Evidence Behind Digital Cognitive-Behavioral Therapy for Insomnia Among Real-World Populations With Chronic Insomnia

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Background

Chronic insomnia is a widespread and serious public health condition affecting approximately 15% of the U.S. adult population (Doghramji, 2006). On the heels of the Coronavirus 2019 (COVID-19) pandemic, insomnia has become even more relevant—and prevalent—with recent research indicating stress, anxiety, and worries related to COVID-19 have resulted in Americans getting significantly less sleep as well as lower quality sleep (Morin & Carrier, 2021). Insomnia is not only associated with long-term and potentially debilitating comorbidities such as depression, obesity, and cardiovascular disease, it is now considered a significant risk factor for numerous metabolic and cardiac conditions, including hypertension, myocardial infarction, heart failure, and type 2 diabetes (Reiman et al., 2017). Chronic insomnia also poses a substantial economic burden on patients and healthcare organizations, with direct and indirect costs in the United States exceeding $100 billion annually (Wickwire et al., 2019).

The most highly recommended insomnia treatment among sleep medicine experts is cognitive-behavioral therapy for insomnia (CBT-I), a nonpharmacologic intervention that involves, among other things, helping patients change thoughts and behaviors that can contribute to or exacerbate insomnia (e.g., having negative expectations for one's ability to get good sleep, spending greater amounts of time in bed) (Baglioni et al., 2020). CBT-I has been endorsed as a first-line treatment for insomnia across global practice guidelines, including those from the United States (Edinger et al., 2021; Qaseem et al., 2016), Europe (Reiman et al., 2017), the United Kingdom (Wilson et al., 2019), and Australia (Ree et al., 2017). CBT-I has repeatedly shown in randomized controlled trials, meta-analyses, and literature reviews to have potent effects against insomnia as well as strong effectiveness on co-occurring anxiety and depression (Gebara et al., 2018; Felder et al., 2020; Ye et al., 2015). Evidence suggests CBT-I is generally as effective in the short term (i.e., 4 to 8 weeks) and even more effective in the long term (e.g., more than 3 months) than sedative hypnotic medication, which, along with sleep hygiene education, comprise the typical treatment offered patients with insomnia (Baglioni et al., 2020; Mitchell et al., 2012).

As research into technology-based healthcare continues evolving, prescription digital therapeutics (PDTs) represent an alternative pathway to treatment for patients who are not referred to or otherwise do not receive CBT-I. In fact, numerous practice guidelines supporting CBT-I have commented on the importance of digitally delivered CBT-I to help extend treatment reach (Table 1). A recent consensus panel guideline developed with input from primary care physicians, psychiatrists, and clinical researchers concurred that insomnia is highly undertreated (Rosenberg et al., 2023). Undertreatment with CBT-I is in part a consequence of the small number of trained CBT-I providers in the United States and around the globe (Thomas et al., 2016; McCarthy et al., 2018). However, as noted in Rosenberg et al.'s (2023) consensus guideline, one of the benefits of CBT-I is its adaptability to a variety of formats, including digital delivery. Because PDTs are software-based treatments that can be accessed from smartphones or tablets, access to a CBT-I becomes much more broadly available. PDTs undergo a rigorous review of clinical evidence from clinical studies to become U.S. Food and Drug Administration (FDA) authorized and are subject to postmarketing requirements, as with many pharmacologic treatments. Patients can be prescribed digital CBT-I in the form of PDTs, which opens the option to providers across sleep medicine and other providers who treat chronic insomnia.

The only FDA-authorized chronic insomnia PDT currently on the market is Somryst® (originally studied as SHUTi), which gained authorization for use from the FDA in 2020 based on pivotal data demonstrating its efficacy and safety in improving insomnia severity in over 1,300 adults (Christensen et al., 2016; Ritterband et al., 2017). Because of the increased interest in the effects of PDTs in actual patients in terms of engagement, health economics, and other outcomes, recent research has sought to build on

the work of these foundational studies by engaging in real-world trials and retrospective analyses to better understand patients' use of and benefits from PDTs outside the clinical trial arena.

Table 1. Sample Listing of Global Practice Guidelines That Support CBT-I

Guideline Organization/Author	Country/Region
American College of Physicians (Qaseem et al., 2016; Brasure et al., 2016)	United States
American Academy of Sleep Medicine (Edinger et al., 2021; Sateia et al., 2017)	United States
Veterans Affairs/Department of Defense (VA/DoD, 2019)	United States
European Sleep Research Society (Reiman et al., 2017)	Europe
British Association of Psychopharmacology (Wilson et al., 2019; Wilson et al., 2010)	United Kingdom
Australasian Sleep Association (Ree et al., 2017)	Australia and New Zealand

Emerging Real-World Clinical Evidence

As an example of large-scale, real-world studies assessing the effects of digital CBT-I, the Digital Real-world Evidence trial for Adults with insomnia treated via Mobile (DREAM; NCT04325464) was launched to assess insomnia severity and sleep diary outcomes from a real-world population's PDT use (Thorndike et al., 2021). DREAM investigators collected data on a wide variety of clinical and patient-reported outcomes associated with the use of digital CBT-I, including but not limited to changes in insomnia severity, sleep diary parameters (i.e., sleep onset latency, wake after sleep onset, total sleep time, and sleep efficiency), excessive daytime sleepiness, depression, anxiety, and quality of life. The DREAM trial, which included over 1,000 patients recruited from 49 U.S. states, recently completed participant enrollment and end of treatment data collection; final results will likely be made public in 2023.

Interim findings from the DREAM study appear to already confirm the clinical effectiveness of digital CBT-I in real-world patients. In interim analyses, use of PDT-delivered CBT-I over 9 weeks (n=993) was associated with significant improvements ($p<0.0001$) in insomnia severity both at end of treatment and 6 months later (baseline to posttreatment Insomnia Severity Index [ISI] score 18.8 vs 11.3; baseline to 6 months 18.8 vs 12.1), as well as significant improvements in sleep diary parameters (Cohen's d effect sizes ranged mostly from 0.88–1.04) (Morin et al., 2022a, 2022b; Figure 1). Improvements were observed regardless of baseline severity of insomnia (Figure 2). At the end of treatment, 46% of patients were considered treatment responders, and nearly 30% achieved insomnia remission. Similarly, at 6 months, about 38% of patients were classified as treatment responders, and approximately 26% had achieved remission. Notedly, improvements in anxiety and depression were also observed with use of Somryst, with medium to large effects at the end of treatment and again 6 months later (all Cohen's d's range=0.45–1.63) (Morin et al., 2022a, 2022b).

Figure 1. Changes in Insomnia Severity With Treatment: DREAM Interim Results (Morin et al., 2022a)

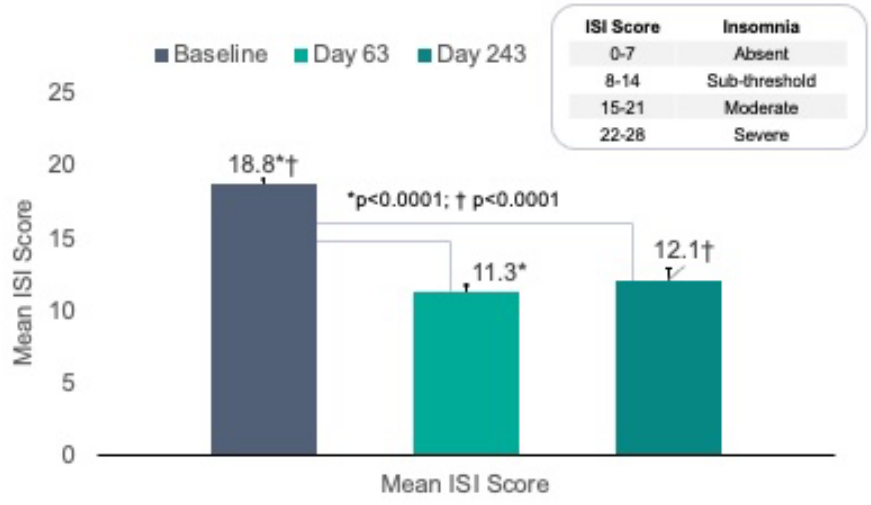
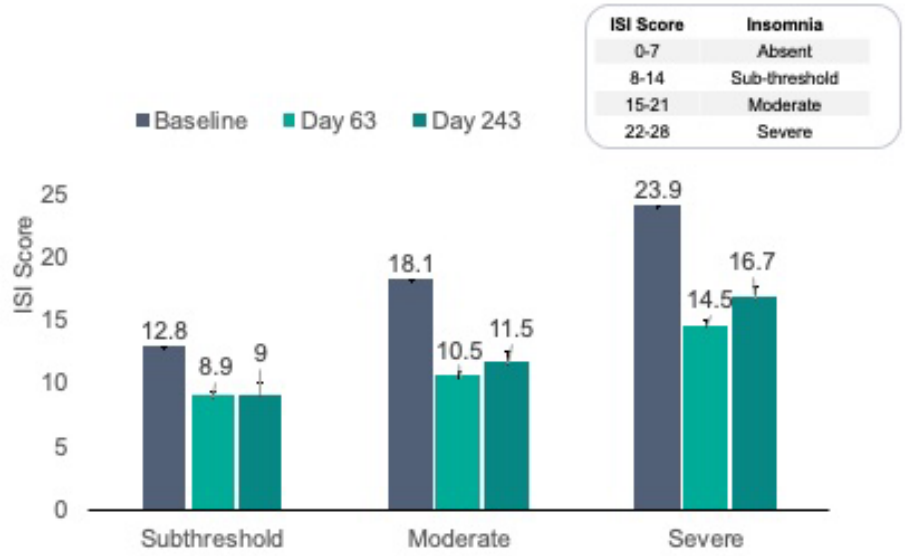


Figure 2. Changes in Insomnia Severity With Treatment by Baseline Insomnia Severity: DREAM Interim Results (Morin et al., 2022a)



The Clinicoeconomics of Treating Chronic Insomnia Through Digital CBT-I

Understanding the clinicoeconomics of digital CBT-I is an important part of real-world research given the substantial financial burden imposed by the disease. Total annual direct and indirect costs of insomnia have been estimated as high as $100 billion, with even higher costs estimated for the numerous patients with insomnia and comorbid conditions (Taddei-Allen, 2020). Payors, policymakers, and patients have a vested interest in understanding the extent to which treatments affect real-world populations not only in terms of improved disease control but also in terms of finances and resource use.

To that end, 2 recently published analyses help illuminate the impact of digital CBT-I on healthcare resource utilization (HCRU) in the chronic insomnia population. First, Forma et al. (2022a) used a pre/post design to look at clinical outcomes and healthcare claims before and after 248 patients accessed the Somryst PDT over a 24-month period. Clinically, insomnia improved, with a 37% decrease in ISI score at the end of the 9 weeks of treatment (decreased from 19.1 to 12.0). Further, almost 59% of patients achieved meaningful treatment response, and nearly 27% achieved insomnia remission. Economic and HCRU data also showed important findings. During the 24 months after accessing the PDT, patients had 52% fewer emergency department visits and 13% fewer outpatient hospital visits than they had in the 24-months before using the PDT. There was also an 18.5% decrease in the number of patients using sleep medication before using Somryst compared with after (52.4% vs 42.7%). Notably, the 24-month total cost savings from using Somryst was $510,678, which amounted to $2,059 in savings per patient (Forma et al., 2022a).

At ISPOR Europe 2022, findings were presented from a similar, more recent analysis that compared 24-month clinical and economic outcomes among 2 groups of patients—those who used Somryst versus a matched control group who did not use the PDT but were treated with sleep aid medication (Forma et al., 2022b). At 24 months following PDT initiation, this case-control analysis—again of 248 matched patients—similarly found numerous reductions in HCRU, including a 59% decrease in emergency department visits, a 55% decline in hospitalizations, a 36% decrease in hospital outpatient visits, a 23% reduction in ambulatory surgical center services, and a 7% decline in office visits. Findings also reported an estimated $8,202 cost reduction per patient compared to controls over a 24-month period (Forma et al., 2022b).

Taken together, these data confirm, using 2 different analytic approaches from claims data, how PDT use resulted in a reduction in healthcare utilization and corresponding cost savings for real-world patients with chronic insomnia. Although the cost reductions cannot be guaranteed to occur in every patient population, these analyses demonstrate trends in decreases in emergency department use, hospitalizations, and other reductions to the overburdened healthcare system during a time when chronic insomnia is becoming more prevalent. This suggests PDT-delivered CBT-I is not only effective but can potentially help reduce patient financial burdens as well.

Digital Trials: The Future of Insomnia Research?

One notable advantage of the DREAM trial that could be leveraged by future real-world PDT studies was its unique design as a fully digitally conducted clinical trial. Digital clinical trials have become an increasingly appealing approach to research as technology-based medicine has advanced—especially as we emerge from the COVID-19 pandemic and continue to witness the benefits of telemedicine in reducing access and treatment gaps (Inan et al., 2021). Indeed, the trial successfully enrolled participants and implemented study interventions during the COVID-19 pandemic, when people frequently experienced significant barriers accessing mental health care (Cenat et al., 2021; Sukut & Ayhan Balik, 2020).

One reason why digital clinical trials are attractive is their potential to help overcome challenges associated with traditional clinical trials that have resulted in low participant enrollment, especially among marginalized populations such as racial/ethnic minorities and rural dwellers. Specifically, digital trials have the potential to improve enrollment by expanding catchment areas (Naik et al., 2020). As a fully decentralized trial, DREAM was able to enroll participants from nearly every U.S. state. Digital clinical trials can also potentially save participants time and money by reducing the need for in-person study visits, meaning participation is easier and more accessible (Naik et al., 2020). They can also make recruitment more efficient by leveraging innovative, technology-based recruitment methods (e.g., use of national social media platforms) and by making participation more appealing due to the reduced burden of in-person visits. In some cases, digital clinical trials may even help save money by making recruitment faster,

data collection and follow-up more efficient, and administrative costs less expensive (Inan et al, 2020; Naik et al., 2020).

In addition to the DREAM study, there is also an ongoing pragmatic trial (NCT04909229) from researchers at Yale University and the Mayo Clinic (Dreyer et al., 2022) that is exploring Somryst, looking at engagement and outcomes with the PDT alongside Fitbit and the Hugo Health data-aggregating platform for data collection. This study was supported by the Medical Device Innovation Consortium on behalf of the National Evaluation System for health Technology Coordinating Center (6292-2019-R2TC-B18) initiative funded by the FDA. While the treatment itself is digital in nature, integrating digital health technologies into remote trial settings allows for linking and aggregating data from multiple sources to provide a more holistic view into patients' experiences and outcomes.

Conclusion

Chronic insomnia has historically been grossly undertreated. The availability of PDT-delivered CBT-I as an effective treatment option could help close treatment access and outcome gaps while offering some degree of relief to the healthcare system through reduced spending and healthcare resource use by patients. However, there is still much to learn about the full range of outcomes that PDTs can generate, which will likely be the subject of research going forward. In the meantime, Pear is excited to be a part of the digital trends and other research working to diminish health inequities, improve quality of care, and ensure patients receive much-needed treatments.

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