The Costs and Value of a Prescription Digital Therapeutic for Chronic Insomnia

The sleep disorder insomnia is characterized by difficulty falling asleep, staying asleep, or both, despite having adequate opportunity to sleep. In the U.S., approximately 30% to 40% of adults experience some form of insomnia symptoms in a year.[1]

The formal diagnosis of insomnia disorder, as defined by the *DSM-5*, occurs in about 6% to 10% of adults.[2] Up to 10% of adults experience short-term insomnia, which lasts from a few days to a few weeks. However, a portion of cases of short-term insomnia will transition to chronic insomnia that can persist for years.[3]

The Clinical and Economic Burden of Insomnia

Insomnia is associated with several medical comorbidities (such as heart disease, gastroesophageal reflux disease, respiratory issues, and chronic pain) and psychiatric disorders (such as anxiety and depression).[4] It also is known to adversely affect individuals' quality of life, academic performance, productivity at work, and other aspects of daytime functioning. Adults who report experiencing insomnia also have a higher incidence of motor vehicle-related accidents and falls.[5]

The sleep disorder has a substantial economic burden, through both direct and indirect costs. Direct costs refer to office visits, medication costs, and testing; indirect costs refer to lost resources, such as absenteeism, presenteeism, work- and non–work-related accidents.[6]

A 2019 study published in *Sleep* calculated the health care utilization costs of insomnia by comparing 151,668 Medicare beneficiaries diagnosed with insomnia to 333,038 beneficiaries without a sleep disorder during the same period.[7] The researchers found that patients with untreated insomnia had higher health care utilization across all point of service locations. Rates of utilization were highest for inpatient care and lowest for prescription fills. Together, this translated to $63,607 more in all-cause costs for patients with insomnia versus controls. The increase was primarily driven by inpatient care ($60,900), followed by relative increases in emergency department ($1,492) and prescription costs ($486).

The Costs of Treating Insomnia

Pharmacotherapy is the most common treatment modality for insomnia, with 4% of U.S. adults taking prescription drugs to treat insomnia each year.[8] The number of prescriptions filled for sleep aids in the U.S. has increased in the past two decades, despite clinical guidelines from the American Academy of Sleep Medicine (AASM) grading the evidence supporting the use of pharmacologic agents in the treatment of insomnia as "weak."[9] Insomnia medications may also carry negative side effects, such as headache, grogginess, difficulty remembering, and difficulty concentrating.[10] In 2019, the U.S. Food and Drug Administration (FDA) issued a boxed warning on common insomnia drugs, including eszopiclone (Lunesta), zaleplon (Sonata), and zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, and Zolpimist), following reports that patients who took one of these nonbenzodiazepine hypnotics suffered serious injury or death from an activity they performed unconsciously.[11]

AASM Clinical Practice Guidelines recommend cognitive behavioral therapy for insomnia (CBT-I) as first-line treatment for all patients with chronic insomnia, including those whose insomnia has not responded to chronic hypnotic medications.[12] In addition, the American College of Physicians (ACP) recommends CBT-I as a first-line treatment for chronic insomnia before turning to pharmacologic therapy.[13]

CBT-I combines cognitive therapy, stimulus control therapy, and sleep restriction therapy, with or without relaxation therapy. It typically is delivered through in-person sessions with a trained therapist, but it can also be delivered virtually through prescription digital therapeutics.[14] Recently, the FDA has focused on the potential for digital health products, including software and mobile apps, to overcome barriers to access, and, in March 2020, it authorized Somryst® as the first prescription-only digital therapeutic cleared to treat adults aged 22 years or older with chronic insomnia.[15]

Somryst is intended to provide a neurobehavioral intervention (CBT-I) in patients 22 years of age and older with chronic insomnia. FDA review was supported by data from two randomized controlled trials evaluating the effectiveness of the therapeutic among more than 1,400 adults with chronic insomnia. In the first trial of 303 patients with chronic insomnia, treatment with Somryst led to clinically meaningful improvements in insomnia severity, sleep onset latency (SOL), and wake after sleep onset (WASO), compared with the active control.*[16] In the second study, which included 1,149 adults with chronic insomnia and depressive

symptoms, a 9-week course of treatment with Somryst resulted in a significant reduction in insomnia severity measurements compared with controls.[17] These benefits persisted over an 18-month period.[18]

Somryst is comprised of a patient-facing therapeutic software application and a clinician-facing dashboard that facilitates health care providers' insight into the patient using Somryst and tracking of patient treatment and progress. The dashboard reports on validated clinical measurements such as the Insomnia Severity Index (ISI), the patient's use of the app, and sleep metrics derived from nightly sleep diaries such as SOL and WASO.

Two posters presented at AMCP 2021, AMCP's annual meeting held virtually on April 12-16, 2021, evaluated the potential value of a prescription digital therapeutic (PDT) for CBT-I in terms of cost-effectiveness and its shown impact on health care payer and employer budgets.[19,20]

The Cost-Effectiveness of Digitally Delivered CBT-I

In the first analysis, researchers led by Fulton Velez, MD, MS, MBA, evaluated the cost-effectiveness of the chronic insomnia PDT compared with other available treatments to inform value assessments and health care decision-making.†[19]

Study methods and design

The analysis compared the PDT with face-to-face CBT-I and branded and generic prescription insomnia medications. Medications included suvorexant, eszopiclone, zolpidem tartrate, ramelteon, and benzodiazepines.

To measure cost-effectiveness, the researchers developed a 3-year Markov model (6-month cycles of remitted/non-remitted health states). Two perspectives were evaluated: U.S. third-party health care payer (direct medical costs) and employer (defined as direct medical costs plus indirect costs of lost productivity).

Insomnia remission (defined as a score <8 on the ISI) served as the measure of clinical effectiveness. The proportions of ISI remitters at 6 and 12 months were derived from the most recent values sourced from clinical trials.

Based on published literature, a health state utility value of 0.8413 was assigned to remitted patients, and a value of 0.7603 was assigned to non-remitted patients.

Regarding costs, the PDT was $900, and researchers assumed that patients were only treated once with the PDT. For CBT-I, they estimated that patients underwent 8 CBT-I sessions, at a cost of $120 per session ($960 total), based on market research. Costs of medication were derived from the Redbook, and, based on published literature, it was assumed that 18.7% of patients taking prescription insomnia medications took them for a short duration (3 months) and 81.3% took them chronically (over the entire year). Cost details are presented in **TABLE 1**.

The PDT and CBT-I were both expected to reduce the use of concomitant insomnia medications from 40.1% at baseline to 33% at 12 months, as observed in the pivotal trials for the PDT.

The model assessed the costs of the PDT, traditional CBT, prescription insomnia medications, and physician visits for chronic insomnia, as well as direct medical costs (6-monthly costs remitted: $983; non-remitted: $1,403) and indirect costs (remitted: $1,315; non-remitted: $1,965).

Results

The study authors reported that the PDT was economically dominant (more effective and less costly) versus branded prescription insomnia medications from both a health care payer and an employer perspective. Looking at generic prescriptions, the PDT was cost-effective (more effective and more costly).

In contrast, the PDT was equally effective to and less costly than, traditional CBT-I from both a health care payer perspective and an employer perspective.

In terms of costs related to clinical outcomes, the comparison of incremental total costs and incremental quality-adjusted life years (QALYs) gained favored the PDT. For example, the incremental cost-effectiveness of the PDT versus generic eszopiclone was $19,852/QALY from a health care payer perspective and $11,871/QALY from an employer perspective (See **TABLE 2** for more comparisons). The researchers added that the costs of managing potential adverse events were excluded from this model, suggesting that the results of the analysis are likely to be conservative regarding costs of PDT versus medications.

"Incremental cost-effectiveness results were most sensitive to the remission rate of comparators, the cost of prescription sleep medications, the adherence rate of prescription sleep medications, and the cost of the PDT," the authors reported. Other sensitivity analyses revealed that the PDT was consistently the dominant treatment option (i.e., more effective and less costly) compared with branded prescription sleep medications. The cost savings with the PDT were greatest when comparing it with branded eszopiclone and zolpidem tartrate.

TABLE 1. Costs of prescription insomnia medications

Treatment	Pack Size (Pills)	Cost per Pack (WAC)	Adherence (%)	Annual Cost
BELSOMRA / suvorexant	30	$365.70	80.0%	$3,561.92
LUNESTA / eszopiclone	30	$470.40	80.0%	$4,581.70
AMBIEN / zolpidem tartrate	100	$1,859.42	80.0%	$5,433.23
ROZEREM / ramelteon	100	$1,296.74	80.0%	$3,789.07
Generic eszopiclone	100	$71.54	80.0%	$696.83
Generic zolpidem tartrate	100	$13.74	80.0%	$40.16
Generic benzodiazepines	100	$11.39	80.0%	$33.28

Presented at the AMCP virtual meeting, April 12 to 16, 2021; corresponds to Table 2 in Poster F26 and Table 2 in Poster F27. [19,20]

TABLE 2. Incremental costs, quality-adjusted life years, and cost-effectiveness

Comparator	Incremental Total Health Care Payer Cost	Incremental Total Employer Cost	Incremental QALYs-Gained	Incremental Health Care Payer Cost-Effectiveness Ratio (ICER)	Incremental Employer Cost-Effectiveness Ratio (ICER)
CBTi	$175	$175	0.0000	PDT Dominates	PDT Dominates
BELSOMRA® / suvorexant	$(6,957)	$(7,402)	0.0555	PDT Dominates	PDT Dominates
LUNESTA® / eszopiclone	$(9,328)	$(9,491)	0.0203	PDT Dominates	PDT Dominates
AMBIEN® / zolpidem tartrate	$(11,461)	$(11,624)	0.0203	PDT Dominates	PDT Dominates
ROZEREM® / ramelteon	$(7,343)	$(7,505)	0.0203	PDT Dominates	PDT Dominates
Generic eszopiclone	$403	$240	0.0203	$19,852	$11,871
Generic zolpidem tartrate	$2,048	$1,885	0.0203	$101,113	$93,092
Generic benzodiazepines	$2,065	$1,903	0.0203	$101,964	$93,943

Corrected version of Table 4 in Poster F26 presented at the AMCP virtual meeting, April 12 to 16, 2021.[19]

TABLE 3. Health care payer cost results for comparators versus the PDT

TREATMENT	YEAR 1	YEAR 2	YEAR 3	TOTAL OVER 3 YEARS
Somryst®	$420,787	$849,886	$1,280,712	$2,551,385
BELSOMRA® / suvorexant	$(108,015)	$(217,607)	$(328,793)	$(654,414)
LUNESTA® / eszopiclone	$(126,752)	$(255,354)	$(385,827)	$(767,933)
AMBIEN® / zolpidem tartrate	$(143,604)	$(289,304)	$(437,124)	$(870,031)
ROZEREM® / ramelteon	$(111,065)	$(223,753)	$(338,079)	$(672,897)
Generic eszopiclone	$(66,492)	$(133,955)	$(202,400)	$(402,847)
Generic zolpidem tartrate	$(49,165)	$(99,047)	$(149,655)	$(297,867)
Other generics	$(48,983)	$(98,681)	$(149,102)	$(296,767)
TOTAL	$(233,288)	$(467,814)	$(710,268)	$(1,411,370)

Presented at the AMCP virtual meeting, April 12 to 16, 2021; corresponds to Table 3 in Poster F27.[20]

TABLE 4. Employer cost results for comparators versus the PDT

TREATMENT	YEAR 1	YEAR 2	YEAR 3	TOTAL OVER 3 YEARS
Somryst®	$706,803	$1,426,093	$2,151,332	$4,284,228
BELSOMRA® / suvorexant	$(148,350)	$(298,867)	$(451,573)	$(898,790)
LUNESTA® / eszopiclone	$(164,853)	$(332,112)	$(501,805)	$(998,770)
AMBIEN® / zolpidem tartrate	$(181,705)	$(366,062)	$(553,102)	$(1,100,869)
ROZEREM® / ramelteon	$(149,166)	$(300,511)	$(454,057)	$(903,734)
Generic eszopiclone	$(117,294)	$(236,300)	$(357,037)	$(710,630)
Generic zolpidem tartrate	$(99,966)	$(201,391)	$(304,292)	$(605,650)
Other generics	$(99,784)	$(201,026)	$(303,740)	$(604,550)
TOTAL	$(254,315)	$(510,176)	$(774,274)	$(1,538,765)

Presented at the AMCP virtual meeting, April 12 to 16, 2021; corresponds to Table 4 in Poster F27.[20]

The Budget Impact of Insomnia Therapeutics

In a second analysis, Dr. Velez and colleagues evaluated the 3-year budget impact of the chronic insomnia PDT from a health care payer and employer perspective.[20]

Study methods and design

The budget impact was expressed as the cost difference between a world with and a world without the PDT. As with the cost-effectiveness analysis, comparators to the PDT included face-to-face CBT-I, branded medications, and generic medications.

For the analysis, the researchers estimated per member per month (PMPM) costs and per patient per month (PPPM) costs over 3 years for an insurance plan with 1 million members. Based on published literature and unpublished clinical data, the annual growth rate of the plan was estimated as 0.73%.

The proportion of adult plan members was 77%, and the prevalence of chronic insomnia among those members was 6%. A large portion (79%) of the members with chronic insomnia were assumed to be treated with prescription insomnia medications.

This budget impact model used the same estimated costs and outcome measures as those in the cost-effectiveness analysis (**TABLE 1**). The authors added that in this study, it was assumed that the PDT took half of its market share from branded products and half from generic products.

Results

The budget impact model results showed that the PDT had a net positive impact on the health care budget, defined as lower costs from both a health care payer and employer perspective (**TABLES 3** and **4**), although the results were slightly more pronounced from the employer perspective.

Key Takeaways:

- Chronic insomnia is associated with increased health care costs.
- Prevalence of insomnia increases with age.
- CBT-I is the recommended first-line therapy for chronic insomnia.
- A prescription digital therapeutic (PDT) for chronic insomnia was shown to be associated with reduced health care costs in budget impact modeling and may help provide more patients with access to CBT-I.
- In cost-effectiveness analyses, the PDT was shown to be either economically dominant (lower cost, more effective) or cost-effective (higher cost, more effective) versus pharmacological therapies or in-person CBT-I.

A world with the PDT was less costly than a world without the PDT, the authors continued, meaning that total costs for a plan with 1 million members, PMPM costs, and PPPM costs were lower in a world with the PDT.

Sensitivity analyses revealed substantial cost savings with the availability of the PDT for both health care payers and employers, accounting for Somryst market share and upfront costs, as well as prices and adherence to prescription insomnia medications.

The authors concluded that the "estimated total costs, PMPM costs, and PPPM costs are lower in a world with the PDT compared to a world without the PDT for the treatment of chronic insomnia." The authors noted that the model does not account for the cost of delayed provision of CBT-I and for additional benefits beyond disease treatment and productivity loss costs.

Conclusion

This cost-effectiveness analysis and budget impact analysis favored the PDT Somryst for the treatment of patients with chronic insomnia, from the perspective of both payers and employers. This information can be used in value assessments and health care decision making, the authors explained.

However, the findings of these analyses are limited by assumptions about disease states and treatment patterns, the researchers noted, writing that "the model represents a simplification of the complex interplay of the factors associated with patient outcomes." Therefore, they concluded, "results should be interpreted with care as clinical data was obtained from individual clinical trials and not from an indirect treatment comparison."

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*Somryst was tested under the name Sleep Healthy Using the Internet (SHUTi), an early version of Somryst with equivalent content. In clinical studies, Somryst demonstrated persistent results at 6- and 12-month follow-ups. Somryst users may not experience any or all of these benefits.

†Dr. Velez is an employee of Pear Therapeutics.

Somryst Important Safety Information: www.somryst.com/#isi-wrap