clinical and translational neuroscience

MDPI

Commentary

Insomnia Guidelines—The European Update 2023

Dieter Riemann [1,2,*], Raphael J. Dressle [1] and Kai Spiegelhalder [1]

[1] Department of Psychiatry and Psychotherapy, Medical Center-University of Freiburg, Faculty of Medicine, University of Freiburg, 79104 Freiburg, Germany
[2] Center for Basics in NeuroModulation (NeuroModulBasics), Faculty of Medicine, University of Freiburg, 79106 Freiburg, Germany
* Correspondence: dieter.riemann@uniklinik-freiburg.de; Tel.: +49-761-270-69190

Abstract: The last ten years have seen the development and publication of numerous national and international guidelines devoted to the diagnosis and treatment of insomnia. These include guidelines by the American College of Physicians (ACP), the American Academy of Sleep Medicine (AASM), the British Sleep Society (BSS), the German Sleep Society (GSS), and the European Sleep Research Society (ESRS). Though coming from very diverse authors and backgrounds, these guidelines by and large agree concerning the therapeutic recommendations: cognitive behavioral treatment of insomnia (CBT-I), a multicomponent psychotherapeutic intervention, is unequivocally recommended as a first-line treatment. In this report, we will focus on the most recent guideline update from the ESRS, which was published in November 2023. After suggesting a careful diagnostic procedure, CBT-I, both applied face to face (F2F) or digitally (dCBT-I), is again recommended as a first-line treatment based on the available evidence. Hypnotic medications like benzodiazepines (BZ), benzodiazepine receptor agonists (BZRA), sedating antidepressants, and others are approved for short-term-treatment of up to four weeks. Orexin receptor antagonists (i.e., daridorexant) and prolonged release melatonin are considered as options for longer-term treatment when carefully considering the advantages and disadvantages. Both light therapy and exercise regimens were viewed as promising; however, they still lack convincing evidence for the time being. Given the fact that not every patient responds satisfactorily or even remits following CBT-I or other treatment options, the research agenda calls for the development and evaluation of new therapeutic avenues and combination therapies.

Keywords: insomnia; diagnosis; treatment; guidelines; CBT-I; hypnotics

Citation: Riemann, D.; Dressle, R.J.; Spiegelhalder, K. Insomnia Guidelines—The European Update 2023. *Clin. Transl. Neurosci.* **2024**, *8*, 10. https://doi.org/10.3390/ctn8010010

Academic Editor: Athina Tzovara

Received: 24 November 2023
Revised: 16 January 2024
Accepted: 24 January 2024
Published: 26 January 2024

1. Introduction

In the last fifty years, all medical diagnostic classification systems have included Insomnia as a diagnostic category. The DSM (Diagnostic and Statistical Manual of the American Psychiatric Association) in its previous versions DSM-III-R [1] and DSM-IV [2] insisted on a distinction between primary and secondary insomnia, whereas the DSM-5 [3] established Insomnia Disorder (ID) as an overarching diagnostic category. The ICSD (International Classification of Sleep Disorders) in its third version [4] (see Table 1) and the current version of the International Classification of Diseases (ICD) of the World Health Organization followed this paradigmatic change. While the ICD in its 10th revision (ICD-10) [5] differentiated between organic and non-organic sleep disorders, the ICD-11 [6] now follows the path suggested by the DSM-5 and ICSD-3.

About 6–10% of the population in industrialized countries is afflicted by ID [7–10], with a higher prevalence in women [7]. ID is characterized by high economical and societal costs [11]. According to Kessler et al. [12], the annual costs of absenteeism from work and reduced work performance alone amount to more than 60 billion dollars in the United States. Thus, ID is probably the most frequent sleep disorder and is accompanied by huge individual and societal costs in terms of disease burden and economic consequences.

Table 1. Diagnostic criteria for chronic insomnia disorder according to ICSD-3 [4].

A.	**The patient reports, or the patient's parent or caregiver observes, one or more of the following:**
	1. Difficulty initiating sleep.
	2. Difficulty maintaining sleep.
	3. Waking up earlier than desired.
	4. Resistance to going to bed on appropriate schedule.
	5. Difficulty sleeping without parent or caregiver intervention.
B.	**The patient reports, or the patient's parent or caregiver observes, one or more of the following related to the nighttime sleep difficulty:**
	1. Fatigue/malaise.
	2. Attention, concentration, or memory impairment.
	3. Impaired social, family, occupational, or academic performance.
	4. Mood disturbance/irritability.
	5. Daytime sleepiness.
	6. Behavioral problems (e.g., hyperactivity, impulsivity, aggression).
	7. Reduced motivation/energy/initiative.
	8. Proneness for errors/accidents.
	9. Concerns about or dissatisfaction with sleep.
C.	**The reported sleep/wake complaints cannot be explained purely by inadequate opportunity (i.e., enough time is allotted for sleep) or inadequate circumstances (i.e., the environment is safe, dark, quiet, and comfortable) for sleep.**
D.	**The sleep disturbance and associated daytime symptoms occur at least three times per week.**
E.	**The sleep disturbance and associated daytime symptoms have been present for at least three months.**
F.	**The sleep/wake difficulty is not better explained by another sleep disorder.**

Since 2016, several national and international guidelines on the diagnosis and treatment of insomnia have been published. These guidelines include the ones of the American College of Physicians (ACP) [13–16], the American Academy of Sleep Medicine [17–19], the German Sleep Society and the European Sleep Society [9,10], the Australasian Sleep Association [20] as well as the British Association for Psychopharmacology consensus statement [21]. Overall, these guidelines make a strong case for Cognitive-Behavioral Treatment for Insomnia (CBT-I) as a first-line treatment for insomnia. Hypnotics are recommended for short term use only and only if CBT-I is not available or ineffective. As potential hypnotics, melatonin, melatonin receptor agonists, benzodiazepines (BZ), benzodiazepine receptor agonists (BZRA), antihistamines, antipsychotics, some sedating antidepressants (e.g., doxepin, trazodone, or trimipramine) and phytotheraputics were considered at that time.

2. Update of the European Guideline for the Diagnosis and Treatment of Insomnia 2023

Since new data related to the diagnosis and treatment of insomnia emerged in the meantime, a task force of the European Sleep Research Society (ESRS) and the European Insomnia Network was commissioned to develop an update of the 2017 guideline [9]. Based on a revision of the German insomnia guideline, this update was published in November 2023 [22] and a brief overview of what is new will be given here. This guideline refers solely to chronic insomnia (duration of symptoms > 3 months) and does not include recommendations for acute insomnia. Recommendations concerning the diagnostic procedure are summarized in Table 2.

Table 2. Diagnostic management of insomnia with or without comorbidities according to the European Insomnia Guideline 2023 [22].

General anamnesis and examination (A)

- Former and present somatic, neurological and mental disorders.
- Personality factors, work and partnership situation, interpersonal conflicts.
- Substance use (medication, alcohol, caffeine, nicotine, illegal drugs).
- Physical examination (if indicated).
- Additional measures (if indicated): Laboratory testing including e.g., blood count, thyroid, hepatic, and renal parameters, CRP, hemoglobin, ferritin and vitamin B12; if indicated: ECG, EEG, CT/MRT, Circadian markers (melatonin, core body temperature).
- The anamnesis should include caregivers if necessary.

Sleep history (A)

- History of the sleep complaints and daytime functioning.
- Information from bed partner/caregivers (snoring, breathing pauses = apneas, periodic limb movements during sleep, nocturnal restlessness, "strange" behaviors).
- Work time/circadian factors (shift- and night work, phase advance, delay).
- Sleep-wake pattern, including daytime sleep (sleep diary, sleep questionnaires).

Actigraphy

- In case of clinical suspicion of irregular sleep-wake schedules or circadian rhythm sleep-wake disorders (**A**).
- In case of clinical suspicion of periodic leg movements in sleep (**A**).
- To assess quantitative rest activity (**A**) and sleep parameters (**C**).

Polysomnography

- In case of clinical suspicion of co-morbid sleep disorders (**A**).
- Treatment-resistant insomnia (**A**).
- In case of clinical suspicion of large discrepancy between subjectively experienced and polysomnographically measured sleep (**B**).

Note: The bold letters refer to the level of evidence. Please refer to Riemann et al. [22] for a detailed description of the grading procedure. A = very strong recommendation, B = strong recommendation, C = weak recommendation, ECG = electrocardiogram, EEG = electroencephalography, computed tomography, MRT = magnetic resonance tomography.

The central parts of the diagnostic procedure include a general anamnesis and examination as well as obtaining a detailed sleep history. Methods like actigraphy and polysomnography may play a certain role, especially for differential diagnosis, but are not essential for the diagnosis of insomnia, which is mainly based on the subjective complaints of afflicted individuals. An important aim of the diagnostic procedure is not only the confirmation of insomnia symptoms, but also a detailed process of determining comorbidities concerning medical or mental illness. Table 3 gives an overview of therapeutic avenues towards ID (with or without co-morbidities) and the recommendations of the task force group.

Based on a careful analysis of the available evidence, it was again recommended that CBT-I should be used as a first-line treatment for insomnia, with or without co-morbidities. In contrast to the earlier version of this guideline [9] the updated version suggests that "CBT-I may be delivered either face to face or digitally", acknowledging the fact that several digital CBT-I interventions have been developed in recent years, empirically tested in randomized controlled studies, and are now available in several European languages (English, German, Dutch, French, Swedish, etc.). In some European countries, digital CBT-I has become "prescribable" as a general health care expense. It is hoped that the digital approach to deliver CBT-I will decisively contribute to a wider availability and dissemination of CBT-I within European health care systems.

Table 3. Recommendations for the treatment of insomnia disorder in adults of all ages according to the European Insomnia Guideline 2023 [22].

Treatment considerations
• Insomnia disorder should be actively treated whenever it presents (A).
• In the presence of comorbidities, clinical judgment should decide whether insomnia disorder or the comorbid condition are treated first or whether both are treated at the same time (A).
Cognitive behavioral therapy for insomnia (CBT-I)
• CBT-I should be provided as the first-line treatment for insomnia disorder in adults of any age, regardless of co-morbidities (A).
• CBT-I may be delivered either in person or digitally (A).
• Sleep restriction and stimulus control are the most active ingredients of CBT-I (B).
Pharmacological interventions
• A pharmacological intervention can be proposed if CBT-I is not effective (**A**).
• BZs and BZRAs can be used in the short-term treatment of insomnia disorder ($\leq$ 4 weeks) (**A**).
• Longer term treatment (off label use) with BZ or BZRA, either daily or preferably intermittently, may be initiated in some cases and the advantages and disadvantages need to be discussed on an individual basis (**B**).
• Low-doses of sedating antidepressants can be considered (off-label use) in the short-term treatment of insomnia disorder; contraindications have to be carefully considered (**B**).
• Longer term treatment of insomnia disorder (without co-morbidities; off-label use) with low dose sedating antidepressants may be initiated in some cases and the advantages and disadvantages need to be discussed on an individual basis (**B**).
• Orexin receptor antagonists can be used for a period of up to three months in the treatment of insomnia disorder (**A**).
• Longer term treatment of insomnia disorder with orexin receptor antagonists may be initiated in some cases and the advantages and disadvantages need to be discussed on an individual basis (**A**).
• Because of insufficient evidence and possible risks antihistamines are not recommended for insomnia disorder treatment (**A**).
• Because of insufficient evidence and in light of their side effects, antipsychotics are not recommended for insomnia disorder treatment (**A**).
• Melatonin (fast release, OTC or as a prescription drug) in general is not effective in the treatment of insomnia disorder (**A**), if no circadian factors are involved.
• Longer term treatment of insomnia disorder with prolonged release melatonin (in patients > 55 years) up to three months may be effective in some cases (**B**).
Other therapies
• Herbal remedies/phytotherapeutics are not recommended for the treatment of insomnia disorder because of insufficient evidence (**A**).
• Light therapy and exercise regimes may be useful as adjunct therapies to CBT-I (**B**).

Note: The bold letters refer to the level of evidence. Please refer to Riemann et al. [22] for a detailed description of the grading procedure. A = very strong recommendation, B = strong recommendation, BZ = benzodiazepines, BZRA = benzodiazepine receptor agonists.

With respect to the pharmacological treatment of insomnia, classical BZ, BZRA, and sedating antidepressants are recommended for short-term use (up to four weeks), as in the earlier version of the guideline. Antihistamines, antipsychotics, and phytotherapeutic substances were not recommended due to lack of evidence or potential adverse effects. Melatonin too, in general, is not recommended for insomnia treatment due to a weak evidence base (exception: in case of circadian factors being involved). Prolonged release melatonin was considered separately, and a positive recommendation was provided for its usage for a duration of up to three months in patients older than 55 years. A major change with respect to pharmacological treatments concerns the recent introduction of daridorexant, a new orexin receptor antagonist, to the European market. The task force, upon weighing the available evidence, recommended daridorexant for treatment periods of up to three months and, upon carefully considering advantages and disadvantages, allowed for even longer treatment periods to be determined on an individual basis. It needs to be seen whether the accumulating clinical experience in the next few years will support

this practice, and especially, whether adverse events might outweigh the clinical benefits of this type of drug.

The task force also judged therapeutic avenues like light therapy and exercise. These strategies were judged promising; however, at present, they lack enough evidence to make a clear positive recommendation.

A final remark relates to the question of non-response/non-remission with all of the available therapeutic options. The guideline [22] clearly states that considering rates of response/remission with any of the therapeutic strategies, probably at least 30–40% of treated patients will not achieve full remission with either CBT-I or hypnotic treatment. Thus, there is a definite need to modify and develop new strategies either on a psychotherapeutic or pharmacological level. Besides that, more data from real-world clinical practice is still needed in addition to well-controlled clinical trials to obtain a more comprehensive understanding of treatment effects. Also, the question whether combination therapies of CBT-I and pharmacotherapy might enhance therapeutic outcomes has not been fully clarified up to now.

Author Contributions: Conceptualization, D.R. and K.S.; writing—original draft preparation, D.R.; writing—review and editing, D.R., R.J.D. and K.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed.; American Psychiatric Association: Washington, DC, USA, 1987.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*, 4th ed.; American Psychiatric Association: Washington, DC, USA, 1998; ISBN 978-0-89042-062-1.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*, 5th ed.; American Psychiatric Association: Washington, DC, USA, 2013; ISBN 978-0-89042-554-1.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*, 3rd ed.; American Academy of Sleep Medicine: Darien, IL, USA, 2014.
5. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*, 10th ed.; World Health Organization: Genève, Switzerland, 1993.
6. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*, 11th ed.; World Health Organization: Genève, Switzerland, 2019.
7. Ohayon, M.M. Epidemiology of insomnia: What we know and what we still need to learn. *Sleep. Med. Rev.* **2002**, *6*, 97–111. [CrossRef] [PubMed]
8. Pallesen, S.; Sivertsen, B.; Nordhus, I.H.; Bjorvatn, B. A 10-year trend of insomnia prevalence in the adult Norwegian population. *Sleep. Med.* **2014**, *15*, 173–179. [CrossRef]
9. Riemann, D.; Baglioni, C.; Bassetti, C.; Bjorvatn, B.; Groselj, L.D.; Ellis, J.G.; Espie, C.A.; Garcia-Borreguero, D.; Gjerstad, M.; Gonçalves, M.; et al. European guideline for the diagnosis and treatment of insomnia. *J. Sleep. Res.* **2017**, *26*, 675–700. [CrossRef] [PubMed]
10. Riemann, D.; Baum, E.; Cohrs, S.; Crönlein, T.; Hajak, G.; Hertenstein, E.; Klose, P.; Langhorst, J.; Mayer, G.; Nissen, C.; et al. S3-Leitlinie Nicht erholsamer Schlaf/Schlafstörungen. *Somnologie* **2017**, *21*, 2–44. [CrossRef]
11. Wickwire, E.M.; Shaya, F.T.; Scharf, S.M. Health economics of insomnia treatments: The return on investment for a good night's sleep. *Sleep. Med. Rev.* **2016**, *30*, 72–82. [CrossRef] [PubMed]
12. Kessler, R.C.; Berglund, P.A.; Coulouvrat, C.; Hajak, G.; Roth, T.; Shahly, V.; Shillington, A.C.; Stephenson, J.J.; Walsh, J.K. Insomnia and the performance of US workers: Results from the America Insomnia Survey. *Sleep* **2011**, *34*, 1161–1171. [CrossRef]
13. Brasure, M.; Fuchs, E.; MacDonald, R.; Nelson, V.A.; Koffel, E.; Olson, C.M.; Khawaja, I.S.; Diem, S.; Carlyle, M.; Wilt, T.J.; et al. Psychological and behavioral interventions for managing insomnia disorder: An evidence report for a clinical practice guideline by the American College of Physicians. *Ann. Intern. Med.* **2016**, *165*, 113–124. [CrossRef]
14. Kathol, R.G.; Arnedt, J.T. Cognitive behavioral therapy for chronic insomnia: Confronting the challenges to implementation. *Ann. Intern. Med.* **2016**, *165*, 149–150. [CrossRef] [PubMed]

15. Wilt, T.J.; MacDonald, R.; Brasure, M.; Olson, C.M.; Carlyle, M.; Fuchs, E.; Khawaja, I.S.; Diem, S.; Koffel, E.; Ouellette, J.; 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*, 103–112. [CrossRef] [PubMed]
16. Qaseem, A.; Kansagara, D.; Forciea, M.A.; Cooke, M.; Denberg, T.D.; Clinical Guidelines Committee of the American College of Physicians. Management of chronic insomnia disorder in adults: A clinical practice guideline from the American College of Physicians. *Ann. Intern. Med.* **2016**, *165*, 125–133. [CrossRef] [PubMed]
17. Sateia, M.J.; Buysse, D.J.; Krystal, A.D.; Neubauer, D.N.; Heald, J.L. 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*, 307–349. [CrossRef] [PubMed]
18. Edinger, J.D.; Arnedt, J.T.; Bertisch, S.M.; Carney, C.E.; Harrington, J.J.; Lichstein, K.L.; Sateia, M.J.; Troxel, W.M.; Zhou, E.S.; Kazmi, U.; et al. Behavioral and psychological treatments for chronic insomnia disorder in adults: An American Academy of Sleep Medicine clinical practice guideline. *J. Clin. Sleep Med.* **2021**, *17*, 255–262. [CrossRef] [PubMed]
19. Edinger, J.D.; Arnedt, J.T.; Bertisch, S.M.; Carney, C.E.; Harrington, J.J.; Lichstein, K.L.; Sateia, M.J.; Troxel, W.M.; Zhou, E.S.; Kazmi, U.; et al. Behavioral and psychological treatments for chronic insomnia disorder in adults: An American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J. Clin. Sleep Med.* **2021**, *17*, 263–298. [CrossRef] [PubMed]
20. Ree, M.; Junge, M.; Cunnington, D. Australasian Sleep Association position statement regarding the use of psychological/behavioral treatments in the management of insomnia in adults. *Sleep Med.* **2017**, *36*, S43–S47. [CrossRef] [PubMed]
21. Wilson, S.; Anderson, K.; Baldwin, D.; Dijk, D.-J.; Espie, A.; Espie, C.; Gringras, P.; Krystal, A.; Nutt, D.; Selsick, H.; et al. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: An update. *J. Psychopharmacol.* **2019**, *33*, 923–947. [CrossRef] [PubMed]
22. Riemann, D.; Espie, C.A.; Altena, E.; Arnardottir, E.S.; Baglioni, C.; Bassetti, C.L.A.; Bastien, C.; Berzina, N.; Bjorvatn, B.; Dikeos, D.; et al. The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023. *J. Sleep Res.* **2023**, *32*, e14035. [CrossRef] [PubMed]