduce diabetes distress, enhance self-care behavior, and improve QoL (**Figure 1**).

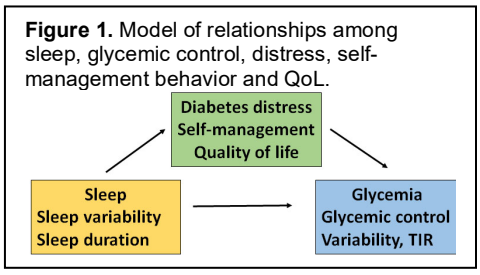

Figure 1. Model of relationships among sleep, glycemic control, distress, self-management behavior and QoL.

Despite data to support a causal relationship between sleep variability and insufficient sleep with abnormal glucose metabolism, very few studies have explored sleep interventions to improve metabolic outcomes. One published study examined the effects of home sleep extension on glucose metabolism in healthy volunteers (n = 16) who were chronic short sleepers.[64] After six weeks of sleep extension (average increase of 44 minutes/day), there was a robust relationship between the increase in sleep duration and improvement in fasting insulin sensitivity. In our randomized cross-over sleep extension study of 21 short-sleeping non-diabetic working-age adults, those who extended their sleep to > 6 h/night for 2 weeks had significant improvement in fasting insulin resistance, early insulin response to glucose, and β-cell function.[12] Another RCT of 42 normal-weight, healthy, short sleepers showed a 21-minute increase in sleep duration for the intervention group. This was associated with decreased intake of fat, carbohydrates, and free sugars.[65]

Perfect et al. conducted a short-term pilot RCT using sleep extension in 79 adolescents with T1D for one week.[66] The sleep extension intervention included didactic information on topics such as the importance of sleep, sleep hygiene principles, control of environmental conditions, management of competing activities and stress reduction, as well as use of a sleep log and actigraphy monitoring.[66] The preliminary results revealed that glucose levels as measured by continuous glucose monitoring in extension participants differed from the fixed-sleep-duration group by 17 mg/dl points (p = .003) during the sleep modification week. Sleep extension resulted in 11 hours more spent in the glucose target range than those in the fixed-sleep condition.[67] This emerging evidence supports the feasibility and efficacy of sleep optimization, as well as a possible dose-response relationship between optimized sleep and changes in metabolic control. Because sleep is linked to

possible mediators of glycemic control (including diabetes distress, diabetes self-management behavior, and QoL), those mediators' influence on glycemic control during sleep optimization need to be examined also.

A.5 Wearable sleep trackers provide a critical opportunity to engage short sleepers

Over the past few years, the public's interest in monitoring sleep has increased immensely, providing an important opportunity to affect sleep in public health. Marketing research reported a 500% annual growth in the wearable fitness tracker market for the past three years.[68] In 2016, over 12% of U.S. adults owned a fitness monitor,[69] and sleep was rated as the most popular feature to track.[69] Our intervention uses data from a wearable sleep tracker (Fitbit) to personalize feedback and promote interaction with remote coaches. Given that individuals often need to forgo other potentially more rewarding activities to extend sleep, sleep-tracking devices provide a way to make sleep extension insightful and rewarding. Companies including Fitbit and Apple have released features such as bedtime reminders and sleep goals. This suggests that consumers are interested in improving sleep, but the impact on sleep and health is unknown.

A.6 Why enhancing adherence to technology-assisted behavioral interventions is key to improvements

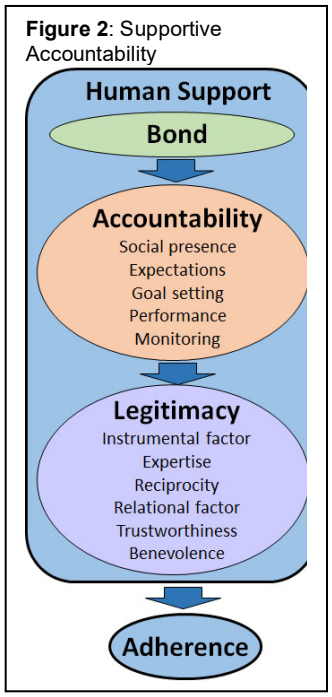

Figure 2: Supportive Accountability

Many technology interventions suffer from high rates of non-adherence.[70] Coached interventions typically show larger effect sizes than unguided interventions, likely due to improved adherence.[71] The process by which human support enhances adherence to behavioral intervention technologies has been termed "Supportive Accountability" (**Figure 2**)[72] and draws on broad empirical literature, including clinical and organizational psychology[73,74] and motivation theory.[75,76] This model suggests that behavioral intervention technology users are more likely to adhere if they are accountable to another person. Accountability is defined as knowing that one will have to justify use or non-use to another individual at some future time.[73] The effects of accountability are enhanced when goal setting and progress are known to another person, goals are process- rather than outcome-focused, and expectations are defined in advance. The model involves qualities of the coach, including legitimacy (the person the user is accountable to has some expertise[74] and is viewed as trustworthy and benevolent). We designed and tested a coaching protocol around these principles[77] that demonstrated the capacity to enhance adherence in a sleep extension intervention (see C.2.7).

A.7 The proposed work will test the efficacy of a 12-week T1D-specific sleep optimization intervention "Sleep-Opt" on the primary outcomes of sleep variability, sleep duration and glycemic control (A1C); and secondary outcomes: other glycemic parameters (glycemic variability, TIR), diabetes distress, self-management behavior, QoL (and other patient reported outcomes) in working-age adults with T1D and habitual short sleep duration or increased sleep duration variability under a randomized controlled design. Working-age adults (18-65 years) often encounter social and family obligations that affect their sleep duration, especially on weekdays, and were shown to have less sleep regularity than older individuals.[78] To determine sustainability of the intervention, follow-up will be performed at the 24th week. **This innovative study will provide insights into the causal relationship of sleep with glycemic control and diabetes distress, self-management behavior, and QoL in individuals with T1D. Our unique technology-based Sleep-Opt is scalable and easily deployed; thus, it could have a wide clinical implication for persons with T1D.**

B. Innovation

Our proposed study will be innovative in that it will study Sleep-Opt on working-age adults with T1D. Innovative features include: (1) Optimizing sleep in T1D. Only one sleep intervention study has been conducted in the T1D population in adolescents. No interventions have focused on working-age adults. **(2) Measuring the effects on glycemic control.** Sleep variability and insufficient sleep contribute to poor glycemic control and glycemic variability. A sleep optimization program to improve glycemic outcomes represents a novel approach to addressing the role of sleep in glycemic control and glycemic variability. Self-management education focuses primarily on modification of diet, activity, and insulin therapy to promote glycemic control. Using sleep hygiene to improve glycemic control adds an important self-management strategy. **(3) Measuring the effects on diabetes distress, diabetes-self management, and QoL.** Poor sleep is related to diabetes distress, poor diabetes self-management, and reduced QoL, which potentially contribute

to poor glycemic control. Sleep optimization offers a unique and practical treatment to improve these outcomes and glycemic control. No such approach currently exists. **(4) Measuring intervention sustainability, as determined by a follow-up period.** No data exist regarding sleep optimization durability in the T1D population. Understanding the long-lasting effects will lead to designing a reinforced intervention with proper timing and optimize the effects of Sleep-Opt.

Sleep-Opt is unique, practical, and scalable. The proposed intervention is based on a theoretical model focused on motivating long-term behavior change. It uses technologies desirable to patients and already part of their daily lives. Using this combination of technology and well-validated behavior change strategies, we can engage patients to learn their behavioral patterns and make lasting changes in their sleep habits. The use of technology and automated support could result in a highly scalable and cost-effective intervention.

C. Approach

C.1 Preliminary Studies

C.1.1 Sleep variability and Insufficient sleep duration are associated with poorer glycemic control in adults with T1D. Dr. Reutrakul, co-I of this study, published a meta-analysis exploring the role of sleep in T1D. In a pooled analysis of 533 adults, those reporting sleeping < 6h had a higher A1C level by 0.24% than those sleeping ≥ 6 h.[3] Dr. Reutrakul's subsequent study explored the role of sleep variability using 5-day actigraphy in 41 adults with T1D.[2] Those with higher sleep variability (standard deviation [SD] of sleep duration > 60 minutes) had significantly higher A1C levels than those with lower sleep variability (median 7.8% vs. 7.2%; **Figure 3).** In addition, higher sleep variability significantly correlated with higher daily insulin requirement (r = 0.386, p = 0.01), suggesting higher insulin resistance in those with greater degree of irregular sleep. Dr. Martyn-Nemeth, PI, studied 30 adults with T1D and found that variability of sleep duration as measured by actigraphy was significantly related to glycemic variability (glucose SD) measured by continuous glucose monitoring (CGM; r = 0.458, p = 0.01).

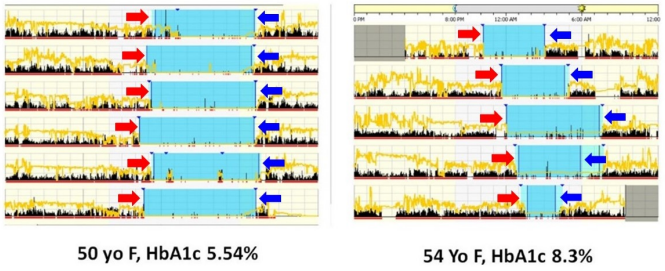

Figure 3: Actigraphy recordings of two T1D patients with different sleep patterns and their A1C. Left: patient with consistent sleep duration and timing. Right: patient with varying sleep duration and timing.

C.1.2 Sleep optimization in short-sleeping non-diabetic adults resulted in improved glucose metabolism. Dr. Reutrakul performed a randomized cross-over study using two-week behavioral sleep optimization aimed at extending sleep duration and promoting sleep hygiene, including sleep regularity, in 21 non-diabetic adults with habitual short sleep (mean 5.3 h/night by actigraphy). Participants who extended their sleep duration to > 6 h/night (N = 8, mean 6.6 h/night) had significantly improved fasting insulin resistance (HOMA-IR; adjusted mean difference [MD] -0.50, p = 0.013), increased early insulin response to glucose (insulinogenic index; MD 0.39, p = 0.001), and improved β-cell function (disposition index; MD 1.07, p = 0.02).[12] This suggested that sleep extension is feasible and has favorable effects on glucose metabolism in short-sleeping adults.

C.1.3 Our newly developed sleep optimization intervention developed for adults with short sleep duration (Sleep Bunny) demonstrated a clinically significant mean sleep increase of 38 minutes.[79]

Table 1. Pilot Sleep Extension trial, 6 weeks

	Intervention N = 10	Control N = 5
Mean Sleep Change	+0:38:36	+0:08:48
Time in Bed	+0:29	+0:08
Sleep Efficacy %	+3.2%	-0.5%
PROMIS - Sleep Disturbance	-7	+4
PROMIS – Sleep-Related Impairment	-1	+8

The intervention included use of a Fitbit, weekly didactic content, interactive tools (e.g., reminders), and coach-delivered feedback.[13] An RCT was conducted with 15 adult participants who were followed for six weeks with a protocol similar to what is proposed. All participants completed 2 periods of actigraphy. Those in the intervention group wore the Fitbit for 85-100% of study days and completed 90% of coaching sessions. Results from the intervention (n = 10) and control (n = 5) groups showed that the intervention was effective at improving sleep duration by a mean of 38 min (**Table 1**), with improvement in sleep efficacy, sleep-related impairment, and sleep disturbance.

C.1.4. T1D Sleep-Opt intervention pilot tested in 8 working adults with T1D, revealed those with high sleep variability responded with improved sleep and glucose parameters.
Using a RCT design, we pilot tested the T1D **Sleep-Opt** intervention and compared it to a healthy living attention control group in 8 adults with objectively measured sleep duration (< 6.5 hours per night) or sleep variability (sleep duration SD > 1 hour per week). The intervention was adapted from the Sleep Bunny sleep extension intervention developed by members of our team.[13] The content was tailored to address both sleep duration and sleep variability as well as content specific to T1D identified from our focus groups.[80] The intervention included use of a Fitbit, weekly didactic content, interactive tools (e.g., reminders), and coach-delivered feedback.[13]. Participants completed 3 periods of actigraphy, continuous glucose monitoring (Abbott Libre®) self-reported questionnaires and a blood draw for A1C at baseline (week 0) at completion of the intervention (week 8) and post-program (week 12). A1C was reduced by 0.16% in the Sleep Opt group compared to 0.3% in the control group. The **Sleep-Opt** group had nearly optimal A1C levels at baseline (5.4-7.3) and could not have safely reduced their glucose levels further. In comparison, the healthy living group began with higher A1C levels (ranging 6.7-9.0). Glycemic variability (CV%) was reduced by 3% in the **Sleep-Opt** group vs. a 4% increase in the control group. Sleep variability improved in both groups. Patient-reported variables demonstrated a greater improvement in the sleep vs. the control group. Fatigue, sleep quality, mood and distress improved in the sleep opt compared to the control group from baseline to post-program. (**Table 2**). There appeared to be a reactive effect in the control group as their objective sleep improved (however subjective sleep and other patient-reported outcomes did not). We plan to address this in the future by providing a questionnaire at the end of the control intervention to evaluate the presence of any sleep behavior changes. We also plan to provide the control group the opportunity to participate in the **Sleep-Opt** intervention at the end of the study. In terms of feasibility, all 8 subjects completed the pilot study and evaluated the program positively. The technology employed was easy to use and the sleep content and coaching calls beneficial. All participants completed 100% of coaching sessions. This pilot study provides proof-of-concept that the **Sleep-Opt** intervention demonstrated improvement in glycemic, sleep and important patient-reported variables.

Table 2. Pilot T1D Sleep Opt, N=8

Mean Change	Intervention N=5	Control N=3
A1C (%)	-0.16	-0.3
Glycemic variability (CV%)	-3.01	+ 4.07
Time in range (%)	+ 8.04	+ 4.33
Sleep duration (min)	+9	+22
Sleep variability (min)	-21	-18
Fatigue (PROMIS)	-4	+7.5
Sleep quality (PSQI)*	-1.4	+5
Mood (CES-D)	-6.7	+5

*lower numbers = improved sleep quality

C.1.5 Our research team consists of investigators from multiple disciplines with expertise that will facilitate successful completion of the project. This application brings together an interdisciplinary team with shared (endocrinology, sleep, CGM technology and glycemic variability measures, chronic illness, and clinical practice) and complementary (behavioral coaching, technology-assisted behavior change, statistical modeling, and Certified Diabetes Educator [CDE®]) expertise. Collectively, the team's research strengths span conceptual, methodological, clinical, and statistical research in self-management and chronic disease. The team has a strong history of collaboration.

C.2 Research plan

C.2.1 Proposed study overview. Figure 4 and Table 3 illustrate the proposed study. We will enroll up to 300 non-shift-working adults aged 18-65 years with a clinical diagnosis of T1D for at least one year who report habitual sleep variability (> 1 hour variation in sleep onset or wake up time/week) or insufficient sleep duration < 6.5 h/night during work- or weekdays. After informed consent is obtained, participants will have a baseline assessment during a 1-week run-in phase. Subjective sleep and objective sleep assessment by wrist actigraphy will be performed to confirm eligibility. Eligible participants will then be randomized to either a Sleep-Opt or healthy living attention control group for 12 weeks. At baseline, diabetes distress, diabetes self-management behavior, quality of life, self-reported fatigue, sleep quality, mood, anxiety, fear of hypoglycemia, daytime sleepiness, and anxiety will be assessed. Glycemic assessments will be performed by A1C, and 1-week continuous glucose monitoring (CGM). At 6 weeks (mid-program) and 12 weeks (end of intervention period), these assessments will be repeated to evaluate the effects of the intervention. At the 24-week follow-up visit, the same assessments will evaluate the program's sustainability.

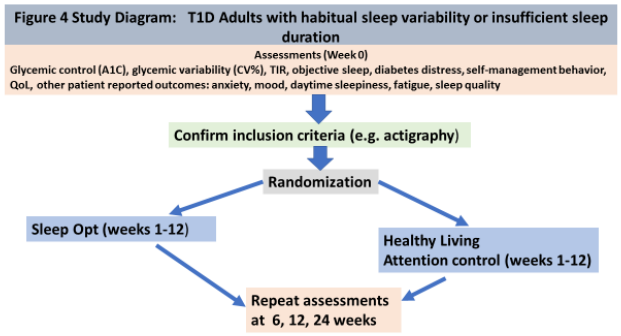

Table 3. Study Overview		Actigraphy	A1C	CGM	Questionnaires
	Baseline week 0	X	X	X	X
Mid-intervention	Week 6	X	X	X	X
Intervention completion	Week 12	X	X	X	X
Follow-Up	Week 24	X	X	X	X

C.2.2 Setting: The study will take place at subjects' home. We will mail study materials and schedule videoconferences for orientation to the study procedures and instruct subjects how to use the study devices.

C.2.3 Participants. We plan to enroll up to 300 subjects. We anticipate a 40% screen failure rate and expect to randomize up to 170 for a final sample of 120 subjects with complete data. Inclusion criteria: working-age adults, 18-65 years with a clinical diagnosis of T1D for at least one year who reported habitual sleep variability (1 hour/week or more) or sleep duration < 6.5 h/night during work- or weekdays (confirmed with actigraphy) with a desire to improve sleep and who own a smartphone compatible with Fitbit. Exclusion criteria: Insomnia symptoms defined as severe as assessed by the Insomnia Severity Index[81] (score ≥ 15), being at high risk for obstructive sleep apnea as assessed by and Stop Questionnaire,[82] history of severe hypoglycemia (defined as hypoglycemic episodes that result in loss of consciousness within the last 6 months, seizures, or requiring emergency room visits or hospitalization), A1C > 10%, rotating shift or night shift work, use of sleep medications/aids, significant renal impairment (estimated glomerular filtration rate < 45 ml/min/1.73 m^2), significant medical morbidities (such as congestive heart failure, cirrhosis, chronic obstructive pulmonary disease requiring oxygen, active treatment for cancer, restless leg syndrome, depression (PHQ8 score greater than or equal to 10), history of stroke with neurological deficits), or breast feeding, pregnant, or planning pregnancy.

C.2.4 Recruitment. Subjects will be recruited through the UIC medical center/university, diabetes clinics in the Chicago metropolitan area through diabetes websites and organizations, using flyers, e-announcements, recruitment letters, listservs and Research Match (www.researchmatch.org), participants from previous studies who have provided consent to be contacted for future studies (Protocols 2014-0477, 2018-0382, and 2022-1130), and the Division of Endocrinology at Cook County Health. At UIC, we (study staff) will identify potentially eligible subjects through the electronic medical record (EMR) system and send recruitment letters and emails. The UIC endocrinology clinic serves approximately 4,000 patients with diabetes per year that reflect a racially, ethnically, and socioeconomically diverse urban population. We have used these same recruitment methods in our previous studies with approximately 20% of study participants recruited through the UIC medical center, while 80% have been recruited through the other sources identified above. We have also drafted a Smartphrase for authorized research staff and providers at both clinics to send to potentially eligible patients via the MyChart Patient Portal in Epic Powerchart EMR. In addition, we will recruit via social media websites such as Facebook and Instagram by posting our flyer to relevant peer support groups for people with Type 1 diabetes and via Facebook Ads. We will work with national Type 1 Diabetes organizations such as the T1D Exchange to share our study via their social media accounts and events. Specific ads will be submitted for approval prior to publishing on social media. Our study will be listed on the UIH Research registry (UIHRR) and The New Normal (TNN) websites. People who are interested in contacting our research staff can email our shared mailbox sleepopt@uic.edu or visit our listing on the UIHRR.

C.2.5 Sample size estimation. We conservatively estimated the minimal detectable difference between treatment arms to be 0.4 to 0.6 standard deviations for our target sample size of 60 per group (after attrition) at the 12-week post-treatment measurement based on a 2-groups pre-post design, α = 0.02, 2-sided, and 80% power. This represents a modest but clinically important change. Table 4 shows projected estimates for attention controls, based on our pilot data with this population, and the treatment group, based on the minimum detectable difference we could detect as statistically significant given our design, target sample size, and correlations between time points of 0.5 to 0.8.[83] Standard deviations from pilot data for A1C (1.07%), sleep

variability (30 minutes), and sleep duration (49 minutes), and the correlation between measurements (r = 0.56 to 0.85) were used for sample size determination.

Table 4. Minimum detectable treatment effects

	Control	Treatment
A1C (%)	7.8	7.4
Sleep variability (minutes)	75	57
Sleep duration (minutes)	355	380

Analyses adjusting for the pre-treatment glucose level and other key covariates (e.g., BMI) will increase power. Aim 2 assesses the main effects of secondary outcomes and, similar to the primary aim, will allow us to detect effect sizes of 0.3 to 0.5 or greater as statistically significant. **Adjustment for multiple testing.** Our primary aim uses an adjusted alpha level for multiple primary outcomes. For secondary aims, exploratory, and hypothesis generating analyses we will publish unadjusted p-values and apply the Benjamini-Hochberg approach to control the family-wise error rate.[84] Aim 3 pertains to correlations between change measures of sleep and glucose control parameters, for which we will be able to detect correlations of the magnitude of .25 or greater as statistically significant.[85]

C.2.6 Procedures –

C.2.6.1 Screening (Week 0). Study staff will conduct initial screening of potential subjects for inclusion/exclusion criteria by telephone. This screening will include age, diagnosis, brief health history, usual sleep patterns and use of sleep aids. Prospective participants will then be provided a link to sign electronic consent form and complete screening questionnaires in REDCap. The questionnaires will assess for exclusionary criterion: insomnia (Insomnia Severity Index), sleep apnea (Stop) and depressive mood (Patient Health Questionnaire (PHQ8). Those who score 15 or greater on the Insomnia Index, at high risk for sleep apnea on the Stop or 10 or greater on the PHQ8 will be excluded. Those with a PHQ8 score of 10 or greater (indicative of a depressive mood) will be offered a list of mental health resources (See Mood Score Script, Ver 1, 3-20-20 and Health Resources, Ver 1, 3-20-20). Anyone who is ineligible but expresses problems with sleep will also be sent a list of Sleep Resources if they are interested (See SleepResources Ver1 8-18-21).

Those who meet study criteria by initial screening will be scheduled for a video conference appointment for the start of the 1-week run-in period (Week 0) to obtain baseline measures, confirm eligibility (A1C, urine pregnancy [for females] and actigraphy for sleep), and apply a CGM device and give instructions on their care. Prior to the video conference appointment, study staff will mail study materials (pregnancy test strips, measurement tape, CGM (FreeStyle Libre Pro CGM and Reader, or Dexcom), Actiwatch, paper sleep log, A1C kit, postage-paid package to return supplies,) to subjects' home.

During the first video conference we will meet for approximately one hour to review the study procedures and instruct a subject how to use the study materials (pregnancy test strips, measurement tape, CGM (FreeStyle Libre Pro CGM and Reader or Dexcom), Actiwatch, A1C kit, paper sleep log, postage-paid package to return supplies). If applicable, (1) a subject (women) will test urine for pregnancy; (2) measure their waist circumference using a measurement tape; and (3) provide eGFR and most recent height and weight from health provider. Then subjects will wear (1) a continuous glucose monitor (CGM) and (2) Actiwatch (3) fill out paper sleep log for one week. The CGM is placed under the skin on their arm using sterile technique. Subjects will be provided instructions on how to care for the CGM. They will also be given an Actiwatch to track their sleep for one week. After one week of wearing the CGM and Actiwatch, subject will remove the CGM and Actiwatch and return them in the mail using the postage-paid package. In addition, subjects will use fingerstick blood sampling to obtain measures of A1C. Following the 1-week run-in period and a confirmation of sleep variability ($\geq$ 1 hr) or mean sleep duration (< 6.5 h/night) during work- or weekdays, A1C results, and other inclusion criteria, subjects will be randomly assigned to the Sleep-Opt intervention or Healthy Living attention control group. We will use permuted blocks of 4, arranged in random order and stratified by sex, A1C and age. The use of permuted blocks preserves balance in randomization over the course of the study (i.e., at any point in time, there will be approximately equal numbers of patients randomized to the intervention or attention control group). The randomization model will be developed by the study statistician (Alana Steffen) and executed through the Research Data Capture (REDCap) data management system. Investigators overseeing intervention and control groups and project director are unblinded; for all other investigators and key personnel, randomization allocation will be concealed through blinded coding within REDCap. During the study period, subjects will continue to receive their usual diabetes care with their health care provider and care for their diabetes as they normally would.

C.2.7 Sleep-Opt Intervention. The goal of intervention will be to decrease sleep variability by at least 30 minutes and/or increase sleep time by at least 30 minutes. The intervention will take place over 12 weeks and be conducted remotely by phone call/video conference (Zoom) at participants' preference. Participants who are randomized to Sleep-Opt will receive the following four components: 1) a wearable sleep tracker; 2) a smartphone application with interactive feedback and tools; 3) didactic content via email lessons, reminders, and notifications; and 4) brief telephone coaching. The components are described below.

C.2.7.1 *Wearable sleep tracker:* Participants assigned to the sleep intervention will receive a Fitbit wearable sleep tracker to allow them to track their sleep and share results with the coach. Data support that consumer sleep trackers provide an estimation of sleep but are less precise than validated actigraphy devices.[86,87] Therefore, sleep sufficiency will be measured with actigraphy, which is validated but does not currently provide real-time feedback to the wearer.[88] Fitbit data will be used in coaching sessions and for providing weekly reports. The interventionist will have access to participants' sleep tracker data through a dashboard using the Fitabase platform. We considered whether it was necessary to provide Fitbits and rather simply rely on coaching for behavior change. We determined that the current popularity of wearable sleep trackers would likely help maintain interest in the intervention, as well as provide more easily actionable data for both the participant and the coach. Additionally, if coaching content can be standardized, future directions of this intervention may include automated messaging, which would pair well with wearable sleep trackers.

C.2.7.2 *Smartphone application:* We will use a commercial sleep tracking application to provide participants feedback on their sleep behaviors. Participants will download the Fitbit smartphone application on their smartphone and participate in a brief training in the intervention orientation session. Participants will be trained to review and edit their Fitbit sleep log each day, thus increasing the validity of the data. Although the Fitbit application has developed the ability to enter sleep goals, these features will not be set on participants' applications. In addition, participants will be able to use other features (e.g. step goals) but not trained or instructed on the use of these application features as part of the intervention.

C.2.7.3 *Intervention content* (**Figure 4**)*:* Participants will receive automated content including didactic lessons for 8 of the 12 weeks with gap weeks included for participants to work on behavior change beginning at Week 5 (see schedule Table 5), individualized progress reports (weekly), and bedtime reminder text messages. The intervention content was developed by psychologists with advanced training in sleep and behavior change (Drs. Baron and Duffecy) and has been piloted in initial user testing**.** The 8 didactic lessons (estimated duration 8-10 min) of written and video didactic content will be delivered via email using REDCap and can be viewed on smartphone, desktop, or tablet. Content from the lessons will be reinforced in the telephone coaching sessions. Participants will receive an automatically generated report each week detailing their days of device usage, average bedtime, wake time, sleep duration, and an encouraging statement linked to the weekly didactic content. Participants will also receive a bedtime reminder via text message via their smartphone 30 min before their scheduled bedtime. They can disable the text reminder for Weeks 7-12.

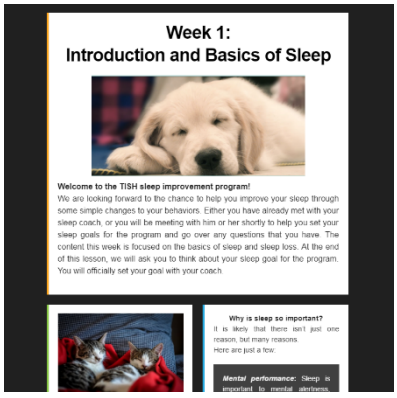

Figure 4. Didactic lessons will be sent weekly to intervention participants via

Table 5. Intervention Didactic Content and Coaching Schedule

Week	Content – Sleep-Opt	Content – Healthy Living	Coaching
1	Intro Basics of Sleep: • Why do we sleep? • How much sleep is recommended? • Consequences of poor sleep with diabetes	Introduction to health living; dental health	20 min engagement session
2	How to Beat Bedtime Procrastination: • What is bedtime procrastination? • Take the bedtime procrastination quiz • How to avoid it	Handwashing	5-10 min call
3	Sleep and Type I Diabetes • Nocturnal hypoglycemia • Nighttime arousals due to diabetes management • Eating/exercise patterns	Preventing infection	5-10 min call
4	Dealing with Weekends and Challenges • The circadian system • What happens on weekends affects your week • What to do when life happens	Body alignment and stretching	5-10 min call
5	Gap week for skill building		

6	Stress and Sleep • What is stress • How does stress affect sleep • How to manage stress	Lung and heart health	5-10 min call
7	Gap week for skill building		
8	The Sleep Environment • Comfort, light and noise • Electronic devices, partners	Health risks of smoking	5-10 min call
9	Gap week for skill building		
10	Effects of Sleep • Benefits of a good night's sleep • What happens if you didn't sleep	Vaccination	5-10 min call
11	Gap week for skill building		
12	Maintaining your Gains • Keeping sight of your goals • Taking note of how you feel • Getting back on track if needed	Cancer screening	Wrap-up session (10 min – week 12)

C.2.7.4 *Coaching:* All participants will be assigned to an interventionist who will be a sleep coach to monitor their progress during the study and provide telephone coaching sessions related to their sleep-related goals. Coaches will be recruited, trained, and supervised by Dr. Duffecy. The coaching protocol developed by Dr. Duffecy is based on the principles of Supportive Accountability.[89] The coaches will establish **legitimacy** by their knowledge of sleep and basic counseling principles. They will establish **goals** with the participants based on the participants' values and beliefs, including the sleep-related goals and usage goals (e.g., number of days wearing the sleep tracker). **Performance monitoring** will be completed through an online dashboard visible to the coaches (Fitabase®). The dashboard will contain data from sleep diaries and the wearable sleep tracker. The first coaching session will be a 20-min engagement session, which includes introductions, rationale for the program, clarifying roles of the coach, and the participants' goals for the program. Coaches (directed by Dr. Duffecy) will provide feedback to the participant based on wearable sleep tracker data. For subsequent coaching sessions, the coach and participant will also have weekly brief (5-10 min) follow-up support calls to troubleshoot any problems with the application or wearable sleep tracker, review progress, problem solve barriers to progress, and set goals. Between sessions, the coaches will be available, mostly via email to troubleshoot any problems with the application or wearable sleep tracker. All coaching sessions, text and email communication will be recorded, and a selection of sessions will be coded for intervention fidelity. The use of coaching has been demonstrated to improve adherence to technology-based interventions.[90,91] Dr. Duffecy has extensive experience in the use of coaching to improve adherence to technology-based interventions.[77,90,92,93]

C.2.8 Healthy Living Attention Control. The research will be conducted remotely by phone call/video conference (Zoom) at participants' preference. The design of the 12-week control group is intended to control for the coach contact in the intervention group, so that we can test the intervention-related components (e.g. motivational enhancement, goal setting, feedback, and sleep education). Dr. Laurie Quinn will train and oversee the coaches for the attention control group. Participants assigned to the health education control group will be provided eight scheduled emails with health education content (e.g. cooking, handwashing, stretching exercises; 8-10 minutes in length) with content written at the 4th grade level or below. Participants will receive eight brief (5- 10 min) telephone contact from the coach (see schedule Table 5) to determine if they received the information and if they had any questions about the materials. The schedule will mirror that of the intervention group. .Coaches will not provide counseling or goal setting but may clarify terms or concepts. Participants in the healthy living control group will be instructed not to change their sleep behavior. They will be eligible to receive the sleep intervention at the end of the study. After the final follow-up session, they will receive a Fitbit wearable fitness tracker.

C.2.9 Measures. Self-report questionnaires will be used to obtain demographic, literacy, health information, menopausal status, food intake, psychological, behavioral and self-management characteristics (**Table 6**).

C.2.9a Primary outcome and additional glycemic measures: Glycemic assessment. 1.) Glycemic control will be assessed using **hemoglobin A1C** (A1C; Home Access Health Corp/Everlywell). A1C is a gold standard marker of glycemic control in T1D reflecting average glucose levels in the previous 90 days. 2) **Glycemic variability using CGM (blinded**) will be conducted using FreeStyle Libre Pro glucose sensor or Dexcom (FDA-approved). The sensor tracks glucose concentrations in the interstitial fluid over 24 h using a thin flexible filament (< 0.4 mm thick) inserted into the upper arm (5 mm depth). The system captures glucose levels every 1 minute and records the data every 15 minutes. Variables we will derive from the CGM are mean glucose level, standard deviation (SD), coefficient of variation (CV), percentage of time spent in range (70-180

mg/dL), percentage of time < 70 mg/dl, and percentage of time spent ≥ 180 mg/dl.[94,95] Interstitial glucose measurements with FreeStyle Libre and Dexcom were found to be accurate compared with capillary blood glucose reference values with a mean absolute relative difference (MARD) of 12% and 9% respectively compared to the gold standard YSI measure of blood glucose.[96] Accuracy of 10% MARD have been approved for self-adjustment of insulin doses in clinical practice.[97] Glycemic measures will be obtained for one week at baseline and Weeks 6, 12, and 24. In our pilot study we experienced a 10% sensor failure rate (less than 15% failure rate reported by the manufacturer and may be due ot the team's expertise in placing these devices). Most sensor failure was due to dislodgement. If dislodgement occurs, we will overnight mail a new sensor to the study participant. The dislodged sensor retains the recorded data. Participants will be instructed to return the sensor. We anticipate a 24-hour disruption in data collection with dislodgement.

C.2.9b Wrist actigraphy to measure behavioral sleep Participants will wear an Actiwatch Spectrum Plus (Respironics, USA) on their non-dominant wrist for one week during baseline assessment, and Weeks 6,12 and 24. Data will be collected in 30-sec epochs. Actiwatch records activity, light exposure, and wear time. Subjects will be asked to keep a daily sleep log and press an event marker on the Actiwatch at bedtime and wake-up time. Data will be downloaded and reviewed with each participant to clarify inconsistencies when the Actiwatch is returned. Rest intervals will be set using reported try-to-fall-asleep times and wake-up times on daily sleep logs or event markers if these times are missing. Using the Immobile Minutes algorithm in the Actiware 6 software, we will derive the following variables: sleep onset, sleep offset, sleep duration, sleep efficiency (a measure of sleep quality), mid-sleep time (time point between sleep onset and wake time), and standard deviation (SD) of sleep duration, an indicator of sleep variability which we previously showed to be related to glucose metabolism.[2]

C.2.9.c Secondary outcomes: Diabetes distress, self-management behavior, quality of life. Diabetes distress will be measured with the Type 1 Diabetes Distress Scale.[98] This 28-item, 6-point Likert scale measures 7 subscales (powerlessness, management distress, hypoglycemia distress, negative social perceptions, eating distress, physician distress, and friend/family distress) as well as provides an overall total distress scale score. Self-management behavior will be measured with the Diabetes Self-Management Questionnaire-Revised (DSMQ-R).[99] This 27-item, 4-point Likert scale measures aspects of self-management behavior and has questions that are specific to those using rapid-acting insulin. Quality of life will be measured with the Diabetes Quality of Life Scale (DQOL), a 46-item, 5-point Likert scale that measures 4 subscales (satisfaction, impact, social/vocational worry and diabetes-related worry).[100] The scales chosen have strong psychometric properties and have been validated in T1D populations.

C.2.9.d Important patient-related variables. Self-efficacy, anxiety, fear of hypoglycemia, mood, fatigue, sleep quality, and daytime sleepiness will be measured with validated instruments: Self-Efficacy for Diabetes Scale,[101] General Anxiety Disorder – 7-item (GAD-7),[102] Hypoglycemia Fear Scale II,[103] Center for Epidemiological Studies Depression Scale (CES-D),[104] PROMIS Fatigue Scale,[105] Pittsburgh Sleep Quality Index,[106] and Epworth Sleepiness Scale.[107] Food intake and timing will be measured by 24-hour dietary recall. Because menopausal status can affect sleep, we will use the STRAW+10 (Stages of Reproductive Aging Workshop+10) criteria for staging menopause for women aged 40 and over.[108] Physical activity will be obtained by activity counts from actigraphy recordings.

Table 6 Measures		
Variables	Measures	Frequency
Demographic, health, and literacy information, caffeine and sleep aid use	Demographic, health questionnaire, menopausal status, Clark Scale, Health Literacy Screener (Newest Vital Sign),[109] Menopausal status (STRAW+10 in women≥40 years[108], caffeine, sleep aid use	Week 0
Subjective sleep indices	Sleep quality (Pittsburgh Sleep Quality Index),[106] Epworth Sleepiness Scale[107]	Week 0
Objective sleep Indices	Sleep duration, sleep efficiency, sleep variability, sleep and wake timing (Respironics Actiwatch Spectrum Plus®). Confirmed with sleep diary (bedtime, disruptions, wake time).	Weeks 0, 6,12, 24
Primary measures: Glycemic Indices Glycemic control Glycemic variability	 A1C CGM (Abbott Libre®; or Dexcom®): glucose variability: coefficient of variation (CV%), time spent in range[94,95]	Weeks 0, 6,12, 24
Secondary measures: Diabetes distress Diabetes Self-Management Quality of life	 T1D Diabetes Distress Scale[98] Self-Management Questionnaire-R[99] Diabetes Quality of Life Scale (DQOL)[100]	Weeks 0, 6,12, 24
Important Patient-Related Variables	Self-Efficacy for Diabetes Scale,[101] General Anxiety Disorder – 7-item (GAD-7).[102] Hypoglycemia Fear Scale II,[103] Center for Epidemiological Studies Depression Scale	Weeks 0, 6,12, 24

	(CES-D),[104] PROMIS Fatigue Scale,[105] 24-hour dietary recall, activity counts from actigraphy recordings.	
Participant Engagement	Number of sessions attended, length of coaching sessions, lessons viewed, Fitbit usage	Weeks 1-12

C.2.10 Data Analysis

Statistical Analysis

We will conduct descriptive analyses of measured variables, evaluate associations among variables, and changes over time. This review of the data will allow us to identify covariates (e.g. age groups, treatment regimen) that may require statistical adjustment in the final models. We will conduct exploratory analyses with baseline cross-sectional data using our de-identified data which may include emerging approaches to capture and analyze sleep and glucose metrics in this rapidly evolving area of research.

Our *overall statistical approach* will be a mixed-effect model for repeated measures (MMRM), recommended for primary analysis of clinical trials with continuous endpoints.[110] Conceptually, MMRM is a more advanced version of repeated-measures ANOVA that can account for the correlation among multiple measurements over time, yet there is no assumption that participants are measured at every time point. Therefore, these models are very flexible at handling missing data. Participants who have a missing observation are not excluded; thus, this produces the intention to treat (ITT) full information maximum likelihood (FIML) model. While missing data will be minimized through careful procedures, some missing data are inevitable with longitudinal studies. We will handle missing data using the FIML approach that is appropriate for data missing at random.[111] We will use inclusive models with auxiliary variables related to missingness among covariates collected at baseline, if needed, to support the missing at random assumption.[112] Multiple imputation will be considered if excessive data are missing among predictor variables, e.g., change in sleep parameters for Aim 3.[112] Sensitivity analyses such as pattern mixture models will be employed if data are suspected to be missing not at random.[113]

Aim 1: Determine the effect of Sleep-Opt, compared to a healthy living attention control group, on the primary outcomes of sleep variability, sleep duration and glycemic control (A1C).

We will conduct MMRM using change from baseline for our primary outcome regressed onto categorical fixed effects for treatment arm, time, their interaction, and the initial baseline measure of the outcome. We will use an unstructured covariance structure to model within-person errors. If convergence problems occur, we will select the best fitting model from among several options, including random coefficients with residual covariance patterns such as autoregressive or exchangeable structure.[110,114] In addition to A1C, we will estimate separate models for parameters from continuous glucose monitoring (glycemic variability, TIR). Sex will be included as a covariate and tested for moderation of the treatment effect. We will also control for BMI, A1C (for other glucose measures), and method of insulin delivery. If treatment arms are found to differ in the distribution of baseline characteristics despite randomization we will conduct sensitivity analyses including these variables as covariates. The primary endpoint will be change differences between groups at 12 weeks, based on least square means using a two-sided test with $\alpha = .05$. We will also assess differences in change from baseline to the 24-week endpoint to assess sustainability of effect.

Aim 2: Determine if Sleep-Opt will result in improved psychological and behavioral secondary outcomes, including diabetes distress, diabetes self-management behavior, and quality of life (QoL). Secondary outcomes will be analyzed with the same approach used in Aim 1.

Aim 3: Determine the contribution of changes in sleep variability and sleep duration during the intervention to changes in glycemic parameters (A1C, glycemic variability, TIR).

Sleep-Opt is designed to reduce sleep variability and extend sleep and duration, and we expect these changes to mediate change in glycemic control. In the context of the Aim 1 models, we will add time-varying sleep parameters, taking into account the average levels per person and the variation at each time point, to understand contributions of between- and within-person differences. We will also examine additional covariates predicting sleep parameters, because level and change in sleep parameters (while influenced by randomized treatment arm) are not experimentally controlled.[115] In addition, we will test moderation of within-person mechanisms by sex, distress, method of insulin delivery, and A1C level using interaction terms. Successful completion of this aim will inform how aspects of sleep are related to the various aspects of glycemic control in general; which glycemic control parameters show reactivity to within-person fluctuations in sleep; and which personal characteristics may be more associated with this reactivity. This will explicate key mechanisms of change and suggest who may benefit most from sleep optimization.

As an additional statistical analysis we will explore the association of actigraphy-derived light and activity with sleep, glucose, and participant characteristics as ambient light may function as a covariate.

Statistical Analysis Addendum

Prior to data analysis the following are revisions were made to the analysis plan.

Multiplicity. The original proposal used alpha=.05 for 3 outcomes in the primary aim. We will use this threshold for all primary and secondary outcomes and provide a post hoc description of familywise error (e.g., families: sleep, CGM, psychosocial outcomes) using Holm's procedure.[116]

Missing data approach. We will conduct our models for aims 1-3 (focal models) using an inclusive strategy incorporating extraneous auxiliary variables to support a conditionally missing at random assumption. We will examine missing data for all variables in our focal models. For variables with substantial missingness (5% or more) we will create a group indicator for missingness (yes, no) and examine effect sizes for extraneous baseline variables, considering those with effect sizes of >|.20| as being related to missingness. We will also consider extraneous baseline variables with partial correlations >|.30| with the variables with substantial missing. We will prioritize variables meeting both criteria, then those meeting only the partial correlation criteria. Variables only related to missingness will not improve the model and will not be considered further.[117] Auxiliary variables will be included as additional outcomes in a way that does not affect interpretation of focal variables. If missing not at random is suspected, we will conduct pattern mixture or selection model approaches as sensitivity analyses. All models will be tested using BLIMP 3 software using Markov chain Monte Carlo estimation; we will report Bayesian median point estimates and 95% credible intervals for treatment effect estimates for previously stated models (i.e., MMRM) for aims 1 and 2 and mediation (indirect) effects from path models for aim 3 (see below).

Intention to treat and per protocol. Modeling for aims are based on the intention to treat principle retaining all individuals in their randomly assigned treatment arm. We will conduct per protocol models if more than 5% of participants did not adhere to the protocol, defined as completing at least 80% of sessions. In these models, we will assess for correlates of engagement and include them as control variables in models excluding the participants who did not complete the protocol.

Models for aims 1 and 2 will provide valuable insight into the potential moderators and timing of change in participants. Aim 3 modeling is revised to use a path analysis approach to test separate parallel multiple mediator models for glycemic outcomes (e.g., A1C, time in range). The indirect effects will be tested with Bayesian 95% credible intervals. Correlates of sleep improvement will be used in these models as control variables and explored as moderators of the mediated effect.

C.2.11 Subject Retention Strategy. We anticipate a 17% attrition rate. We expect to randomize up to 170 subjects to obtain complete data on 120 subjects. This estimate is based on our previous work. All efforts will be made to retain participants and reduce burden of participation. Assessment visits and coaching calls will be flexibly scheduled according to participant needs. Parking and/or transportation costs will be reimbursed. Participants will be allowed to mail back actigraph and CGM devices to reduce office visits. Participants will receive $100 for participation, incrementally paid across visits. Participants will also be allowed to keep the Fitbit device as an additional incentive for program completion. Those in the attention control group will receive a Fitbit at the end of the study. Parking will be provided for anyone who chooses to complete their data collection visits in-person.

C.2.12 Treatment Fidelity Strategy All coaching sessions (Sleep-Opt and Healthy Living attention control) will be recorded for training and fidelity monitoring (audio or videorecording). All coaches will be trained until they reach a criterion of adherence to the treatment protocol before being assigned study participants. Each quarter, Dr. Duffecy will review approximately 10% of conducted sessions quarterly and code them for adherence using previously developed rating scales.[90] Items include aspects of the session content (e.g., eliciting questions or problems about the intervention, setting goals), structure of the session (e.g., sets an agenda), and therapeutic process (e.g., uses open-ended questions, appropriate session pacing). Control sessions will be reviewed for the presence of sleep-related content or health advice. If any sleep or health advice (other than direction to the source website) is provided, this will trigger re-training. Drs. Duffecy and

Quinn will provide bi-weekly supervision to the coaches for their respective groups, providing back data regarding treatment fidelity as well as troubleshooting any clinical issues. A manual of operations will be developed, and staff will be trained on study procedures. All interactions with participants will be scripted when possible. Protocol violations will be reviewed by the staff and reported to the IRB. All interactions by staff with participants will be logged, and emails will be archived.

C.2.13 Study Timeline (See Table 11).

Table 11. Study Timeline Year 1	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	Cumulative Number of active Subjects
Study set-up	X	X	X	X	X	X							
*Sleep-Optimize subjects							2	2	2	2	2	2	
*Control subjects							2	2	2	2	2	2	
Total active subjects							4	8	12	16	20	24	
Total subjects YEAR 1							**4**	**8**	**12**	**16**	**20**	**24**	24
Year 2	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	
*Sleep-Optimize subjects	2	2	2	2	2	2	2	1	1	2	2	2	
*Control subjects	2	2	2	2	2	2	2	1	1	2	2	2	
Total active subjects	24	24	24	24	24	24	24	22	22	24	24	24	
Total subjects YEAR 2	**28**	**32**	**36**	**40**	**44**	**48**	**52**	**56**	**60**	**64**	**68**	**72**	72
Year 3	1	2	3	4	5	6	7	8	9	10	11	12	
*Sleep-Optimize subjects	2	2	2	2	2	2	2	1	1	2	2	2	
*Control subjects	2	2	2	2	2	2	2	1	1	2	2	2	
Total active subjects	24	24	24	24	24	24	24	22	22	24	24	24	
Total subjects YEAR 3	**76**	**80**	**84**	**88**	**92**	**96**	**100**	**102**	**104**	**108**	**112**	**116**	116
Year 4	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	
*Sleep-Optimize subjects	2	2	2	2	2	2	2						
*Control subjects	2	2	2	2	2	2	2						
Total active subjects	24	24	24	24	24	24	24	20	16	12	8	4	
Total subjects YEAR 4	**120**	**124**	**128**	**132**	**136**	**140**	**144**						144
Year 5	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	
Data cleaning	X	X	X										
Data analysis			X	X	X	X	X	X					
Manuscript preparation						X	X	X	X	X	X		
Final study reports										X	X	X	
Total active subjects *Newly enrolled subjects													

C.2.14 Potential Study Problems and Alternate Approaches. 1) Changes in diabetes treatment regimen is a potential influencer in glycemic control during the study period. The participants in the study will receive diabetes treatment per the usual care by their physicians. We will collect the modalities of treatment, changes in treatment, and totally daily insulin doses as covariates when analyzing the primary outcomes. **2**) Design consideration regarding the length of the intervention and A1C measurement: The intervention was designed for a12-week period to achieve the best possible outcomes based on previous behavioral interventions and feedback from pilot study participants.[59] **3**) The intervention requires smartphones; this could limit the accessibility to non-smartphone users. However, the number of smartphone users has grown significantly in the last decade. It was estimated that 77% of US adults owned a smartphone in 2016, up from 35% in 2011, making the smartphone one of the most quickly adopted consumer technologies.[118] This number is expected to grow; thus, smartphone accessibility will become less of a limitation in the near future. **4**) Obstructive sleep apnea is screened by questionnaire and not the gold standard polysomnography in this study. It is possible that subjects with sleep apnea will be included in the study. However, this will not pose harm to the subjects, and sleep apnea and sleep duration independently contribute to glycemic control.[3,119] **5.)** In our pilot study we experienced a 10% sensor failure rate. (This is less than that reported by the manufacturer and may be due to the research team's expertise in placing these devices). Most sensor failure was due to dislodgement by the participant. If dislodgement occurs, we will overnight mail a new sensor to the study participant. The dislodged

sensor will retain the recorded data. Participants will be instructed to return the sensor. We anticipate a 24 hour disruption in data collection with dislodgement.

C.2.15 Future Directions. Once the intervention is determined beneficial, future directions include deploying sleep optimization to other age groups in T1D, as well as other population with dysglycemia, such as those with type 2 diabetes and gestational diabetes. In the future, using automated prompts with or without human interaction could increase the scalability of this approach. Sleep optimization could be incorporated as a component of standard medical care of T1D.

3.1 Protection of Human Subjects

1. Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design
Study Design. The purpose of this study is to determine the efficacy of a T1D-specific sleep optimization intervention (Sleep-Opt) on the primary outcomes of glycemic control (A1C), sleep variability and sleep duration; and secondary outcomes: other glycemic parameters (glycemic variability, time in range); diabetes distress, self-management behavior, quality of life (QoL) and other patient reported outcomes in working-age adults with T1D and habitual high sleep variability or short sleep duration. The human subjects involved in this research will be working-age adults, 18-65 years with type 1 diabetes (T1D) who report habitual sleep variability (sleep duration SD > 1 hour per week) or sleep duration <6.5h/night during the work days with a desire to improve sleep. To achieve these aims, we will conduct a randomized controlled trial comparing a sleep intervention to a healthy living attention control group.

Study population. We plan to enroll up to 300 subjects. We anticipate a 40% screen failure rate and expect to randomize up to 170 for a final sample of 120 subjects with complete data. Inclusion criteria include 18-65 years of age, with a clinical diagnosis of T1D for at least one year, report habitual sleep variability (1 hour/week or more) or sleep duration <6.5h/night during the work days or week days (confirmed with actigraphy), with a desire to sleep longer, and who own a smartphone compatible with Fitbit. Exclusion criteria include insomnia symptoms defined as severe insomnia symptoms as assessed by the Insomnia Severity Index (score ≥ 15), being at high risk for obstructive sleep apnea as assessed by Stop Questionnaire,[82] a history of severe hypoglycemia (defined as hypoglycemic episodes that result in loss of consciousness within the last 6 months, seizures, or requiring help from others), A1C > 10%, rotating shift or night shift work, use of sleep medications/aids, significant renal impairment (estimated glomerular filtration rate < 45 ml/min/1.73 m^2), significant medical morbidities such as congestive heart failure, cirrhosis, chronic obstructive pulmonary disease requiring oxygen, active treatment for cancer, depression (PHQ8 ≥ 10), history of stroke with neurological deficits, breastfeeding, pregnant or planning pregnancy.
Convenience sampling will be used to recruit subjects throughout the Chicago metropolitan area. We expect that approximately 20% of participants will be recruited from the University of Illinois Medical Center and the remaining from the Chicago metropolitan area. This number is based on our previous study recruitment outcomes. Participants will be randomized to the intervention group or an attention control group to minimize bias. Randomization will be computer-generated in permuted blocks of 4, arranged in random order and stratified by sex. The randomization model will be developed by the study statistician (Dr. Steffen) and will be executed through the REDCap data management system.

Site/Setting. Subjects' home is the study site. All study materials will be mailed to subjects' home and subjects and study staffs will meet via video conference for orientation to the study procedures and instruct subjects how to use the study materials. During the study period, subjects will continue to receive their usual diabetes care with their health care provider. Subjects will be encouraged to discuss any questions regarding blood glucose management with their diabetes health care provider.

b. Study Procedures, Materials, and Potential Risks
Study Procedures
The sleep optimization intervention employs a wearable sleep tracker (Fitbit), 8 weekly online lessons (over a 12-week period), an interactive smartphone application, and 8 brief telephone counseling sessions tailored to T1D. The intervention will address three specific aspects: sleep variability, sleep duration, and TID-related

sleep issues such as nocturnal hypoglycemia. Those randomized to the healthy living attention control group will receive 8 weekly online healthy living information lessons (over a 12-week period), and 8 brief phone calls from a health education coach (equal in time and attention to the intervention group). Participants in both groups will be evaluated for sleep parameters, primary outcomes of glycemic control, sleep variability and sleep duration, and secondary outcomes (glycemic variability, time in range, diabetes distress, self-management behavior, QoL and other patient reported outcomes) at baseline (Week 0), Week 6 (mid-treatment), Week 12 (end of treatment), and Week 24 to test the sustainability of the intervention.

Sources of Materials

Data will be collected from study subjects only for research purposes as follows: (1) self-reported data from questionnaires and the most recent estimated glomerular filtration rate (eGFR), height, and weight from health provider; (2) a fingerstick blood for A1C and urine for pregnancy; (3) continuous glucose monitoring (CGM) from a glucose sensor placed under the skin; (4) wrist actigraphy; (5) Intervention data from the Fitbit and other technologies, as well as coaching calls.

1. Self-reported data will include information collected: (a) during recruitment to establish study eligibility and (b) demographic (age, sex, race, ethnicity), health (diabetes duration, comorbidities, menopausal status, use of sleep aids and caffeine, eGFR, height, weight), key study variables (diabetes distress, self-management behavior, quality of life); and related patient-reported outcomes (anxiety, mood, fatigue, subjective sleep, daytime sleepiness, self-efficacy, hypoglycemic fear, 24 hour dietary recall) collected from questionnaires.
2. Specimens: A1C determined from a fingerstick blood by using standardized procedures. Pregnancy (to confirm eligibility) will be determined from a urine sample using standard procedures. All specimen collection will be conducted by subjects instructed by a trained member of the study personnel using standards for blood borne pathogens.
3. Continuous interstitial glucose levels to calculate glycemic variability and time in range will be obtained from a CGM sensor placed under the skin using standard procedures by trained study personnel. The sensor transmits the glucose levels to a receiver (the size of a quarter) that the subject wears for one week.
4. Sleep parameters obtained through actigraphy (size of a wristwatch worn on non-dominant wrist) will include sleep duration, sleep efficiency, and sleep timing. Standard deviations of these parameters will be calculated and used to reflect sleep variability.
5. Program evaluation obtained from questionnaires and interview.
6. Data collected via the intervention, including frequency and length of use of technologies and coaching data
7. Data to evaluate program outcomes will include (1) recruitment (number recruited, screened, eligible, consented) and (2) retention (attendance and completion rate records) maintained by study personnel.
8. CCTS UIC-Circle data on UI Health patients that may be eligible to participate in our study. This data will be used to mail invitations to participate (See Section C.2.4). The data elements provided by the CCTS will include full name, age, gender, race, ethnicity, address, phone number, and email address if available. Once received from the CCTS the data will be stored securely in REDCap and a Box-Health folder.

Potential Risks

The potential risks to subjects include:

1. Bleeding, irritation, discomfort, or infection at the fingerstick site and CGM insertion sites. The risk for these problems is very minor and is minimized by following standardized procedures using trained study personnel.
2. Loss of confidentiality. Standard procedures will be used to avoid breaches in confidentiality. We expect this risk to be low.
3. Completing self-report measures on diabetes distress and mood may cause subjects some emotional distress.
4. Risks associated with the intervention may include irritation due to wearing the Fitbit or actigraphy devices.

5. Loss of privacy. Private locations will be used to collect data at all times.

No other risks are currently identified.

2. Adequacy of Protection Against Risks

a. Informed Consent

Subjects (18-65 years) will be recruited from a Chicago metropolitan area university medical center, diabetes clinics, Research Match, local diabetes websites, and organizations, using flyers, e-announcements, and recruitment letters and emails. Potentially eligible interested subjects will be screened by trained study personnel for inclusion and exclusion criteria. Written informed consent will be obtained via online (REDCap) prior to performing any research procedures. The informed consent process will begin when potential subjects are contacted. The researcher will explain the study purpose, procedures, benefits, risks, confidentiality, and research subject's rights. After all questions have been answered and the subject verbally agrees to participate, written consent will be obtained at the via online (REDCap). A copy of the signed consent will be provided to the subject either mail and/or email.
A waiver of informed consent will be requested for the purpose of identifying eligible patients for recruitment from the University of Illinois Health System data base.

b. Protections Against Risk

Methods to minimize risk include:

1. Minimization of bleeding, irritation, discomfort, or infection at the fingerstick site (e.g. A1C) and insertion site (for CGM). The risk for these problems is very minor and is minimized by following standardized procedures. CGM placement and fingerstick will be done using sterile technique and standardized procedures. These will be performed by subjects instructed by trained personnel. Subjects will be instructed to observe their CGM insertion site daily and contact the research personnel if there are signs of bleeding, irritation, redness, or pain.
2. Loss of confidentiality. Strict procedures will be put into place to minimize the risk of breach of confidentiality. All study staff will be trained on methods of maintaining subject confidentiality. Subjects will be assigned a unique code number. A master list that links the subject identity to the data will be kept by the principal investigator (PI) and stored in a locked office separately from the data. **Data storage**: All data will be stored and analyzed by code number. This consists of coded questionnaires, A1C results, actigraphy, and CGM recordings. The coded data will be entered into a password-protected computer with a secure server for analysis. Hard copy (paper copy) data (blood draw results) will be stored in a locked office. Questionnaire data will be collected using Research Electronic Data Capture (REDCap). No identifiers (except subject ID) will be included. Only members of the research team will be able to access these data. **Procedures during data collection:** Privacy will be provided during recruitment by screening potential subjects in a private setting. The screening data that contain personal identifiers will be kept separate from the coded study data and stored in a locked office. All data collection and study procedures will take place in a private location. All data collected via the intervention (e.g., internet intervention materials, data entry, etc.) will be transmitted using Transport Layer Security (TLS) encryption to prevent eavesdropping and tampering with information while it is in the transmission pipeline. To prevent unauthorized access to internet sites, they will be password-protected.
3. Because people with T1D are always at risk for hypoglycemia, study staff will instruct study participants to have fast-acting carbohydrate available should a they develop hypoglycemia during a meeting session (either intervention or attention control group).
4. Completing self-report measures on distress and mood may cause subjects some emotional distress. The risk is minimal. In our previous studies with the same population, no subjects reported emotional distress with these measures. However, study staff will be aware of the possibility and address any concerns that are voiced.
5. Should a subject require medical or other professional intervention due to an adverse event or illness, treatment may be obtained through the UIC Medical Center, the subject's regular doctor, or the treatment center or clinic of their choice. Subjects will be provided contact information for the PI should they want to talk to her about their illness or injury.

6. To prevent coercive contact from the application and coach, all email outreach is pre-scripted, and user contact information is never revealed. Outreach emails will state that the coach has noticed they have not worn the Fitbit in a few days and ask if they would like troubleshooting help or to return to the program. It will not include any coercive language or pressure. Email communication will be limited to pre-scripted content reminders and participant outreach.
7. Participants will be informed that they may discontinue the intervention at any time. If an adverse event is experienced, participants will be instructed to contact Dr. Duffecy or Dr. Quinn. Phone numbers will be provided through which one of the investigators can be reached 7 days/week, 24 hours/day.

c. Vulnerable Subjects
Vulnerable subjects will not be included in the study (fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals or others who may be considered vulnerable populations).

3. Potential Benefits of the Proposed Research to Human Subjects and Others

There may be no direct benefits to participating in the study. However, subjects in the intervention group may increase sleep duration and experience increased glucose control. The potential in future is that this study may advance the knowledge of sleep interventions to extend sleep duration and improve glucose control. The possible risks are no greater than those experienced in normal day-to-day life.

3.3 Data Safety Monitoring Plan
This study will involve working adults (aged 18 to 65 years) with type 1 diabetes (T1D) who experience high sleep variability or insufficient sleep duration. We plan to enroll up to 300 subjects for a final sample size of 120. Subjects will be enrolled and will complete a 1-week run-in period to collect baseline data, actigraphy to measure sleep, and continuous glucose monitoring (CGM) to calculate baseline glycemic variability. Following the run-in period, eligible subjects will be assigned to one of two groups: attention control group = 12 weeks or intervention group = 12 weeks.
The risk associated with this study is minimal for the interventions and data collection methods employed in the study. The potential for a serious adverse event is very low. Drs. Martyn-Nemeth, Reutrakul, and Quinn are experts in the clinical care of people with diabetes. Dr. Steffen has extensive experience with advanced statistics. Dr. Martyn-Nemeth will assure that participants are fully informed and consent freely, and Drs. Martyn-Nemeth and Steffen will monitor the safety of the study as described below.

Monitoring Plan
The PI, Dr. Martyn-Nemeth, will be the primary monitor and a Data Safety Monitoring Committee will share the responsibility of monitoring the data.

- A Data Safety Monitoring Committee (DSMC) will be appointed to provide oversight and monitoring of the data on an annual basis. The DSMC will consist of: (1) Mary Kapella, PhD, RN, Associate Professor Emeritus and past Director of Sleep Center, Department of Biobehavioral Health Science, College of Nursing; (2). Ulf Bronas, PhD, Associate Professor, Biobehavioral Health Science, College of Nursing; (3) Dr. Eileen Collins, PhD, Dean, College of Nursing, (4) Terry Unterman, MD, Professor, Division of Endocrinology, Department of Medicine at UIC, and (5) Dr. Chang Park, PhD, statistician, Department of Population Health Nursing Science, College of Nursing. Drs. Martyn-Nemeth and Steffen will meet with the DSMC annually and will present both a written and verbal report. The report will include a summary of cumulative recruitment, randomization, cumulative retention and attrition rate, study group demographics, adverse events, and data completeness and quality. A written report of the meeting will be compiled that summarizes the review of data and outcomes, as well as any recommendations with respect to modification of the protocol.
- Process for Adverse Events. Throughout the study, the PI and Co-Is will monitor the participants for adverse events (AEs). Dr. Martyn-Nemeth and study staff will review AEs individually in real time and consult with co-investigators as needed. All AEs or unanticipated problems will be reported to the UIC IRB and/or study sponsor as required based on the respective policies and procedures.
- Procedures for monitoring study safety. The facility has protocols in place for responding to emergency events and serious adverse events. These protocols will be followed for the study. All study personnel involved in conducting the research, including recruitment and screening for eligibility, data management, and provision of interventions, will receive training that will address: (1) overview of the

study objectives and procedures, (2) background and training on collecting data free from bias, (3) protection of human subjects and confidentiality, bloodborne pathogen training and infection control procedures (4) instructing study participants in performing fingersticks and placing CGM sensors using infection control procedures, and (5) data and intervention monitoring.

- Procedures for maintaining study compliance. The PI will assure that informed consent is obtained prior to performing any research activities, all subjects meet eligibility criteria, and the study is conducted according to the IRB-approved research plan. Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal quality assurance process. Quality control will include annual data verification and protocol compliance checks, as well as checks for missing data by study personnel. Protocol adherence will be monitored by the PI by auditing 50% of the cases for compliance with IRB requirements, informed consent requirements, verification of source documents, and compliance with the study protocol. To ensure reliability of data entry, a random sample of data entries will be reviewed and compared with the raw data, and the results will be recorded. An acceptable error rate will be < 0.3%. Results of the audit will be documented. Research meetings will be scheduled to assure the quality of the conduct of the research and promote communication among study team members and good data management activities.

Treatment Fidelity Monitoring

All coaching sessions (Sleep-Opt and Healthy Living attention control) will be recorded for training and fidelity monitoring. All coaches will be trained until they reach a criterion of adherence to the treatment protocol before being assigned study participants. Biannually , Dr. Duffecy will review approximately 10% of conducted sessions quarterly and code them for adherence using previously developed rating scales.[90] Items include aspects of the session content (e.g., eliciting questions or problems about the intervention, setting goals), structure of the session (e.g., sets an agenda), and therapeutic process (e.g., uses open-ended questions, appropriate session pacing). Control sessions will be reviewed for the presence of sleep-related content or health advice. If any sleep or health advice (other than direction to the source website) is provided, this will trigger re-training. Drs. Duffecy and Quinn will provide bi-weekly supervision to the coaches for their respective groups, providing back data regarding treatment fidelity as well as troubleshooting any clinical issues. A manual of operations will be developed, and staff will be trained on study procedures. All interactions with participants will be scripted when possible. Protocol violations will be reviewed by the staff and reported to the IRB. All interactions by staff with participants will be logged, and emails will be archived.

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