Article published online: 2024-10-23

Medical Professionals and Pharmacological Intervention for the Treatment of Insomnia: A Cross-Sectional Study

Antonios Liaskopoulos[1] Vasileios Kakouris[2] Nikolaos Liaskopoulos[3,4] Andreas S. Lappas[3,5] Nikolaos Christodoulou[3] Myrto Samara[3]

[1] Psychological Applications in Health Postgraduate Studies, Faculty of Health Sciences, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece
[2] Department of Psychology, School of Philosophy, National and Kapodistrian University of Athens, Greece
[3] Department of Psychiatry, Faculty of Medicine, University of Thessaly, Larisa, Greece
[4] Psychiatric Clinic, General University Hospital of Larissa, Larissa, Greece
[5] Department of Geriatric Psychiatry, Aneurin Bevan University Health Board, Newport, Wales, United Kingdom

Address for correspondence Antonios Liaskopoulos, BA, MSc (e-mail: antonisliask@yahoo.gr).

Sleep Sci

Abstract

Objective To explore the preferences of medical practitioners concerning various medications and other remedies to manage insomnia, and to ascertain whether these preferences are associated with their respective medical specialties.

Materials and Methods Employing the snowball sampling technique, we administered two versions of a questionnaire to an international group of medical professionals, including trainees and specialists from diverse medical backgrounds.

Results Zopiclone, zolpidem, and mirtazapine were evaluated as the most effective treatments for insomnia, while physicians would typically avoid using other tricyclic antidepressants, dual orexin receptor antagonists, and tryptophan for insomnia treatment. Noteworthy statistical correlations between physicians' specialty and preferred drug therapy, were observed in three out of five cases: 1) first-line drug treatment for short-term intervention against insomnia; (2) second-line treatment for long-term intervention; and 3) cases involving the elderly.

Discussion Psychiatrists demonstrated a greater preference for antipsychotics and antidepressants for the treatment of insomnia compared with other physicians. Conversely, other medical professionals exhibited a preference for benzodiazepines and Z-drugs (zopiclone and zolpidem). Although Z-drugs were evaluated as the most effective in the treatment of insomnia, in the clinical practice, physicians administer or would administer antidepressant or antipsychotic drugs more often (mirtazapine and quetiapine respectively). Regarding Dual Orexin Receptor Antagonists (DORAs), the high prevalence of "Do not know/No opinion" answers implies that our sample was not familiar with this innovative treatment.

Keywords
- preference
- insomnia
- drugs

received
December 8, 2023
accepted after revision
July 24, 2024

DOI https://doi.org/10.1055/s-0044-1791238.
ISSN 1984-0659.

© 2024. Brazilian Sleep Association. All rights reserved.
This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Approximately 1 in 3 people each year complain of insomnia symptoms.[1] According to one study,[2] in 74% of these cases, the patients report insomnia for at least 1 year, with the most vulnerable groups being women, the elderly, and people with a history of chronic insomnia.

A recent survey[3] found that insomnia affects around 30% of the population of the United States, and 5 to 15% of these individuals experience chronic insomnia. In Greece, the percentage of insomnia in the general population has been estimated at around 25%,[4] while a more recent survey[5] on middle-aged people showed that this percentage amounts to 18.3% and, among the elderly population, another study[6] has reported that the percentages range from 39.2 to 45%.

Every year, insomnia leads to approximately 5.5 million people visiting a physician,[7] and their request is usually expressed through complaints of difficulties starting and maintaining sleep, waking up early in the morning or during the night or simply low-quality sleep, that does not provide rest.[8]

According to the European Sleep Research Society's European guideline for the diagnosis and treatment of insomnia,[9] whose target audience includes all clinicians involved in the management of this condition, the diagnostic procedure for insomnia and its comorbidities should include a clinical interview consisting of the current sleep history, which specifically includes sleep habits such as sleep/wake schedules, bedtime routine, sleep environment, nocturnal behavior, and work schedules. It is also important to obtain a brief social and medical history to identify any predisposing factors, such as factors that cause an acute episode of insomnia and those that lead to the maintenance of the problem, when the condition becomes chronic.[8] The assessment can be performed through self-report methods, such as sleep diaries and questionnaires, and electronic devices such as actigraphy, a device worn on the wrist that records movements during sleep, as well as other personal monitoring devices whose results have, however, often been accused of being misleading and inaccurate.[10]

Nevertheless, in case of suspicion of the existence of other sleep disorders due to a physical problem, medical tests are strongly recommended, specifically polysomnography, as it is the most reliable method of assessing and identifying insomnia.[9]

Regarding the therapeutic approach, cognitive-behavioral therapy (CBT) is proposed as the first choice, with strong effectiveness for all ages and, if not available or ineffective, pharmacological interventions are applied, with benzodiazepines, benzodiazepine receptor agonists, and some antidepressants being indicated for short-term treatments (shorter than 4 weeks), while antihistamines, antipsychotics, melatonin, phytotherapeutics, and complementary or alternative treatments (such as light therapy, homeopathy, and acupuncture) are contraindicated due to insufficient reliability.[9]

Antagonists (daridorexant; used for up to 3 months) and prolonged-release melatonin (used for up to 3 months in patients $\geq$ 55 years) were added to the updated European Insomnia Guideline,[11] while fast-release melatonin continues to be contraindicated. The joint statement of five Italian scientific societies[12] also agrees with these guidelines, with the addition of Z-drugs (zopiclone and zolpidem), and the strict labeling for short-term use of pharmaceutical interventions (shorter than 4 weeks).

In a report[13] aiming to create a clinical practice guideline after 35 randomized controlled trials (RCTs) of pharmaceutical substances, the American College of Physicians suggested the use of eszopiclone, zolpidem, and suvorexant, while benzodiazepines, antidepressants, and melatonin did not appear to be effective options and showed increased risks for the development of dementia as well as injuries. After 1-year, the American Academy of Sleep Medicine recommended, in the Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults,[14] the use of the following drugs: suvorexant, eszopiclone, zaleplon, zolpidem, triazolam, temazepam, ramelteon, and doxepin; and they did not recommend the use of the following drugs: trazodone, tiagabine, diphenhydramine, melatonin, tryptophan, and valerian.

A more recent meta-analysis of 64 systematic reviews on the effectiveness of pharmacotherapies for insomnia[15] found that zolpidem, suvorexant, doxepin, and melatonin were systematically effective, while temazepam, triazolam, zopiclone and trazodone were sometimes effective for treatments shorter than 16 weeks. Numerous studies conducted during the last decade have focused on determining the preferred pharmaceutical intervention among medical practitioners to manage insomnia, including benzodiazepines, Z-drugs, antidepressants, antihistamines, antipsychotic agents, orexin receptor agonists (ORAs), and melatonin receptor agonists (MRAs). Not all studies, however, come to the same conclusion, and suggestions and opinions on the effectiveness of drugs for the treatment of insomnia differ due to the absence of a commonly-accepted framework.

Benzodiazepines and Z-drugs have been used systematically for insomnia treatment as they bind to the receptor complex of neurotransmitter gamma-amino butyric acid (GABA), causing anxiety reduction, sleepiness, and muscle relaxation, although each substance targets a different receptor subset.[16] A meta-analysis of 105 RCTs in adults using benzodiazepines and Z-drugs[17] showed that the two classes of drugs had similar effect sizes in improving both objective and perceived sleep quality, and that Z-drugs were safer compared with benzodiazepines, for they caused fewer side effects. Furthermore, a meta-analysis of 24 studies on the effectiveness of benzodiazepines and Z-drugs in people older than 60 years of age[18] showed that benzodiazepines were more effective in reducing the number of awakenings and increasing total sleep time, although they caused more cognitive side effects. It has also been observed that both benzodiazepines and Z-drugs increase the risk of falling in the elderly, although Z-drugs carry a lower risk of dependence and memory loss.[19] A cross-sectional study conducted in France[20] has shown that physicians prefer benzodiazepines and Z-drugs for the treatment of insomnia. It is also noteworthy that Z-drugs have been prescribed to 1% of the

 © 2024. Brazilian Sleep Association. All rights reserved.

Greek general population at least once over the course of a year.[21] Some professionals seem to prefer Z-drugs over benzodiazepines and other drug treatments.[22] Meanwhile, some studies suggest that other drug treatments are preferred over benzodiazepines,[23,24] while others mention a reluctance toward both benzodiazepines and Z-drugs.[25]

At the same time, several studies endorse the advantageous effects of specific antidepressant drugs for individuals suffering from insomnia. The reasons that have led to the use of antidepressants for the treatment of insomnia were their previous use in the treatment of chronic pain, which results in the reduction of pain-related sleep disturbances, the improvement of sleep problems in patients suffering from depression, and the absence of a specific time limit on their use, making them a promising solution for the long-term treatment of disorders such as chronic insomnia.[26] These dative tricyclic antidepressants (TCAs), mirtazapine, mianserin, and antagonists targeting serotonergic 5-HT2 receptors (such as trazodone and nefazodone), demonstrate sleep-improving properties.[27]

The clinical practice of the past decade (2003–2015) has shown that both TCAs – especially amitriptyline – and other antidepressants (particularly trazodone) are commonly used off-label for the treatment of insomnia.[27,28] Indeed, in an online survey using a case vignette, 80% of the respondents, who were clinicians, preferred the off-label use of sedative antidepressants such as trazodone and other medications not approved by the United States Food and Drug Administration (FDA), such as melatonin, for the treatment of insomnia.[25]

A recent meta-analysis[29] on the effects of antidepressants on insomnia treatment found that the drugs significantly improved total sleep duration compared with placebo, the dropout rate was low, but significant side effects were observed, mainly next-day somnolence. Furthermore, a meta-analysis of 31 studies[30] compared the efficacy of benzodiazepines, Z-drugs, and antidepressants, concluding that benzodiazepines showed the highest efficacy, followed by Z-drugs and, finally, antidepressants. It is also worth mentioning that the off-label use of antipsychotics has been pursued as a therapeutic approach to manage insomnia as well.[31,32] A meta-analysis of 21 clinical trials[33] confirmed the effectiveness of quetiapine in increasing sleep duration, especially in cases of comorbid insomnia with other disorders, but the side effects were frequent and severe to such an extent that they led patients to abandon the treatment.

Furthermore, a case study[34] examining a patient with persistent and chronic insomnia demonstrated that with a progressive increase in quetiapine dosage due to the decline of its effect over time, the treatment of the disorder was effective and without serious side effects. This finding implies that quetiapine shows great potential as an alternative in selected cases of treatment-resistant insomnia.[34]

It should be mentioned that prescriptions of ORAs and MRAs have increased over time.[35] Orexin is a neuropeptide that plays a crucial role in the maintenance of arousal through the continuous stimulation of wake-promoting brain centers, meaning that antagonists to the orexin receptors could reduce wakefulness, thus helping to treat insomnia.[36,37]

A meta-analysis[38] has demonstrated that Dual Orexin Receptor Antagonists (DORAs), at appropriate dosages, exhibit both efficacy and safety in the treatment of insomnia. For instance, suvorexant 20 mg, filorexant 5 mg, and lemborexant 10 mg were pointed out for their beneficial outcomes.[38] In fact, experts in the field of insomnia acknowledge the positive effects of both lemborexant and suvorexant as the first-line treatment for insomnia.[39] A systematic review and network meta-analysis concur that lemborexant exhibits the most favorable profile concerning efficacy, acceptability, and tolerability, both in the context of the short and long-term treatments for insomnia, despite the fact that its safety data were still inconclusive.[40]

Overall, melatonin did not show significant benefits[40] and further support from scientific evidence is required to prove its effectiveness in primary insomnia, while it appears to exhibit some efficacy in the context of secondary insomnia.[41] A meta-analysis of 24 RCTs[42] confirmed the inefficacy of melatonin for the treatment of insomnia, but another meta-analysis of 22 studies[43] concluded that melatonin, to a lesser extent, and ramelteon, to a greater extent, are effective for the treatment of insomnia. Finally, melatonin is milder compared with other drugs, and it seems appropriate for children and adolescents, as it reduces their insomnia without significant side effects.[44]

In light of these considerations, a survey to explore physicians' preferences regarding the treatment of insomnia in different real clinical practice scenarios was conducted. The present study specifically aims to highlight the differences in the prescription of medications for the treatment of insomnia among psychiatrists and non-psychiatrists, as well as to look for possible explanations behind these differences. To our knowledge, the present is the first study to explore the association between drug preference and medical specialty. The knowledge of previously unrevealed pharmacological patterns among medical professionals concerning insomnia treatment can be used to enhance physicians' education regarding pharmaceutical substances and to establish proper pharmaceutical practices in the future regarding insomnia treatment.

Materials and Methods

Participants

In the present cross-sectional study, the snowball sampling technique was employed in data collection. This process took approximately 45 days to complete. The questionnaires were initially administered to local National Health Service hospitals and health centers in Greece. The questionnaires were also dispatched to randomly chosen medical professionals from publicly-available databases and other online sources, and were also promoted on relevant, medicine-orientated social media platforms. At the same time, medical professionals practicing in other countries, with some level of acquaintance with the authors of the current study, were invited to complete the questionnaire. No email addresses or personal data were obtained in any case. The final sample consisted of 149 participants who filled out the survey,

 © 2024. Brazilian Sleep Association. All rights reserved.

encompassing trainee or qualified psychiatrists, general practitioners, surgeons, and physicians in a medical specialty or other medical fields.

The survey obtained official approval from the Committee for Bioethics and Ethics of the School of Medicine at Aristotle University of Thessaloniki (under identification number 43/2023). Prior to the commencement of the study, informed consent was obtained from all participants, and we ensured that they were provided with comprehensive and pertinent information regarding the purpose and objectives of the research.

Measures

The survey included:

a) sociodemographic and occupational characteristics of the respondents (such as, gender, country of practice, specialty, years of active clinical experience, whether they had practiced medicine in the previous year, their main working environment, and their familiarity with sleep disturbances);
b) physicians' perceptions of the therapeutic efficacy in treating insomnia of various pharmacological interventions using a 5-point Likert scale (0 = insufficient; 5 = very sufficient) plus the option "Do not know/No opinion";
c) physicians' initial and secondary drug choice for the short- and long-term treatments of insomnia for adult and elderly patients; and
d) whether clinicians would avoid certain drugs and the reasons for doing so.

Statistical Analysis

A descriptive analysis was initially conducted to summarize the characteristics of the study participants using percentages for the categorical variables and mean and standard deviation (SD) values for the continuous variables and counts. Similarly, we also analyzed the clinicians' opinion regarding the efficacy of various drugs to treat insomnia, which was the main outcome of interest in the present study, as well as their preferences in different patient scenarios: 1) their first-line drug preference for short-term insomnia treatment; 2) their second-line drug preference for short-term insomnia treatment; 3) their first-line drug preference for long-term insomnia treatment; 4) their second-line drug preference for long-term insomnia treatment; and 5) their drug preferences when treating elderly patients with insomnia.

The original 5-point Likert scale was converted to a 3-point scale, retaining the "Do not know/No opinion" option. To ensure statistical precision in the assessment of the mean and SD values, the "Do not know/No opinion" answers were excluded and treated as "Missing Value" in the IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, Unted States) software, version 29.0.2.0. This methodological approach may result in weaker correlations among the variables.[45] However, correlations were not a primary concern, as the focus was on each drug independently, and the mean and SD values were presented in a descending order.

Next, an attempt was made to link the participants' specialties with the first- and second-line drugs for the short- and long-term treatments of insomnia. The pharmaceutical interventions were clinically grouped as follows: 1) benzodiazepines/ Z-drugs; 2) antidepressants; 3) mild approaches (antihistamines, melatonin, 5-HTP, herbs)/other (referral to specialist, no opinion); 4) antipsychotics; and 5) DORAs. The medical specialties were also merged as psychiatrists and non-psychiatrists. All specialties are presented in detail in ►**Supplementary Table S1** (online only). All statistical analyses were performed using the Microsoft Excel (Microsoft Corp., Redmond, WA, United States) and the IBM SPSS Statistics for Windows software.

Results

Sociodemographic Variables of the Respondents

A total of 149 (58.4% male and 41.6% female) respondents completed the current study). The sample was predominantly composed of medical professionals practicing in Greece (69.8%), and the rest were from abroad. Half of the sample (50.3%) consisted of trainee or qualified psychiatrists, whereas the other half, of non-psychiatrists. Practically all of the participants (95.3%) were active, and most had more than 10 years of active clinical practice (57.7%). The percentages of participants who reported being fully familiar with sleep disorders and who indicated they did not have patients with sleep disturbances within their practice were small, of 4.7 and 2% respectively. Most of the participants (38.9%) had a small number of insomniac patients (1 to 25%), and most (46.3%) also reported the National Health Service Hospital (publicly funded hospital) as their main work environment. Additional information can be found in ►**Supplementary Table S1** (online only).

Physician's perception of the Efficacy of Various Drugs in Treating Insomnia

►**Table 1** illustrates the opinions of the participating physicians regarding the efficacy of specific drug regimens in treating insomnia. Zopiclone, zolpidem, mirtazapine, quetiapine, and lorazepam were evaluated as the most effective options. Notably, zopiclone, zolpidem, and zaleplon demonstrated high mean ratings (of 2.6 ± 0.54, 2.59 ± 0.56, and 2.46 ± 0.57 respectively). However, it is worth mentioning that almost half of the respondents had no opinion about zopiclone and zaleplon. On the contrary, Zolpidem received higher recognition, with only 8.72%of respondents indicating a lack of familiarity with the substance. Mirtazapine, quetiapine, and lorazepam also showed high mean ratings, while the proportions of "Don't know/No opinion" answers were relatively low, standing at 12.08%, 8.05%, and 2.68% respectively.

Nutritional products (herbs) and supplements (tryptophan) were evaluated as the most inefficient substances to treat insomnia, with mean ratings of 1.75 and 1.69 respectively. Most clinicians were not familiar with DORAs (87.25%), doxepin (76.51%), tryptophan (73.83%), zaleplon (62.42%), and other TCAs (53.69%).

 © 2024. Brazilian Sleep Association. All rights reserved.

Table 1 Physicians' opinions regarding the efficacy of various drug regimens in the treatment of insomnia.

Drug	Mean	Standard deviation
Zopiclone	2.6	0.542
Insufficient	1.34%	
Moderately sufficient	18.79%	
Very sufficient	33.56%	
Do not know/No opinion	46.31%	
Zolpidem	2.59	0.564
Insufficient	3.36%	
Moderately sufficient	30.87%	
Very sufficient	57.05%	
Do not know/No opinion	8.72%	
Mirtazapine	2.55	0.585
Insufficient	4.03%	
Moderately sufficient	31.54%	
Very sufficient	52.35%	
Do not know/No opinion	12.08%	
Quetiapine	2.48	0.583
Insufficient	4.03%	
Moderately sufficient	39.60%	
Very sufficient	48.32%	
Do not know/No opinion	8.05%	
Lorazepam	2.47	0.602
Insufficient	5.37%	
Moderately sufficient	40.94%	
Very sufficient	51.01%	
Do notkKnow/No opinion	2.68%	
Zaleplon	2.46	0.571
Insufficient	1.34%	
Moderately sufficient	17.45%	
Very sufficient	18.79%	
Do not know/ No opinion	62.42%	
Alprazolam	2.39	0.656
Insufficient	8.72%	
Moderately sufficient	38.93%	
Very sufficient	44.30%	
Do not know/No opinion	8.05%	
Trazodone	2.38	0.661
Insufficient	6.71%	
Moderately sufficient	28.86%	
Very sufficient	32.89%	
Do not know/No opinion	31.54%	
Dual orexin receptor antagonists	2.37	0.597
Insufficient	0.67%	
Moderately sufficient	6.71%	
Very sufficient	5.37%	
Do not know/ No opinion	87.25%	
Bromazepam	2.36	0.629
Insufficient	6.71%	
Moderately sufficient	39.60%	
Very sufficient	36.24%	
Do not know/No opinion	17.45%	
Other benzodiazepines: oxazepam, temazepam, flurazepam, triazolam, and clonazepam	2.25	0.623
Insufficient	6.71%	
Moderately sufficient	37.58%	
Very sufficient	23.49%	
Do not know/No opinion	32.21%	
Melatonin	2.18	0.603
Insufficient	9.40%	
Moderately sufficient	53.02%	
Very sufficient	24.83%	
Do not know/No opinion	12.75%	
Doxepin	2.09	0.612
Insufficient	3.36%	
Moderately sufficient	14.77%	
Very sufficient	5.37%	
Do not know/No opinion	76.51%	
Antihistamines	2.04	0.588
Insufficient	14.09%	
Moderately sufficient	61.07%	
Very sufficient	18.12%	
Do not know/No opinion	6.71%	
Amitriptyline	2.03	0.576
Insufficient	11.41%	
Moderately sufficient	51.68%	
Very sufficient	14.09%	
Do not know/No opinion	22.82%	
Agomelatine	1.99	0.484
Insufficient	6.71%	
Moderately sufficient	42.28%	
Very sufficient	6.04%	
Do not know/No opinion	44.97%	
Other tricyclic antidepressants	1.96	0.580
Insufficient	8.72%	
Moderately sufficient	30.87%	

 © 2024. Brazilian Sleep Association. All rights reserved.

Table 1 (*Continued*)

Very sufficient	6.71%	
Do not know/ No opinion	53.69%	
Herbs (valerian, lavender)	1.75	0.608
Insufficient	25.50%	
Moderately sufficient Very sufficient Do not know/No opinion	42.95% 6.71% 24.83%	
Tryptophan	1.69	0.521
Insufficient	8.72%	
Moderately sufficient	16.78%	
Very sufficient	0.67%	
Do not know/No opinion	73.83%	

Physicians' Preferred Drug Intervention in Different Clinical Scenarios

►**Supplementary Table S2** (online only) presents the frequency with which specific drugs were preferred under different clinical scenarios in a descending order. For a comprehensive analysis of these scenarios, please consult the "Materials and Methods" section of the present article. Mirtazapine was in the top five positions across all five scenarios, while quetiapine and alprazolam appeared in the top five positions in four scenarios. More details regarding specific answers per scenario are presented in ►**Supplementary Table S2** (online only).

Drugs that Clinicians Avoid

►**Table 2** presents certain drugs that physicians would avoid prescribing when treating insomnia. Physicians would specifically avoid the category "other tricyclic antidepressants" (mean: 1.96 ± 0.58), DORAs (mean $\pm$ SD $= 2.37 \pm 0.60$), herbs (mean $\pm$ SD $= 1.75 \pm 0.61$), and tryptophan (mean $\pm$ SD $= 1.69 \pm 0.52$) the most. It should be mentioned that, although DORAs had a high mean value regarding efficacy (2.37), almost 1/3 of the participants (29.53%) would be reluctant to administer them. The reasons for avoiding specific drugs are presented in ►**Supplementary Table S3** (online only).

Association between Physicians' Specialty and Drug Preference

Statistical significance was observed in three out of the five scenarios presented to the participants: first-line drug treatment for short-term intervention against insomnia; second-line drug treatment for long-term intervention; and cases involving the elderly. For the other two scenarios – second-line drug treatment for short-term intervention against insomnia and first-line treatment for long-term intervention –, it appears that the physicians' specialty does not correlate with their preference for a specific drug regimen. ►**Tables 3** to **5** include only the drug categories in which the differences were statistically significant.

►**Table 3** shows a statistically significant difference between psychiatrists and non-psychiatrists: the former group prefers antipsychotic drugs as the first-line treatment for short-term intervention against insomnia. ►**Table 4** indicates the results regarding the second-line drug treatment for long-term intervention against insomnia. Psychiatrists prefer antidepressants and nonpsychiatrists, benzodiazepines or Z-drugs, and the difference was statistically significant. Likewise, in case of elderly patients, the same pattern appears, in which psychiatrists prefer antidepressants, while non-psychiatrists prefer benzodiazepines or Z-drugs (►**Table 5**). The scenarios and drug categories in which no correlation between physicians' specialties and specific drug regimens was observed were excluded from these tables.

Table 2 Drugs physicians' avoid when treating insomnia.

Drug	n (N = 149)	Frequency (%)
Other tricyclic antidepressants	48	32.22%
Dual orexin receptor antagonists	44	29.53%
Tryptophan	40	26.85%
Herbs (valerian, lavender)	38	25.50%
Alprazolam	35	23.49%
Doxepin	35	23.49%
Other benzodiazepines: oxazepam, temazepam, flurazepam, triazolam, clonazepam	34	22.82%
Amitriptyline	25	16.78%
Antihistamines	22	14.77%
Bromazepam	22	14.77%
Agomelatine	21	14.10%
Zaleplon	21	14.10%
Lorazepam	21	14.10%
Quetiapine	19	12.75%
Trazodone	15	10.10%
Would prescribe them all	14	9.40%
Zolpidem	12	8.05%
Zopiclone	11	7.38%
Mirtazapine	8	5.37%
Melatonin	7	4.70%
None of above	2	1.34%
Aripiprazole	1	0.67%

Discussion

The present is the first study to investigate differences in attitudes and preferences of pharmacotherapy for the treatment of insomnia between psychiatrists and non-psychiatrists. A general comment would be that, in many cases, psychiatrists prefer antipsychotic and antidepressant drugs for the treatment of insomnia, while non-psychiatrists favor

 © 2024. Brazilian Sleep Association. All rights reserved.

Table 3 First-line drug treatment for short-term insomnia intervention.

First-line drug	Specialty		
Treatment for short-term intervention		Psychiatrists	Non-psychiatrists
	Antipsychotics	n (N= 149)	n (N = 149)
		9	1

Table 4 Second-line drug treatment for long-term insomnia intervention.

Second-line	Specialty		
Drug treatment for long-term intervention		Psychiatrists	Non-psychiatrists
		n (N= 149)	n (N= 149)
	Benzodiazepines/Z-drugs	12	28
	Antidepressants	37	20

Table 5 Drugs used in insomnia treatment for elderly patients.

Drug	Specialty		
Treatment for elderly patients		Psychiatrists	Non-psychiatrists
		n (N= 149)	n (N= 149)
	Benzodiazepines/Z-drugs	10	30
	Antidepressants	23	12

benzodiazepines or Z-drugs. Potential explanations for this tendency are examined below.

Insomnia can be interpreted either as a symptom or causal factor of a mental health disorder.[46] Among 280 patients who experienced their first psychotic episode, 63 of them (22.6%) also exhibited clinically-significant insomnia,[47] while other researchers mention that chronic insomnia exists before depression, it is a risk factor for the new onset or relapse of depression, and it could persist even after remission.[48] Indeed, some scholars report that depression causes insomnia,[49] others claim that insomnia can directly or indirectly trigger depressive symptomatology.[50] The direction of causality is still unclear; therefore, a cause-and-effect relationship between the two cannot be established at present.[49] Taking all of these factors into account, psychiatrists may interpret insomnia as a symptom of an undisclosed mental health disorder, which justifies their preference for antipsychotic and antidepressant drugs. This hypothesis is supported by the literature.[51]

The results of the present study indicate that nonpsychiatrists prefer benzodiazepines and/or Z-drugs for the treatment of insomnia. There is some evidence to suggest that nonpsychiatric physicians are not always familiar with the risks and benefits of Z-drugs and benzodiazepines. A survey[52] found that physicians and nurses acknowledge some of the benefits of Z-drugs and benzodiazepines – in reducing the time to fall asleep, nocturnal time spent awake, and alleviating fear or agitation –, with 24 and 10% of them respectively being unable answer most of the questions about the risks and benefits of Z-drugs and benzodiazepines retrospectively. Additionally, a survey[53] examining potentially inappropriate medications prescribed by family practitioners to elderly patients revealed that zopiclone, zolpidem, and diazepam were the top-three inappropriate drugs, which were the most frequently prescribed for the wrong reason. The rationale behind this trend was the family practitioners' lack of knowledge regarding the potential risk of prescribing inappropriate medications.

In the present survey, in two out of three questions (concerning second-line drug treatment for long-term insomnia intervention and insomnia in elderly patients), the number of nonpsychiatrists who chose benzodiazepines/Z-drugs over the other medications was more than double the number of psychiatrists (►**Tables 4** and **5**). Taking into account the fact that benzodiazepines/Z-drugs are not recommended for long-term use and should be prescribed with caution to elderly patients,[54] this trend might be due to them not realizing that they could mistakenly prescribe the wrong medication. On the other hand, there is a widespread belief among psychiatrists that benzodiazepines are only suitable for short-term treatments, as they think that in the long term these drugs lead to the development of tolerance to the treatment and sometimes even dependence, with withdrawal symptoms after discontinuation.[8] In fact, this belief is not based on existing data, since, after the long-term use, only 15 to 40% of patients show withdrawal symptoms, rebound insomnia, and increased anxiety, and it has even been established that addiction is also due to biological factors of certain patients that are related to specific subtypes of the GABA neurotransmitter.[16,55,56] Another possible explanation about why psychiatrists seem to dislike

 © 2024. Brazilian Sleep Association. All rights reserved.

benzodiazepines is that their patients are likely to have a chronic/persistent form of the disorder or comorbidity with other psychiatric disorders and have already tried other treatments without success, so psychiatrists choose antidepressants or antipsychotics, which appear to be more effective in these cases.[26,33,34]

In the current survey, physicians evaluated Z-drugs as the most efficient regimen for the treatment of insomnia. In ►**Table 1**, it is evident that zopiclone and zolpidem received the highest evaluations, with mirtazapine ranking third. However, mirtazapine was among the top-five preferred drugs in all five scenarios for insomnia treatment, while zopiclone and zolpidem were only among the top-five drugs in one scenario (►**Supplementary Table S2**). Practically, this means that mirtazapine is preferred for both the short and long-term treatments of insomnia, as a first-line or second-line treatment for all age groups. On the other hand, although doxepin has been proved to be effective for the short- and long-term treatments, with relatively few side effects (drowsiness and headache) [57,58] and positive results documented in children and adolescents,[59] it does not seem to be preferred by psychiatrists in the present research. This may be due to ignorance, as 76.5% did not know it or had no opinion, in contrast to the rest of the antidepressants that were used and considered effective.

It should also be noted that one of the most popular prescriptions (with rates higher than those of Z-drugs) was of the antipsychotic drug quetiapine, which has emerged as one of the preferred drugs in four out of five scenarios. Interviews conducted with family physicians[60] showed that they favored the quetiapine alternative for patients with complex psychosocial problems with the goal of avoiding benzodiazepine dependence, confirming the results of previous research,[26,33,34] but they were highly unaware of the drug's potential side effects and risks. Quetiapine has been associated with incorrect use or abuse, resulting in poisoning or overdose, and significant side effects, such as extrapyramidal symptoms, diabetes, cardiovascular, ophthalmological, and skin problems, as well as withdrawal syndrome; moreover, its cost is very high.[61] However, according to another research,[62] the negative effects of quetiapine when prescribed specifically for insomnia have been rather overestimated and, in fact, the increasing rates of its prescription are due to the desire of the patients themselves, who actively demand it.

Another noteworthy finding is that newer drugs, such as lemborexant, suvorexant, and daridorexant, which act by inhibiting both OX1R and OX2R, presented a high percentage of "Do not know/No opinion" answers (87.25%). However, these drugs facilitate both sleep onset and sleep maintenance without the risk of dependence symptoms.[63,64] Additionally, the cost-effectiveness of DORAs seems to be high. In terms of cost-effectiveness, studies have shown the dominance of lemborexant over suvorexant and zolpidem,[65] as well as the superiority of suvorexant over zolpidem,[66] suggesting lemborexant and suvorexant as good options for insomnia treatment. Despite the superiority of DORAs in terms of results and cost-effectiveness, in the current study we found that medical professionals did not prefer these medications for insomnia (►**Table 2**), because they might have limited awareness about their existence or their beneficial outcomes. Another possible explanation for that lies in the fact that the DORAs have not yet been approved by regulatory bodies in many countries and, as a result, physicians do not know them.

The present research, as a survey of attitudes and preferences, seeks to identify both pharmaceutical preferences and deviations from guidelines regarding insomnia treatment. At the same time, we have tried to recognize the reasons for these preferences by mentioning some possible explanations and to offer directions for policy making and future research. Indeed, the high percentages of "Do not know/ No opinion" answers to questions regarding DORAs underline the need for a follow-up survey to examine if acceptance and use of these drugs will increase among prescribers in the future, based on the emerging evidence suggesting their effectiveness. As a result, the findings of the current study seem to suggest that improved awareness of physicians regarding novel treatment options (such as DORAs) and their beneficial outcomes may benefit patients.

However, the present research has several limitations, which mainly concern the sample size and the way in which the variables were categorized during the statistical analysis. Initially, although an effort was made to ensure representativeness in the sample, the final number of 149 participants is considered rather limited for a cross-sectional study and resulted in underrepresentation of certain pharmacotherapy options. Due to this, to extract statistically meaningful results, broader categories were created (such as grouping benzodiazepines and Z-drugs into a single category). However, this can be interpreted as a methodological error, because these drugs neither share the same pharmacological profile nor the same pharmacokinetics. Additionally, the over-representation of Greek respondents introduced a bias into the study. Apart from the fact that our sample from abroad was small, they had some level of acquaintance with the authors of the current study. Moreover, conclusions are tentative, because association does not infer causality. As a result, further investigation of the issue with a larger sample is suggested.

Funding
The authors declare that they did not receive funding from agencies in the public, private or non-profit sectors to conduct the present study.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Johnson EO. Epidemiology of Insomnia: from Adolescence to Old Age. Sleep Med Clin 2006;1(03):305–317
2 Morin CM, Bélanger L, LeBlanc M, et al. The natural history of insomnia: a population-based 3-year longitudinal study. Arch Intern Med 2009;169(05):447–453
3 Matheson EM, Brown BD, DeCastro AO. Treatment of Chronic Insomnia in Adults. Am Fam Physician 2024;109(02):154–160. https://www.aafp.org/pubs/afp/issues/2024/0200/chronic-insomnia-adults.html. [Internet]

 © 2024. Brazilian Sleep Association. All rights reserved.

4 Paparrigopoulos T, Tzavara C, Theleritis C, Psarros C, Soldatos C, Tountas Y. Insomnia and its correlates in a representative sample of the Greek population. BMC Public Health 2010;10(01):531
5 Kyrtsopoulos M, Tsiptsios D, Karapepera V, et al. A Questionnaire-Based Cross-Sectional Study of Insomnia among Middle-Aged Adults from Greece's Northeastern Fringe, Thrace. Maedica (Buchar) 2023;18(03):404–412. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10674121/. [Internet]
6 Tsaras K, Tsiantoula M, Papathanasiou IV, Papagiannis D, Chatzi M, Fradelos EC. Predictors of Depression and Insomnia in Community-Dwelling Elderly People: A Cross-Sectional Evidence of Their Bidirectional Relationship. Cureus 2021;13(03):e13965
7 Matheson E, Hainer BL. Insomnia: Pharmacologic Therapy. Am Fam Physician 2017;96(01):29–35. https://www.aafp.org/pubs/afp/issues/2017/0701/p29.html. [Internet]
8 Krystal AD, Prather AA, Ashbrook LH. The assessment and management of insomnia: an update. World Psychiatry 2019;18(03):337–352. https://onlinelibrary.wiley.com/doi/pdf/10.1002/wps.20674. [Internet]
9 Riemann D, Baglioni C, Bassetti C, Bjorvatn B, DolencGroselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. Journal of sleep research [Internet]. 2017;26(06):675–700. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28875581
10 Gruwez A, Libert W, Ameye L, Bruyneel M. Reliability of commercially available sleep and activity trackers with manual switch-to-sleep mode activation in free-living healthy individuals. Int J Med Inform 2017;102:87–92. https://www.sciencedirect.com/science/article/pii/S1386505617300692. [Internet]
11 Riemann D, Espie CA, Altena E, et al. The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023. J Sleep Res 2023;32(06):e14035
12 Palagini L, Manni R, Aguglia E, et al. Expert Opinions and Consensus Recommendations for the Evaluation and Management of Insomnia in Clinical Practice: Joint Statements of Five Italian Scientific Societies. Front Psychiatry 2020;11:558
13 Wilt TJ, MacDonald R, Brasure M, et al. Pharmacologic Treatment of Insomnia Disorder: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians. Ann Intern Med 2016;165(02):103–112
14 Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: An American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med 2017;13(02):307–349
15 Rios P, Cardoso R, Morra D, et al. Comparative effectiveness and safety of pharmacological and non-pharmacological interventions for insomnia: an overview of reviews. Syst Rev 2019;8(01):281. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6857325/
16 Cheng T, Wallace DM, Ponteri B, Tuli M. Valium without dependence? Individual $GABA_A$ receptor subtype contribution toward benzodiazepine addiction, tolerance, and therapeutic effects. Neuropsychiatr Dis Treat 2018;14:1351–1361
17 Buscemi N, Vandermeer B, Friesen C, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. J Gen Intern Med 2007;22(09):133513–50
18 Glass J, Lanctôt KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ 2005;331(7526):1169
19 Capiau A, Huys L, van Poelgeest E, van der Velde N, Petrovic M, Somers A. Therapeutic dilemmas with benzodiazepines and Z-drugs: insomnia and anxiety disorders versus increased fall risk: a clinical review. Eur Geriatr Med 2023;14(04):697–708
20 Driot D, Ouhayoun S, Perinelli F, et al. Non-drug and drug alternatives to benzodiazepines for insomnia in primary care: Study among GPs and pharmacies in a Southwest region of France. Therapie 2019;74(05):537–546
21 Siafis S, Fountoulakis KN, Fragkidis V, Papazisis G. Prescribing Z-drugs in Greece: an analysis of the national prescription database from 2018 to 2021. BMC Psychiatry 2023;23(01):370. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10214344/
22 Siriwardena AN, Apekey T, Tilling M, Dyas JV, Middleton H, Ørner R. General practitioners' preferences for managing insomnia and opportunities for reducing hypnotic prescribing. J Eval Clin Pract 2010;16(04):731–737
23 Begum M, Gonzalez-Chica D, Bernardo C, Woods A, Stocks N. Trends in the prescription of drugs used for insomnia: an open-cohort study in Australian general practice, 2011-2018. Br J Gen Pract 2021;71(712):e877–e886. https://bjgp.org/content/71/712/e877.short. [Internet]
24 Takeshima M, Aoki Y, Ie K, et al. Physicians' attitudes toward hypnotics for insomnia: A questionnaire-based study. Front Psychiatry 2023;14:1071962
25 Sorscher AJ, Siddiqui AA. Pharmacotherapy for Chronic Insomnia: A Brief Survey of PCP Attitudes and Preferences. J Sleep Disord Treat Care 2016;5(01):x
26 Everitt H, Baldwin DS, Stuart B, et al. Antidepressants for insomnia in adults. Cochrane Database Syst Rev 2018;5(05):CD010753
27 Wichniak A, Wierzbicka A, Walęcka M, Jernajczyk W. Effects of Antidepressants on Sleep. Curr Psychiatry Rep 2017;19(09):63. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5548844/. [Internet]
28 Wong J, Motulsky A, Abrahamowicz M, Eguale T, Buckeridge DL, Tamblyn R. Off-label indications for antidepressants in primary care: descriptive study of prescriptions from an indication based electronic prescribing system. BMJ 2017;356:j603. https://www.bmj.com/content/356/bmj.j603. [Internet]
29 Liu Y, Xu X, Dong M, Jia S, Wei Y. Treatment of insomnia with tricyclic antidepressants: a meta-analysis of polysomnographic randomized controlled trials. Sleep Med 2017;34:126–133
30 Winkler A, Auer C, Doering BK, Rief W. Drug treatment of primary insomnia: a meta-analysis of polysomnographic randomized controlled trials. CNS Drugs 2014;28(09):799–816
31 Asnis GM, Thomas M, Henderson MA. Pharmacotherapy Treatment Options for Insomnia: A Primer for Clinicians. Int J Mol Sci 2015;17(01):50
32 Chow ES, Zangeneh-Kazemi A, Akintan O, Chow-Tung E, Eppel A, Boylan K. Prescribing Practices of Quetiapine for Insomnia at a Tertiary Care Inpatient Child and Adolescent Psychiatry Unit: A Continuous Quality Improvement Project. J Can Acad Child Adolesc Psychiatry 2017;26(02):98–103. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5510938/. [Internet]
33 Lin CY, Chiang CH, Tseng MM, Tam KW, Loh EW. Effects of quetiapine on sleep: A systematic review and meta-analysis of clinical trials. Eur Neuropsychopharmacol 2023;67:22–36. https://www.sciencedirect.com/science/article/pii/S0924977X22008987?via%3Dihub#sec0024
34 Cornelis C, Van Gastel A, Dumont G, et al. A case of dose escalation of quetiapine in persistent insomnia disorder. Acta Clin Belg 2017;72(05):346–348
35 Okuda S, Qureshi ZP, Yanagida Y, Ito C, Homma Y, Tokita S. Hypnotic prescription trends and patterns for the treatment of insomnia in Japan: analysis of a nationwide Japanese claims database. BMC Psychiatry 2023;23(01):278
36 Janto K, Prichard JR, Pusalavidyasagar S. An Update on Dual Orexin Receptor Antagonists and Their Potential Role in Insomnia Therapeutics. J Clin Sleep Med 2018;14(08):1399–1408. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6086961/
37 Kumar A, Chanana P, Choudhary S. Emerging role of orexin antagonists in insomnia therapeutics: An update on SORAs and DORAs. Pharmacol Rep 2016;68(02):231–242
38 Xue T, Wu X, Chen S, et al. The efficacy and safety of dual orexin receptor antagonists in primary insomnia: A systematic review and network meta-analysis. Sleep Med Rev 2022;61:101573
39 Takaesu Y, Sakurai H, Aoki Y, et al. Treatment strategy for insomnia disorder: Japanese expert consensus. Front Psychiatry 2023;14:1168100

 © 2024. Brazilian Sleep Association. All rights reserved.

40 De Crescenzo F, D'Alò GL, Ostinelli EG, et al. Comparative effects of pharmacological interventions for the acute and long-term management of insomnia disorder in adults: a systematic review and network meta-analysis. Lancet 2022;400(10347)170–184. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00878-9/fulltext. [Internet]

41 Low TL, Choo FN, Tan SM. The efficacy of melatonin and melatonin agonists in insomnia - An umbrella review. J Psychiatr Res 2020; 121:10–23

42 Choi K, Lee YJ, Park S, Je NK, Suh HS. Efficacy of melatonin for chronic insomnia: Systematic reviews and meta-analyses. Sleep Med Rev 2022;66:101692

43 Maruani J, Reynaud È, Chambe J, Palagini L, Bourgin P. Pierre Alexis Geoffroy. Efficacy of melatonin and ramelteon for the acute and long-term management of insomnia disorder in adults: A systematic review and meta-analysis. J Sleep Res 2023;x:x

44 Wei S, Smits MG, Tang X, et al. Efficacy and safety of melatonin for sleep onset insomnia in children and adolescents: a meta-analysis of randomized controlled trials. Sleep Med 2020;68:1–8

45 Denman DC, Baldwin AS, Betts AC, McQueen A, Tiro JA. Reducing "I Don't Know" Responses and Missing Survey Data: Implications for Measurement. Med Decis Making 2018;38(06): 673–682

46 Freeman D, Sheaves B, Waite F, Harvey AG, Harrison PJ. Sleep disturbance and psychiatric disorders. Lancet Psychiatry 2020;7 (07):628–637

47 Subramaniam M, Abdin E, Shahwan S, et al. Prevalence, correlates and outcomes of insomnia in patients with first episode psychosis from a tertiary psychiatric institution in Singapore. Gen Hosp Psychiatry 2018;51:15–21

48 Vargas I, Perlis ML. Insomnia and depression: clinical associations and possible mechanistic links. Curr Opin Psychol 2020;34:95–99

49 Franzen PL, Buysse DJ. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dialogues Clin Neurosci 2008;10(04):473–481

50 Staner L. Comorbidity of insomnia and depression. Sleep Med Rev 2010;14(01):35–46

51 Stolk L. New drug: daridorexant for insomnia. Ge-Bu. 2022;75–78 (10):1

52 Heinemann S, Brockmöller J, Hagmayer Y, Himmel W. Why Z-drugs are used even if doctors and nurses feel unable to judge their benefits and risks-a hospital survey. Eur J Clin Pharmacol 2020;76 (02):285–290

53 Voigt K, Gottschall M, Köberlein-Neu J, Schübel J, Quint N, Bergmann A. Why do family doctors prescribe potentially inappropriate medication to elderly patients? BMC Fam Pract 2016;17 (01):93. Doi: 10.1186/s12875-016-0464-2

54 Panes A, Pariente A, Bénard-Laribière A, et al. Use of benzodiazepines and z-drugs not compliant with guidelines and associated factors: a population-based study. Eur Arch Psychiatry Clin Neurosci 2020;270(01):3–10

55 Hood SD, Norman A, Hince DA, Melichar JK, Hulse GK. Benzodiazepine dependence and its treatment with low dose flumazenil. Br J Clin Pharmacol 2014;77(02):285–294

56 Krystal AD. A compendium of placebo-controlled trials of the risks/benefits of pharmacological treatments for insomnia: the empirical basis for U.S. clinical practice. Sleep Med Rev 2009;13 (04):265–274

57 Lankford A, Rogowski R, Essink B, Ludington E, Heith Durrence H, Roth T. Efficacy and safety of doxepin 6 mg in a four-week outpatient trial of elderly adults with chronic primary insomnia. Sleep Med 2012;13(02):133–138

58 Yeung WF, Chung KF, Yung KP, Ng THY. Doxepin for insomnia: a systematic review of randomized placebo-controlled trials. Sleep Med Rev 2015;19:75–83

59 Shah YD, Stringel V, Pavkovic I, Kothare SV. Doxepin in children and adolescents with symptoms of insomnia: a single-center experience. J Clin Sleep Med 2020;16(05):743–747. Doi: 10.5664/jcsm.8324

60 Kelly M, Dornan T, Pringsheim T. The lesser of two evils: a qualitative study of quetiapine prescribing by family physicians. CMAJ Open 2018;6(02):E191–E196

61 Montebello ME, Brett J. Misuse and associated harms of quetiapine and other atypical antipsychotics. In:Non-medical and illicit use of psychoactive drugs.. Springer; 2015:125–139

62 Waal H, Vold JH, Skurtveit SO. Quetiapine abuse – myth or reality? Tidsskrift for Den norskelegeforening [Internet]. 2020; Available from: *https://tidsskriftet.no/en/2020/09/kronikk/quetiapine-abuse-myth-or-reality*

63 Moline M, Asakura S, Beuckman C, et al. The abuse potential of lemborexant, a dual orexin receptor antagonist, according to the 8 factors of the Controlled Substances Act. Psychopharmacology (Berl) 2023;240(04):699–711

64 Muehlan C, Vaillant C, Zenklusen I, Kraehenbuehl S, Dingemanse J. Clinical pharmacology, efficacy, and safety of orexin receptor antagonists for the treatment of insomnia disorders. Expert Opin Drug Metab Toxicol 2020;16(11):1063–1078

65 Ikeda S, Azuma MK, Fujimoto K, et al. Cost-effectiveness analysis of lemborexant for treating insomnia in Japan: a model-based projection, incorporating the risk of falls, motor vehicle collisions, and workplace accidents. Psychol Med 2022;52(13):2822–2834

66 Nishimura S, Nakao M. Cost-effectiveness analysis of suvorexant for the treatment of Japanese elderly patients with chronic insomnia in a virtual cohort. J Med Econ 2018;21(07):698–703

 © 2024. Brazilian Sleep Association. All rights reserved.