



Objective Clinical Measures of Sleep in Real-World Settings

Abstract

Sleep is essential for maintaining physical and brain health. The disruptions in sleep can be indicative of primary sleep disorders or symptoms of underlying conditions. Polysomnography (PSG), although the reference standard, is limited in real-world settings due to its intrusive nature and logistical challenges.

The Digital Medicine Society (DiMe) launched a multistakeholder project to establish a set of core digital measures for sleep applicable across various therapeutic areas. This study outlines the clinical relevance of such measures, emphasizing their importance for clinicians and researchers.

This paper describes the physiological underpinnings of sleep and identifies key sleep-related measures across different therapeutic areas. Through a narrative review of sleep and how it is impacted in various conditions, it aims to highlight the possibility of measures that can aid in the transition from lab-based assessments to remote, real-time monitoring of sleep patterns and disturbances.

This work details the structure of sleep cycles, introduces aggregate measures of sleep, and describes the impact of sleep disruptions across various conditions including cardiovascular diseases, sleep-disordered breathing, depression, and neurological disorders. These insights are critical for developing standardized digital tools that can provide accurate, yet less invasive sleep assessments.

The development of digital measures of sleep offers a promising avenue for enhancing the understanding and management of sleep across a spectrum of diseases. This study provides foundational knowledge and a framework for future research aimed at integrating these measures into routine clinical practice, thereby improving patient outcomes through innovative, patient-centric approaches.

Keywords: Sleep, Digital Health Technologies, Polysomnography, Clinical Measures, Therapeutic Areas, Remote Monitoring.

Introduction

Sleep is fundamental to physical and brain health throughout the lifespan, and its disruptions may be features not only of primary sleep disorders but can also be indicators or symptoms of various underlying conditions across many therapeutic areas. Subjective sleep assessments, such as questionnaires and sleep diaries, have been valuable for capturing the patient experience and estimating likelihood for some disorders. Lab-based polysomnography (PSG) is the accepted standard used to

objectively assess sleep and, where appropriate, link physiological changes in sleep to subjective assessments.

However, when it comes to wider therapeutic implications of sleep health, lab-based PSG has limitations in usability for studying sleep physiology and does not adequately measure aspects of behavioral disorders in real-life (“natural”) settings. Today, the rapidly improving field of digital health technologies (DHTs) can enable longitudinal assessments of sleep parameters. Along with these evolving technologies, however, come the challenges of identifying the gaps and selecting the right tools to address the clinical questions at hand.

Recognizing these challenges, the Digital Medicine Society (DiMe) has initiated a multistakeholder collaboration to define the core digital measures of sleep that are applicable across different therapeutic areas and cover concepts that are important to clinicians, researchers, patients, caregivers and the general population. This endeavor strives to provide stakeholders with the critical parameters for sleep and sleep disturbance, aspiring to establish a well-defined set of digital sleep measures that can be leveraged for short-term and longitudinal remote monitoring.

In this first review, we detail one aim of this overall project: to define the sleep measures that are important to clinicians and clinical researchers. This aim is achieved through the following objectives:

- 1) Outline sleep physiology and describe aggregate measures
- 2) Identify clinically-relevant sleep-related measures across select therapeutic domains

In achieving these objectives, readers will have the context (objective 1) through which to understand clinically relevant measures (objective 2).

The second article in the series will focus on the landscape of sensing technologies capable of capturing clinical measures of sleep.

Sleep architecture

Sleep architecture refers to the structural organization of sleep states, or “stages”, including wakefulness (W), non-rapid eye movement (NREM; comprising N1 [light sleep], N2, and N3 [deep sleep]), rapid eye movement (REM). Wake ranges from full alertness to drowsiness. Typically occurring as a transition from W, N1 periods are short in duration and can be easily disrupted. N2 periods are longer and are characterized by entering into a deeper sleep, including a drop in temperature, relaxed muscles, slowed breathing and heart rate, and the presence of EEG sleep spindles (~12 hz oscillations lasting 0.5-2s). A healthy individual will usually spend around half of their sleep period in this state. From both animal and human studies, it is generally well accepted that N2 and sleep spindles are associated with memory consolidation [1,2,3]. N3 is the deepest state of sleep, lasting 20-40 minutes per cycle and decreasing in duration as the night progresses. N3 and REM sleep are associated with memory processes and with the subjective feeling of restorative sleep [4]. Further, N3 may also be associated with increased glymphatic flow, enabling the brain to remove waste more effectively[5]. In contrast to the NREM stages, REM sleep is

characterized by complete relaxation of most voluntary muscles alongside rapid movement of the eyes. The first REM period typically appears after the first hour of sleep and usually lasts just a few minutes. REM episodes then occur with some periodicity, increasing in duration over the course of the night. A healthy individual will typically experience more N3 during the earlier half of the night and more REM in the latter half. Periods of wakefulness, or arousals, may occur at any time of the sleep period; however, they most often follow a period of N2 or REM.

In a typical night, a healthy individual will experience approximately 4-6 sleep cycles of ~70-120 minutes each. Simplistically, the cycles progress through N1, N2, and N3, before moving back to N2 followed by a period of REM, after which the cycle repeats. Sleep architecture can be presented graphically as a hypnogram (see Figure 1).

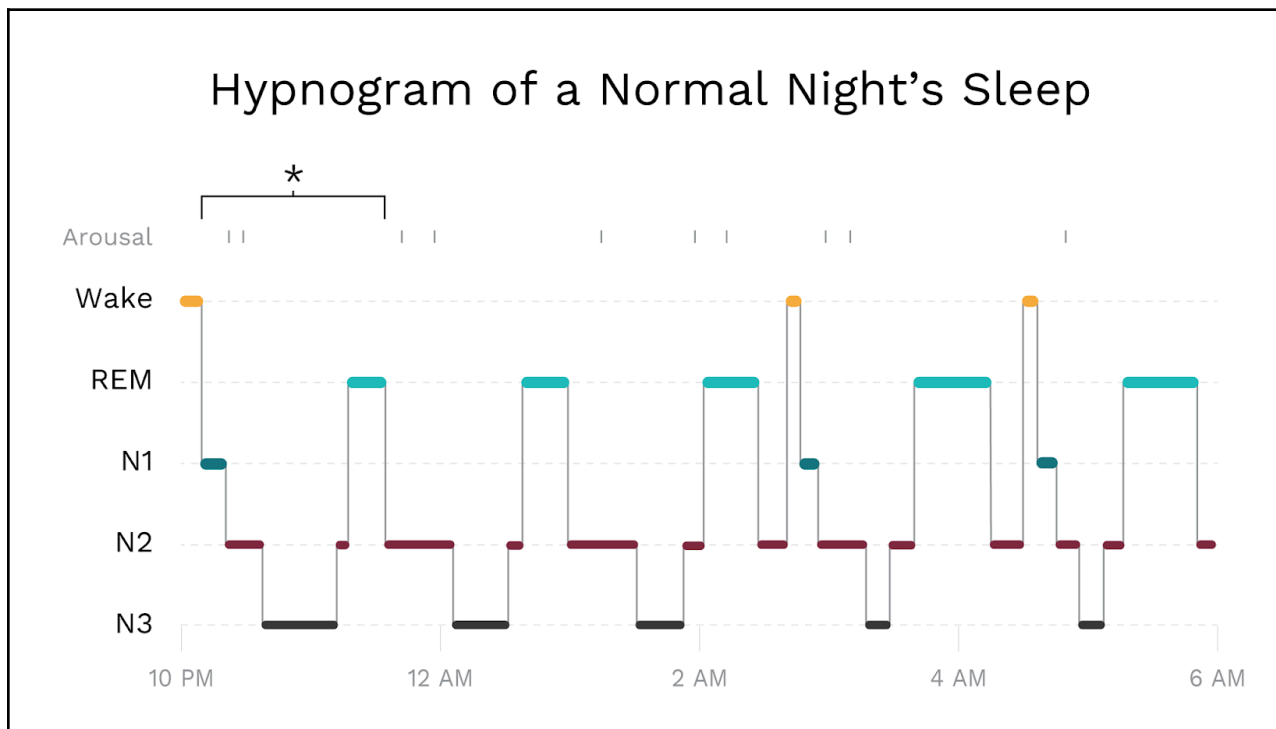


Figure 1: An example of a hypnogram (smoothed for simplification) depicting a typical night of sleep for a healthy adult

* Represents one complete sleep cycle commencing with the onset of sleep (N1) and concluding with end of the REM period

Aggregate Measures of Sleep

The complexities of sleep architecture can be summarized using aggregate measures and indices. For example, the hypnogram data can be used to derive measures such as total sleep time, sleep stage durations and percentages, sleep efficiency, sleep onset latency, and wake after sleep onset (see Figure 2). Various sleep-related event indices can be calculated; for example, the arousal index represents the number of arousals per hour of total sleep time.

Figure 2: Key aggregate measures of sleep

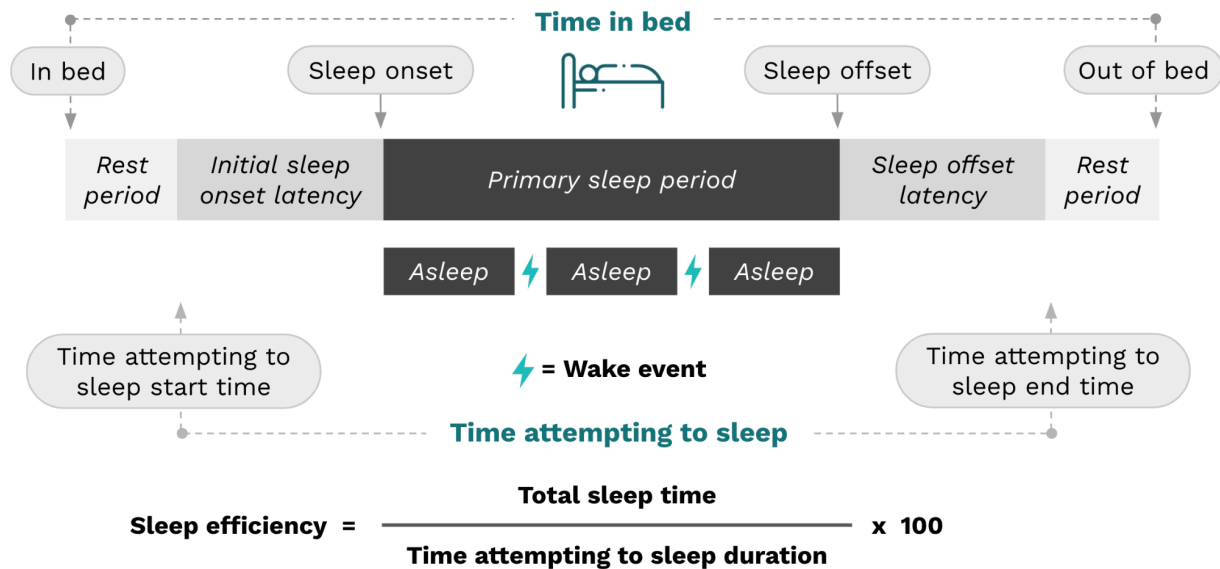


Table 1. Broad descriptions of some aggregate measures currently used in the literature

| Measure | Explanation | Comment |
|--|--|---|
| Time in Bed (TIB) Time <i>Other terms</i> Time Attempting To Sleep (TATS) per ANSI/CTA/NSF 2052.1; major sleep period, rest interval, assumed sleep interval | Time interval when subjects are attempting to sleep | Measuring intent is the key difference between the terms. Intent can be measured explicitly (self-report), inferred (algorithmically), or assumed as the time at which someone first gets into bed |
| Primary Sleep Period <i>Other terms</i> true sleep period / minutes, O-O (Sleep Onset - Sleep Offset) interval | Time interval from sleep onset to sleep offset; note that Sleep Period is always shorter than TIB / TATS | There may be awakenings during the sleep period, but the sleep offset used in this definition is typically the one where the individual intends to start their wake period and does not return to sleep |

| | | |
|--|---|---|
| (initial) Sleep Onset Latency (SOL) a.k.a. Initial Sleep Latency (ISL), a.k.a. Latency to Persistent Sleep (LPS) | The number of minutes from the start of TIB it took a participant to fall asleep. | Note that there are other sleep onsets through the night if the participant woke up, but the first one is a measure of choice for many clinical cases. Sleep onset is not always pronounced as a start of continuous block of sleep. It is also difficult to define when the intention to sleep starts as described per TIB. LPS also takes into account how well the sleep episode persists (e.g. > 10 min) |
| Total Sleep Time (TST) | Total number of minutes that were scored as sleep during TIB May be defined/refer to either "Sleep minutes during TIB" or "True sleep minutes" | In some cases, N1, as a transitional phase, is counted as Wake contributing to potential discrepancy |
| Wake after Sleep Onset (WASO) | Number of minutes scored as awake during the sleep onset - sleep offset interval | WASO does not on its own characterize sleep fragmentation, it just counts the total number of minutes in W state that occur after sleep onset and prior to the final sleep offset |
| Sleep Efficiency (SE) | Proportion of minutes a subject was asleep during the sleep period | SE can be defined in several ways; a simplified formula is $SE = TST / (TATS)$. |

Although aggregate measures and indices are often defined in the context of the overnight rest period, it is important to note that A) the rest period may not necessarily take place at night; and B) a given 24-hour period may also include one or more naps resulting in multiple rest periods. Real-world sleep monitoring increases relevance of the multiple rest periods. This also depends on the therapeutic area of interest.

Sleep measures across select therapeutic domains

Having described sleep architecture, normal sequence of sleep cycles, and aggregate measures of sleep continuity and quality, the remainder of this review will focus on clinical manifestations of disrupted sleep across a broad range of therapeutic conditions. We selected the conditions based on therapeutic focus, prevalence of the sleep-related symptoms, severity of the associated sleep quality health risks, and size of the affected population.

Primary Sleep Disorders

Primary sleep disorders include sleep disruptions not attributable to another medical or psychiatric condition. The most common Primary sleep disorders include insomnia disorder (ID) and obstructive sleep apnea (OSA). Central disorders of hypersomnolence (CDH) are also considered due to the significant need for real-life monitoring. The full classification of Primary sleep disorders is summarized by International Classification of Sleep Disorders, 3rd ed., ICSD-3-TR [6]. In this review, we only focus on select cases given that the primary sleep disorders have a dedicated community of researchers and are covered extensively elsewhere [7].

Insomnia

Insomnia disorder is defined as a complaint of difficulty falling or staying asleep associated with significant distress or impairment in daytime function and occurs despite an adequate opportunity for sleep (see ICSD-3TR; DSM5). Diagnosis of ID is typically derived from clinical interview and subjective scales following complaints of trouble falling and/or staying asleep, excessive daytime sleepiness, and/or cognitive difficulties.

Research studies of objective measures in ID have focussed primarily on sleep onset latency (SOL) and wake after sleep onset (WASO), as well as the duration of N3 and REM sleep stages, total sleep time (TST), and sleep efficiency (SE). Although PSG is a way of capturing these measures, the current guidance does not advise the procedure given the subjective nature of ID [8]. Minimally-intrusive longitudinal measurements, taken in real-life settings, may be more appropriate for understanding the sleep complaint. The depth of the PSG lab assessment can be replaced by prolonged periods of observation, which allow tracking of weekly and seasonal variations as well as associated measures of daytime activities. The well-established subjective Consensus Sleep Diary and the Pittsburgh Sleep Quality Index (PSQI) are weakly correlated with the objective measures [9], suggesting that the subjective instruments may be measuring different constructs related to sleep (e.g., a psychological perception of well-being rather than actual sleep parameters).

Objective measures relevant to insomnia: Sleep Onset Latency; Wake After Sleep Onset; Total Sleep Time; Sleep Efficiency; Time In Bed; Longitudinal regularity of sleep; N3 duration; REM duration.

Sleep-related breathing disorders

Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder, characterized by partial or complete collapse of the upper airway [10, 11], leading to intermittent reduced (hypopnea) or absent (apnea) airflow. Apnea leads to intermittent reductions in blood oxygen saturation typically followed by an arousal in order to restore airway patency, resulting in sleep fragmentation and a reduction in slow wave (N3) and REM sleep [12]. In many, the highest incidence of apneas/hypopneas occurs during REM sleep.

OSA is one of the most studied sleep-related conditions due to its significant adverse consequences and associated mortality. Sleep-specific measures for OSA include N3 and REM duration, apnea/hypopnea index (AHI) and the arousal index (AI). In addition, a range of physiological measurements during sleep are relevant, predominantly airflow and blood oxygen saturation from which individual apneas/hypopneas can be obtained.

The limitations of the diagnostic and prognostic value of the AHI, and similar metrics based on event counts, are increasingly recognized, leading to an active quest for more precise clinical markers to evaluate OSA severity [13]. As such, hypoxic burden, arousal intensity, heart rate response, and respiratory event duration are becoming relevant measures in this condition [14]. Beyond diagnostics, monitoring OSA in real-life settings requires robust measures that can be captured in home settings with minimal setup.

Objective measures relevant to sleep-disordered breathing: N3 duration; REM duration; arousal index. Physiological measures captured during sleep include the AHI, Respiratory Disturbance Index (RDI), Respiratory Event Index (REI), Oxygen Desaturation Index (ODI), which collectively rely on identification of individual respiratory events; hypoxic burden; respiratory event duration; arousal intensity. Notably, the latter measures require specialized equipment that can capture, at least, respiratory effort and blood oxygenation.

Central disorders of hypersomnia (CDH)

CDH includes narcolepsy type 1 (narcolepsy with cataplexy; NT1), narcolepsy type 2 (narcolepsy without cataplexy; NT2) and idiopathic hypersomnia (IH). All CDH present with idiopathic excessive daytime sleepiness (EDS) with a variety of symptoms. NT1 distinguishes itself due to the significant loss of orexinergic (OX)/hypocretin-producing neurons in the brain, resulting in cataplexy (the sudden loss of muscle tone associated with a rapid drop in heart rate variability[15], and significantly disturbed nighttime sleep in addition to EDS during the day. Sleep in narcolepsy, particularly NT1, presents with rapid transitions (within seconds) between different states that makes manual scoring difficult. IH is diagnosed by the presence of EDS with unknown origin, sleep inertia - especially in the mornings - and in some cases, long nighttime sleep. Another distinguishing factor of IH is that daytime napping is typically unrefreshing, whereas for NT1/NT2 daytime naps seem to help. Diagnostics as per the ICSD-3-TR criteria include a patient interview and an overnight PSG, followed by a Multiple Sleep Latency Test (MSLT). The presence of early-onset REM periods (within 15 minutes of sleep onset), is a diagnostic hallmark of narcolepsy.

Extended PSGs (36-48 hours) tend to help differentiate between these hypersomnias [16,17], however, this adds burden to patients and is impossible to execute in clinical studies.

Objective measures relevant to CDH: Sleep onset latency; REM onset latency; sleep fragmentation

Cardiovascular conditions

Heart failure

Heart failure (HF) is a condition where an individual's heart is no longer functioning at full capacity and is no longer able to supply enough blood for the body to meet its needs. HF is associated with a disproportionately high prevalence of fragmented sleep, sleep deprivation, and sleep disordered breathing (SDB) [18]. AHA guidelines have identified sleep deprivation and poor sleep quality as barriers to self-care and treatment adherence in patients with HF.

In most cases, sleep disturbances in HF are captured with patient reported outcome instruments. Practitioners may request routine PSG in patients with chronic HF in order to classify the presence and type of SDB along with capturing sleep onset latency and sleep efficiency. Sleep evaluation can also be used prognostically: one prospective study has demonstrated that WASO > 40 min and N2 duration < 44% of TST were independent predictors of a combined endpoint of death or a cardiac event in patients with previous decompensation of HF [19]. Sleep quality as a risk factor leading to HF and sleep disturbance in post-HF patients are two areas of research which will likely advance in the near future.

Objective measures relevant to heart failure: sleep onset latency; sleep efficiency; wake after sleep onset; apneas; hypopneas, N2 duration.

Stroke

Stroke is an acute event with high severity that may result in lasting brain damage, long-term disability, and death. The role of sleep in helping to regulate cardio-vascular, renal, and metabolic systems is very significant. Nocturnal hypertension, in particular, is a major risk factor for stroke. First, it makes sense to consider sleep before and after the stroke incidence: 1) it is important to understand if there is a contribution of poor sleep quality to the risk of stroke, and 2) how stroke affects sleep function after the event. Secondly, stroke events follow circadian rhythmicity and show evening-morning distribution [20].

Persistent insufficient sleep and frequent interruptions (such as wakings and arousals) are suspected to be risk factors for the development of stroke. Conversely, it is well described that stroke could lead to the development of sleep disorders. Decreases in sleep efficiency and total sleep time and increased sleep onset latency have been found to occur in patients who suffered stroke. Sleep architecture is also altered following ischemic stroke in different cerebral locations, in particular reductions in slow wave sleep (N3) and REM sleep [20]. Finally, sleep disorders, such as ID, OSA, restless leg syndrome (RLS), and/or periodic leg movement during sleep (PLMS) may negatively influence recovery from stroke [21].

Objective measures relevant to stroke: total sleep time; sleep onset latency; sleep efficiency; arousal index; wake after sleep onset; REM duration and fragmentation; N3 duration.

Cardiac arrhythmias

Cardiac arrhythmias are irregularities in heartbeat that may impair the blood flow to the body. As in most cardiovascular conditions, the relationship between the pathophysiology and sleep function is bidirectional. One straightforward observation based on retrospective data from 403,187 UK biobank subjects found that healthy sleep reduces risks of developing Atrial Fibrillation (AF) and bradycardia after correcting for traditional risk factors [22]. The reverse effect of cardiac arrhythmias on sleep is mostly indirect through breathing-, depression-, and anxiety-related comorbidities. In particular, frequent palpitation (feeling of “pounding heart” or missing beat) may interfere with the sleep effort. Another link in comorbidity is prominent between OSA and cardiac arrhythmias [23].

Apart from EEG, electrocardiophysiological measures are one of the best physiological markers of sleep dynamics, especially if considered together with respiration [24]. This points to a tight relationship between neurophysiology of sleep and cardiac rhythm modulation [25]. In terms of objective sleep disturbance, a large 2018 study including 4553 participants of which 526 were patients with atrial fibrillation showed that these patients had more frequent nighttime awakenings. In a sample of patients with PSG recordings (n=1127), an association between decreased REM sleep and later atrial fibrillation was found [26]. Interestingly, insomnia symptoms predicted an increased risk of later atrial fibrillation.

Objective measures relevant to cardiac arrhythmias: wake after sleep onset; REM duration; sleep onset latency; total sleep time; heart rate variability; blood pressure variability, respiration rate.

Depression

Major Depressive Disorder (MDD) is diagnosed when an individual experiences at least 5 of the 9 depressive symptoms (depressed mood and/or loss of interest or pleasure, changes affecting appetite or weight, sleep, psychomotor activity, energy level, feelings of guilt, concentration ability, or suicidality; at least one of the symptoms must be either depressed mood or loss of interest or pleasure), nearly every day during the same 2-week period, that represents a change from previous functioning. Changes in sleep architecture associated with MDD are one of the most commonly reported issues.

The most common sleep complaints in MDD are insomnia and difficulty maintaining sleep, predominantly due to rumination. Patients also report hypersomnia as mentioned above, alongside fatigue, complaints of non-restorative sleep, excessive daytime sleepiness and sleep continuity issues [27, 28]. However, this is combined with a population who have poor insight into their own sleep and often incorrectly estimate aspects of their sleep onset latency and total sleep time [29]. Alongside these aspects of sleep disruption, the architecture also shows change in patients

with MDD. Reductions in slow wave N3 sleep, and in particular decreased time to first REM (REM onset latency), increased time spent in REM sleep, and increased REM density, or the amount of rapid eye movements during REM episodes are observed [30,31]. Such observed alterations in REM sleep have been shown to be predictive of MDD and treatment efficacy [32,33].

Alongside the sleep disturbance associated with MDD itself, the associated treatments can also have an impact on sleep. For instance, tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and monoamine oxidase inhibitors can be REM suppressing, which can result in a further delay in REM onset latency and decreased REM episodes in the early portion of sleep. However, some classes of antidepressants also have a negative impact on sleep, some reporting insomnia as a common side effect [34].

Objective measures relevant to depression: total sleep time; sleep onset latency; N3 duration; REM duration; REM density; REM onset latency; REM episodes.

Menopause

The menopausal transition is a phase of hormonal changes experienced by women, often with considerable impact on quality of life. It reflects the natural decline of sex hormone production as a consequence of ovarian aging. Physiologically, this transition stretches over a time period of several years (perimenopause) which is characterized by increased variability in sex hormone levels and menstruation.

The majority of women experience multiple symptoms associated with menopause. Vasomotor symptoms (VMS, i.e., hot flushes and night sweats), sleep disturbances, and mood changes are some of the most commonly reported symptoms, with VMS and sleep disturbances reported in approximately two thirds of women [35,36]. Sleep disturbances related to menopause most often are characterized by difficulties falling asleep and/or night-time awakenings. These symptoms often influence the overall quality of life and have an impact on family, relationships, intimacy, jobs, physical and mental health and wellbeing. While sleep disturbances associated with menopause are often of milder degree than required for a formal diagnosis of insomnia disorder, their high prevalence in an otherwise healthy and productive population makes it a topic of high societal and health-economic relevance.

Objective measures relevant to menopause: total sleep time; sleep onset latency; wake after sleep onset; skin/body temperature.

Parkinson's Disease

Parkinson's disease is a neurodegenerative condition characterized by motor features such as tremor, bradykinesia, rigidity, and postural instability. Among sleep disorders seen in PD patients are insomnia, excessive daytime sleepiness (EDS), restless legs syndrome (RLS), REM sleep behavior disorder (RBD), sleep apnea and circadian abnormalities [37,38,39]. While insomnia and EDS can sometimes display a bi-directional relationship, PD-related neurodegeneration and dysautonomia may influence sleep, including dysregulation of sleep/wake cycle in hypothalamus, dopamine deficiency, dystonia, loss of REM atonia, RLS, nocturia, anxiety, depression, and long-term effects of medication.

In the absence of other major comorbidities (such as depression), the causal relationship between disturbed sleep and onsets of neurodegenerative diseases, with PD being in majority of cases, can be convincingly established [40]. Excessive daytime sleepiness in PD patients is a significant concern, especially in early disease development when it could be manifested by sleep attacks, due to interference with normal daytime functions like driving [41,42]. The strength of the link between RBD, PD progression, and EDS depends on PD phenotype - not all patients develop the symptoms on the same severity level [43].

There are three main avenues in longitudinal monitoring of sleep disturbances in PD: micro-changes in sleep architecture (such as lower slow EEG density and a higher ratio of slow REM EEG frequencies) alongside macro-changes in sleep architecture (e.g., a reduction in TST and SE, and decreases in the duration of N3 and REM and an increased REM latency). Nocturnal limb and body movements have also been shown to be key sleep-related impacts of Parkinson's disease.

Objective measures relevant to Parkinson's Disease: total sleep time; sleep efficiency; N3 duration; REM duration; REM onset latency; sleep period movement frequency.

Discussion

This work outlines sleep measures, encompassing sleep staging, sleep-related events, and aggregate sleep measures, utilizing an array of tools ranging from the reference standard of sleep measurement (PSG) to at-home metrics (DHTs). In addition, aggregate measures of sleep are reviewed as they currently appear in the literature. Although these measures are based on PSG assessment, there is the possibility of using less intrusive technologies apt for remote data capture within home settings.

The cornerstone for sleep assessment/classification has been in-lab PSG. However, its applicability in depicting a typical night's sleep is limited due to its cost, patient burden, and logistical challenges.

In exploring the impact of sleep across selected key therapeutic areas, we identified several clinical measures of sleep function and associated disorders where it would be advantageous to measure using digital health technologies. The commonality in measurements across these therapeutic areas underscores the potential for a more generalized understanding of sleep's clinical implications (Table 2). However, despite the common use of some of these measures, standardization across the field is variable, as shown by the confluence of terms and definitions in Table 1.

The longitudinal advantage of digital sleep measures captured by at-home digital health technologies, especially when compared to PSG, provides for a holistic, 24/7, and more patient-centric approach to sleep assessment. This resonates with the evolving paradigm of healthcare due to the pandemic in 2020, but also transcends the conventional episodic evaluations. A transition towards a paradigm of more continuous measurement is not without challenges, yet the promise it holds for a better understanding and management of sleep across a spectrum of diseases is compelling.

Table 2: Key Measures of Sleep Architecture and Continuity

| |
|--|
| |
|--|

| Measurement parameter | Therapeutic area | | | | | Comment |
|---|------------------|--------|---|---|--------|---|
| | S D | C V | D | M | P D | |
| Sleep stages/ Hypnogram | ● | ● | ● | ● | ● | Once sleep stages are assigned to each 30-second epoch, they can be summarized in many ways such as total duration of each stage or the percentage of each stage within the sleep period. If a hypnogram can be reliably created, many aggregated measures can be derived - including the measures below in this table. For some sleep disorders, higher resolution sleep staging (<30-second epochs) is needed to evaluate the microarchitecture of sleep. |
| Sleep onset latency | ● | ● | ● | ● | ● | The duration (in minutes) between the beginning of TIB until sleep onset, defined as the first epoch scored as sleep. The definition of sleep onset varies across technologies. |
| Total sleep time | ● | ● | ● | ● | ● | The total duration (in minutes) of all epochs scored as sleep within the TIB period. |
| Sleep efficiency | ● | | ● | | | TST expressed as a percentage of TIB. Alternative denominators have been proposed, such as the sleep period (see Table 1). |
| Wake after sleep onset | ● | ● | ● | ● | ● | The total duration (in minutes) of all epochs scored as wake between sleep onset and sleep offset <i>or</i> between sleep onset and the end of the TIB period. |
| Awakenings, arousals and micro-arousals | ● | ● | | | | Awakenings are identified according to epochs scored as wake during the sleep period, whereas arousals are events occurring within epochs identifiable as abrupt shifts in EEG frequency (>16Hz) for at least three seconds preceded by at least 10 seconds of stable sleep. Microarousals are arousals of shorter durations and thus will not be captured in 30-second epoch aggregations. |

TIB: Time in Bed (see Table 1); TST: Total Sleep Time

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