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REVIEW

Non-pharmacological Approaches for Management of Insomnia

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Abstract
Insomnia is a prevalent sleep problem associated with a constellation of negative health-related outcomes and significant socioeconomic burden. It commonly co-occurs with psychiatric and medical conditions, which may further exacerbate these comorbid conditions and hinder treatment response. There is much empirical evidence to support the clinical efficacy of non-pharmacological treatment for insomnia, especially cognitive behavioral therapy for insomnia (CBT-I), in managing insomnia in a wide range of populations. This article reviews the research on the efficacy of CBT-I for primary insomnia and insomnia comorbid with other psychiatric and medical conditions, the empirical evidence regarding different CBT-I treatment modalities, the implementation of CBT-I across different age groups, and some initial evidence on the sequential combination of insomnia treatments. A brief overview of other non-pharmacological treatment with regard to complementary alternative medicine is also provided.

Key Words Sleep · Insomnia · Treatment · Non-pharmacological · Cognitive behavioral therapy · Comorbidity

Introduction

Insomnia is a prevalent sleep problem in the general population and represents one of the most debilitating and costly public health concerns [1, 2]. Insomnia disorder can occur in any age group, with predominance in females emerging during adolescence [3, 4]. Although several psychological and neurophysiological models have been proposed to conceptualize the development of insomnia, the etiology and underlying mechanisms remain unclear. There are typically two major treatment options for insomnia, including non-pharmacological and pharmacological approaches. This review will focus on the non-pharmacological approaches for treating insomnia, especially on the evidence of cognitive behavioral therapy for insomnia (CBT-I) in different age groups and clinical populations, as well as its various treatment modalities.

Overview of Insomnia

Insomnia is a sleep disorder characterized by difficulty in sleep initiation, difficulty in sleep maintenance or early morning awakening, occurring at least 3 times per week for at least three months, with significant personal distress, and daytime functional impairments (Diagnostic and Statistical Manual of Mental Disorder 5th edition, DSM-V). The prevalence of insomnia varies extensively across different studies, with a point prevalence ranging from 4% to 36% in adolescents [4–11], and 9–50% in adults [12–15], depending on the ethnicity, symptomatic timeframe (2 weeks, 1 month, or 3 months), and diagnostic criteria (DSM-IV vs. DSM-V). It is a chronic medical condition with persistence rates varying from 11% to 60% over 1-year interval [16–19], and 15% to 40% over 5-year follow-up [20, 21].

Insomnia is increasingly recognized as a major public health concern and is associated with a constellation of negative outcomes, including daytime functional impairments; a higher likelihood of physical and mental comorbidities,

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such as depression, anxiety, hypertension, diabetes mellitus, and cardiovascular diseases; an increased risk for accidents and suicide; and impaired quality of life [14, 22–25]. It may result in substantial personal distress and burden not only for the affected individuals but also for their families and the society [2, 26, 27]. For example, it is estimated that annual cost related to insomnia was 63.2 billion due to the loss of productivity in the USA in the year of 2008 [2].

Etiology of Insomnia

The causes of insomnia are multifactorial. Extensive effort has been made to understand the etiology and pathophysiology of insomnia, and the majority of the models were formulated based upon several psychophysiological and behavioral constructs sharing a key component: "hyperarousal" [28]. The hyperarousal model of insomnia postulates that high arousal would alter individual's cognitive, physiological, and psychological states, leading to disturbed sleep [28–30]. A recent complementary view suggests that individuals with persistent hyperarousal are more prone to the "instability of rapid eye movement (REM) sleep," which results in sleep fragmentation and sleep complaints [31]. Among the psychological-behavioral models that conceptualize the development and maintenance of insomnia, the Spielman's "3-P" model is one of the widely cited frameworks. This model delineates the development of insomnia through the progression from acute to chronic insomnia as a result of three closely interactive factors: predisposing, precipitating, and perpetuating factors. Predisposing factors refer to the genetic, physiological, and psychological risk factors that may increase individual's vulnerability to the onset of insomnia. Precipitating factors include the physiological, psychological, and environmental stressors that may trigger the acute onset of sleep disturbance. Perpetuating factors refer to the distorted cognitions about sleep and insomnia, and maladaptive behaviors that individuals with insomnia tend to adopt as a way to cope with their sleep problem, but often inadvertently exacerbate their sleep difficulty.

CBT-I

Insomnia often runs a chronic course. However, pharmacological treatments for sleep problems are generally recommended for short-term use [32, 33]. Due to the limitations of the drug treatments, including potential dependence and tolerance under long-term usage [34, 35], as well as the recognition of hyperarousal factors in the insomnia trajectory, non-pharmacological approach has received increasing attention in the past decade. In particular, cognitive behavioral therapy for insomnia (CBT-I) has emerged as the most prominent non-pharmacological treatment approach and is recommended as the first-line treatment for chronic insomnia in adults by American Academy of Sleep Medicine [36, 37] and American College of Physicians [38]. CBT-I is a multi-component treatment targeting behavioral, cognitive, and physiological factors that perpetuate insomnia and aims to modify and alter maladaptive behaviors and distorted beliefs about sleep and insomnia [39, 40]. It often comprises of four to eight weekly sessions (50–90 min) led by trained therapists covering the following topics: stimulus control, sleep restriction, relaxation techniques, cognitive therapy, and sleep hygiene education. CBT-I can be delivered in different formats, such as face-to-face individual or group therapy, guided or unguided digitally delivered self-help format.

There have been a proliferation of randomized controlled trials (RCTs) to evaluate the efficacy of CBT-I in treating chronic insomnia in adults. Collective evidence emanated from multiple systematic and meta-analyses supported that CBT-I is an efficacious treatment in a wide range of populations with medium to large effect sizes [41–47]. Its effect on improving sleep is comparable to medication in a short-term but is more sustainable in a long run [48–50]. In general, 70 to 80% of the participants with chronic insomnia were found to show an improvement of insomnia symptoms after the intervention, 50% achieved clinically meaningful outcomes (e.g., sleep latency less than 30 min, reduction of hypnotic use), and 30% became good sleepers [51]. The positive outcomes were evident in several self-reported sleep parameters, particularly wakefulness-related variables, such as sleep onset latency (SOL) and wake after sleep onset (WASO) [40]. For example, Trauer et al. analyzed 20 RCTs conducted in the adult population and estimated that the average reduction of SOL and WASO after treatment was about 19 min (95% CI, 14.1 to 23.9) and 26 min (95% CI, 15.5 to 36.5), respectively [46]. The improvement was able to maintain over a relatively long follow-up period (e.g., 24 months) [49]. Notably, total time in bed (TIB) was often shortened immediately after treatment due to the introduction of sleep restriction technique, which also contributed to the mild improvement in total sleep time (TST) throughout the treatment period [38, 46], but the effect on sleep duration seemed to augment over time as individuals progressively increased their sleep efficiency (SE) [46]. A recent review conducted by van Straten and colleagues, comprising a large number of RCTs ($N = 87$) and a large sample size ($N = 6303$), also supported the effectiveness of CBT-I regardless of the comorbidity, age range, and concurrent use of sleep medications [45]. The improvements on SOL, WASO, and SE after CBT-I were more pronounced with moderate to large effect sizes when measured subjectively by using sleep diary [52]. It is noteworthy that objective sleep measurements were rarely included in the CBT-I trials. Few studies have incorporated either actigraphy or PSG measurement, and their sample sizes tend to be small. In addition, the results on the objective sleep improvements were mixed, with no evidence of

improvement in polysomnography-based parameters but some evidence based on the actigraphy data, showing a small effect in reducing SOL and a moderate effect in reducing TST [52]. Moreover, the positive improvements in sleep-related variables also resulted in beneficial effects on daytime symptoms including mood, daytime sleepiness, fatigue, and overall quality of life with small to medium effect sizes, while physical functioning showed no significant improvement [53].

CBT-I for Insomnia Comorbid with Psychiatric Disorders

Insomnia commonly co-occurs with a wide range of psychiatric disorders, with the estimated prevalence rates of 80–90% in depression and anxiety, and 70% in post-traumatic stress disorder (PTSD) [54–57]. In the past, insomnia was traditionally conceptualized as a "symptom" or "secondary" to the psychiatric illnesses. However, multiple lines of evidence have indicated an independent and distinct trajectory of insomnia in the context of psychiatric comorbidity. For example, sleep disturbance does not necessarily resolve along with the improvement of psychiatric problems and is commonly reported as a residual symptom in psychiatric patients who have been treated for their daytime depressive symptomatology [58]. Moreover, the presence of insomnia may interact with mood symptoms, exacerbate the comorbid psychiatric conditions, hinder the treatment response, and lead to an increased risk of relapse and recurrence of the psychiatric comorbidities [59–61]. The collective evidence therefore suggests the need to provide independent, target treatment for insomnia in the context of comorbid psychiatric conditions [62, 63].

Given the high comorbidity of insomnia and psychiatric disorders, as well as the potential impact of insomnia in the trajectory of mood problems, the dissemination of CBT-I in psychiatric population has received substantial interests in the past 20 years. The most commonly studied psychiatric comorbidities include depression, anxiety, PTSD, and alcohol or hypnotic dependence. The findings generally support the positive effects of CBT-I on improving insomnia symptoms, mood and functioning outcomes in comorbid psychiatric conditions [43, 64, 65].

Depression

Patients with depression who experience sleep disturbances often report more severe mood symptoms. Poor sleep often precedes the new onset or recurrence of depression and also presents as a common residual symptom in patients remitted from depression. For example, approximately 70% of depressed patients continue to complain about sleep disturbances following the antidepressant treatment [56, 58]. The bidirectional and complex association between insomnia and mood problems underscores the need to specifically tackle sleep problem in comorbid insomnia and depression. Manber et al. conducted two randomized controlled trials (RCTs) to evaluate the effects of CBT-I in addition to conventional antidepressant medication in depressed patients [66, 67]. Their studies showed that CBT-I as an adjunct treatment to antidepressant was superior to antidepressant plus control therapy in reducing insomnia severity while achieving a comparable rate of remission of depression [67]. Similar results on the clinically added benefits of CBT-I were also reported when using the abbreviated version of CBT-I (two sessions) [68]. The brief CBT-I plus treatment as usual (TAU) was found to result in a reduction of insomnia symptoms and improved SE, and depressive symptoms as compared to TAU alone in patients with residual depression and refractory insomnia [68]. Furthermore, it is also encouraging to note that CBT-I was found to reduce depressive symptoms with an effect size (moderate to large) comparable to that of depression-specific psychological treatment [69]. Taken together, the existing evidence collectively suggests that CBT-I is beneficial for patients with major depressive disorder in both sleep and mood aspects.

Anxiety

Similar to depression, anxiety is often associated with insomnia. Their close association is likely related to the shared underlying mechanisms [59]. In particular, anxiety-related cognitive processes may maintain insomnia. For example, excessive worries about sleep could activate and trigger emotional or physiological arousals, resulting in sleeplessness [70]. The sleeplessness could reciprocally generate a higher level of worries and anxiety. Indeed, patients with insomnia not only worry about their overall sleep problems but also have a generally higher anxiety level.

Despite the interplay between insomnia and anxiety, it is surprising to note that there have been limited studies to investigate the effect of CBT-I with a specific focus on insomnia comorbid with anxiety disorders. A meta-analytic review of 72 studies with anxiety-related measures showed that CBT-I has a moderate effect on improving anxiety (Hedges'g = 0.41) [71]. The impact was similar among patients with anxiety problems (e.g., a high level of trait anxiety, excessive pre-sleep cognitive arousal) (Hedges'g = 0.47) and those with subclinical anxiety symptoms (Hedges'g = 0.40) [71]. However, when additionally combining anxiety treatment into CBT-I, such a combination strategy was not found to further improve anxiety symptoms or enhance treatment outcomes of insomnia [71, 72]. It might be possible that some of the techniques in CBT-I designed to reduce arousal (e.g., relaxation and constructive worry techniques) already have some therapeutic effects on anxiety. Nonetheless, there have been

only a handful of RCTs exclusively focusing on individuals with comorbid insomnia and anxiety disorders, which limited the generalizability of CBT-I to this clinical population.

Post-traumatic Stress Disorder

Insomnia is often implicated in the development of PTSD and also represents a ubiquitous and chronic symptom associated with this specific psychiatric disorder. Sleep disturbance before the traumatic event may increase the likelihood of the development of PTSD, while the occurrence of PTSD could exacerbate sleep problems [73], highlighting the important role of sleep disturbance in the clinical course of PTSD. In a recent meta-analysis on the effect of sleep intervention in PTSD patients, 5 out of 11 studies implemented CBT-I as the core treatment component [74] and showed a significant reduction of self-reported insomnia (Hedges'g = 1.15), PTSD (Hedges'g = 0.58) and depressive symptoms (Hedges'g = 0.44). For example, Talbot et al. evaluated the efficacy of CBT-I compared to waiting-list group in patients with comorbid insomnia and PTSD. While PTSD symptoms were found to improve in both arms, CBT-I group showed additional improvement in sleep as evidenced by higher SE and a higher remission rate of insomnia (41% vs. 0%) [75]. When CBT-I was combined with imagery rehearsal therapy (IRT), a technique specifically targeting nightmares, other than the beneficial effect on sleep, 50% of the patients from the sleep treatment group achieved a remission of PTSD compared to 0% in the TAU group [76]. This implies the importance of specifically addressing sleep problems including insomnia and nightmares among PTSD patients.

Alcohol Dependence

Patients with alcohol dependence (AD) report a wide range of sleep-related disturbances, particularly insomnia. It is estimated that 36% to 91% of AD patients experience sleep disturbances during both active use and withdrawal stages [55, 77–79]. Although alcohol can produce an initial effect on facilitating sleep onset, it significantly disrupts sleep continuity with increased wakefulness. The development of tolerance related to excessive and prolonged use of alcohol further increases sleep latency and sleep fragmentation [80]. Furthermore, insomnia is associated with a higher likelihood of subsequent relapse of AD. Previous research conducted in individuals recovering from AD has shown that CBT-I led to considerable improvements in sleep onset latency, insomnia symptoms, and sleep hygiene practice, but there were no significant differences in the relapse rate and the number of days abstinent from alcohol between CBT-I and control groups [81–83]. However, these studies were limited by a high attrition rate (~ 40%) [82, 83] and a small sample size (ranging from 17 to 60). As such, there is a need for more research to confirm the effectiveness of CBT-I in patients with substance use disorders [84].

CBT-I for Insomnia Comorbid with Medical Conditions

The estimated prevalence of insomnia varies from 41% to 67% among patients with comorbid medical condition, such as heart disease, chronic pain, cancer, and hypertension [25, 85]. The presence of sleep disturbance in the context of medical comorbidities might arise directly from the pathophysiology of the medical disease itself, or as a result from the substantial emotional and physical burden related to the illnesses or the side effect of the medications. The potential additional burden of comorbid insomnia on the medical condition may lead to decreased quality of life, impaired immune function, and more severe symptomatology [64, 86]. In particular, cancer and chronic pain are the two medical problems that have received relatively greater attention.

Cancer

A substantial percentage (50–60%) of cancer patients report insomnia [87], which is not surprising due to the significant distress and burden associated with this potentially fatal condition. The association between insomnia and cancer may be complex and multifactorial. It is hypothesized that biological (e.g., inflammation, circadian disruption) and psychological (e.g., depression and anxiety) factors as well as the side effects of the cancer treatments (e.g., pain, fatigue) could all contribute to the high prevalence of insomnia in cancer patients [87, 88]. In addition, the presence of insomnia could further reduce quality of life, increase fatigue, impair immune system, and also lower the survival rate in cancer patients [89]. A recent meta-analysis examining the effects of CBT-I specifically in cancer patients revealed small-to-medium effect in improving SOL ($d = 0.43$), SE ($d = 0.53$), and WASO ($d = 0.41$) as measured by sleep diary and large effect in reducing self-report insomnia symptoms ($d = 0.77$) [90]. The positive sleep changes were found to maintain at 6-month follow up. These positive changes were similarly observed across different treatment modalities (group, individual, and internet), intervention duration (varying from five to eight sessions), and stage of illness/cancer treatment [90]. There is also concomitant improvement in functional outcomes following insomnia treatment, such as improved quality of life, cancer-related fatigue, and mood symptoms [91]. There is some preliminary promising evidence suggesting

that psychotherapy may extend the survival time of cancer patients [92]. There is a need for further research to examine the long-term outcomes of CBT-I in cancer patients.

Chronic Pain

Chronic pain can be caused by numerous medical problems, such as arthritis, fibromyalgia, and spondylosis. There is evidence suggesting that people with chronic pain are 18 times more likely to have insomnia [93]. About 53–90% of people with chronic pain report insomnia problems [93–96]. Disturbed sleep could provoke pro-inflammatory responses, enhance pain experience, reduce pain tolerance, and exacerbate somatic symptoms [97–99]. Traditional pharmacological treatment for chronic pain only offers a modest reduction in pain, and sleep disturbance remains as one of the most distressing symptoms following the active pain treatment [100, 101]. Insomnia in the context of chronic pain is often under-diagnosed and under-treated. A recent meta-analysis evaluating the efficacy of non-pharmacological treatment of insomnia for patients with chronic pain has identified 9 RCTs incorporating CBT-I as the core treatment component. Consistent with the previous research on other comorbid medical or psychiatric conditions, the findings in general favored CBT-I with medium to large effect sizes ($d = 0.78$, 95% C.I. 0.42 to 1.13) in improving sleep quality, and the positive sleep gains were able to maintain for up to 12 months [102]. A modest pain reduction ($d = 0.18$, 95% C.I. 0–0.36) and moderate fatigue reduction ($d = 0.38$, 95% C.I.: 0.08 to 0.69) were also noted in the short-term [102].

Special Considerations of CBT-I in Comorbid Psychiatric and Medical Conditions

Patients with comorbid psychiatric and medical conditions may require specific clinical attention due to the complex interplay between the illnesses. The refinement and adaptation of CBT-I in the context of specific comorbid illnesses may maximize the treatment effect and optimize the concomitant improvement related to the comorbid conditions. However, the majority of the previous studies on CBT-I in comorbid conditions did not report any specific modification of the treatment content concerning the special needs of each disorder. For example, a relatively low compliance and a high dropout rate are often observed in non-pharmacological treatment of insomnia in patients with comorbidities [82]. Another example is the obstacles of implementing CBT-I in depressed patients, who might have difficulties in complying with some of the behavioral strategies, such as sleep restriction technique due to anhedonia, a lack of motivation, and low energy [103]. Moreover, previous evidence also indicated that insomnia patients with one or more comorbid psychiatric and medical conditions are less likely to respond to CBT-I treatment and are often unable to complete the treatment [64, 72, 86]. Therefore, further refinement and modification of CBT-I, such as adding motivation enhancement component or disease-specific management strategies, may be needed in order to enhance the treatment outcomes.

CBT-I Across Different Age Groups and Insomnia Subtypes

Insomnia is a prevalent health-related problem across the lifespan. While the majority of the previous research focused on CBT-I in middle aged adults, there has been emerging evidence suggesting the promising effect of CBT-I in other age groups, such as youth and older adults.

CBT-I in Youth

Adolescence is a critical developmental period associated with substantial psychological and physiological changes. There is a parallel increase of the risk of developing sleep problems, with 3.6-fold and 2.1-fold increase of the prevalence of insomnia in adolescent girls and boys, respectively [4]. Although there have been a limited number of CBT-I trials conducted in the youth population, the available data consistently supported the positive effects of CBT-I in improving both objectively and subjectively measured SOL (objective: 16.2 min, subjective: 21.4 min) and SE (objective: 2.8%, subjective: 5.3%) regardless of the format of the treatment (e.g., digitally delivered, group-based). Interestingly, subjective TST was also found to be improved in adolescents following the CBT-I treatment, and such an effect was not often seen in adults [104]. It might be possible that youths are more severely affected by sleep deprivation than adults, and the restoration of normal sleep following CBT-I treatment may enable them to acquire longer sleep. Additionally, the sleep restriction component was often not emphasized in the CBT-I intervention among youths given that sleep restriction is already "imposed" on adolescents during weekdays, particularly due to early school start time [105, 106]. The existing studies suggest that sleep-related improvement in youths was associated with the concurrent positive changes in daytime sleepiness, as well as depressive and anxiety symptoms [104], implying that CBT-I could be a promising approach to address sleep problems and improve mood symptoms and daytime functioning in adolescents.

CBT-I in Older Adults

Older population is another vulnerable group who often reports persistent insomnia, possibly due to the changes in sleep architecture with aging effect and a relatively high rate of comorbidities [107]. Approximately 30–40% of adults aged above 65 years old complain of sleep disturbance [108]. Special considerations might be needed in the implementation of CBT-I strategies in the elderly as there are often high comorbidities of psychiatric, medical, and other sleep disorders. Cognitive decline might also be a factor that warrants an adaptation of the standard CBT-I intervention. Among the few available studies, Morin et al. conducted the initial trial testing the efficacy of CBT-I compared with pharmacotherapy (temazepam) for late life (mean age: 65 years) insomnia [49]. This study demonstrated that CBT-I delivered in a group format produced similar effects as pharmacological treatment in a short term and the sleep improvements were able to sustain in favoring the CBT-I group over a long-term follow-up [49]. The short- and long-term efficacy of CBT-I was also demonstrated in Sivertsen et al.'s study, which compared the effectiveness of individual based CBT-I with pharmacological treatment (zopiclone) [50]. A recent study has shown some promising evidence that CBT-I improved not only sleep but also depressive symptoms in older adults [109].

CBT-I Across Different Insomnia Subtypes

The variable responses towards CBT-I might be partly explained by the heterogeneity of insomnia [110, 111]. A recent study has identified at least 5 stable insomnia subtypes; some of which are more prone to mood problems [112]. It is unclear whether treatment response to CBT-I differs among these various insomnia subtypes, but there has been some evidence suggesting blunted response to CBT-I in insomnia patients with objective short sleep duration (< 6 h) [111], which is considered as the most biologically severe phenotype of insomnia [113]. Nonetheless, it remains inconclusive as some studies did not show any difference in treatment response to CBT-I between those with short and normal sleep duration in adults [114] and elderly [115] with insomnia. The limited application of objective measurements including both actigraphy and polysomnography in CBT-I studies might explain the paucity of data in this area, and further research is needed to investigate the potential differences between insomnia subtypes in response to CBT-I treatment, so as to provide evidence for future development of phenotype-specific insomnia treatment.

CBT-I Across Different Cultures

Cultural factors might influence people's attitudes and beliefs about sleep, which in turn translate to culturally specific sleep behaviors. For example, an hour-long nap during noon (siesta) is a tradition in Oriental and Mediterranean cultures, such as China, Italy, and Spain. In addition, shorter nocturnal sleep duration, which is primarily driven by late bedtime, is often seen in East Asian compared to Oceanian counterparts, with Hong Kong having the latest bedtime [116, 117]. Given the potential contribution of cultural factors in one's behaviors, it has been generally suggested that cultural differences should be addressed during psychotherapy so as to provide culturally specific treatment content and strategies to the patients. Although CBT-I has been tested in different countries, only a few studies specifically mentioned the considerations of cultural factors in the treatment. For example, Birling et al. has developed a mixed protocol of individual and group formats of CBT-I, and culturally attuned relaxation and cognitive components (e.g., necessity to sleep at noon) [118]. Although this culturally adapted CBT-I program produced positive changes in diary-measured SOL, WASO, and TST, the study was limited by a lack of the control group. Nonetheless, previous research showed that the treatment outcomes of CBT-I were generally promising across different countries [46], with a significant improvement of sleep, albeit that cultural-specific factors were rarely addressed or mentioned. The necessity of having culturally adapted CBT-I has not been widely researched as compared to other CBT interventions. Given the vital role of cultural consideration in practice [119], future studies are needed to explore what constitute the effective cultural adaptions and the basis for these adaptions in delivering CBT-I.

CBT-I in Different Formats

CBT-I is conventionally delivered face-to-face by trained therapists on an individual basis. However, this mode of treatment delivery is labor-intensive and has limited the availability and dissemination of CBT-I at a large scale. It is also the major reason that CBT-I is still not widely adopted in the clinical practice despite its strong empirical evidence. Thus, alternative forms of CBT-I have been developed to overcome the limitations and increase the accessibility and feasibility of the treatment in recent years. There is emerging evidence showing that telemedicine delivery of CBT-I is another alternative option that is not inferior to traditional face-to-face modality [120].

These alternative modalities, which mainly involve the delivery of CBT-I via website or mobile app [121–123], are constructed in a structured, content-specific, and even interactive way with either guided, automated feedback, or no-support mode [124, 125]. Previous studies showed that up to 80% of the participants completed the digital CBT-I, indicating an acceptable adherence to the self-help format [126]. Other approaches of delivering CBT-I include booklets [127], emails [128], videotapes [129], and telephone consultations [130]. Although some studies indicated a superior effect of face-to-face treatment to other alternative modalities (e.g., internet-delivered) [131], growing evidence suggests comparative efficacy of different treatment modalities in improving sleep, with small-to-large effect on sleep quality ($d = 0.41$), SE ($d = 0.40$), WASO ($d = 0.55$), and SOL ($d = 0.86$) [132]. Due to its comparative efficacy with traditional format (e.g., delivered face-to-face), digital CBT-I has been suggested as the entry step (low intensity) treatment in a stepped-care model, an approach proposed as a solution to address the high demand of insomnia treatment services [126, 133].

Apart from different modalities, brief behavioral treatment for insomnia (BBTI) or single component of CBT-I (e.g., Sleep Restriction Therapy, SRT, or Stimulus Control Therapy, SCT) represents another approach to make the intervention more practical in the clinical setting [134, 135]. These alternative forms were developed to be shorter in treatment duration (e.g., two face-to-face sessions followed by two follow-up phone calls), behaviorally focused, and easily deliverable by healthcare professionals even with minimal prior sleep training [134]. A recent review evaluating the effectiveness of BBTI in the patients with insomnia demonstrated that the brief version of CBT-I led to sleep improvements as measured by sleep diary (i.e., reduced SOL and WASO, increased SE). There was also some initial evidence showing that BBTI resulted in sustained sleep improvements at 6-month follow-up [134]. However, the evidence was limited to the older population with modest sample size. To maximize its practical values in clinical practice, the implementation of BBTI should be further studied in other age groups and the clinical populations with comorbidities [134].

Combination and Sequential Treatment for Insomnia

Despite the promising evidence of CBT-I in treating insomnia, 20–30% of the patients did not respond [51, 136]. A combination of drug and psychological interventions have been proposed to maximize therapeutic gains, especially among difficult and resistant cases [137–139]. For example, insomnia patients who received both CBT-I and sleep medication have reported added value in sleep improvement (i.e., longer sleep duration) during the active treatment period [139], which was not often observed when only CBT-I treatment was prescribed. This initial combined treatment group when continuously being provided with CBT-I showed better sustained outcome than those who subsequently received medication or a combination of both treatments [139]. However, it remains unclear which approach serves the best first-stage intervention given that both CBT-I and drug treatment produce equivalent short-term benefits. A recently published trial has demonstrated that after the provision of behavioral therapy or zolpidem as the initial treatment option, sequentially adding cognitive therapy or trazodone could maximize the treatment outcomes for those who did not remit with the first-stage therapy [138]. The differential effects of various treatment sequences suggest the need to further evaluate the best treatment algorithms for patients with insomnia disorder. In addition, prescribing treatments that match individual patients' characteristics, with the consideration of one's comorbid conditions, disease severity, and patient's own preference, might be a promising personalized medicine approach that merits further research in the management of insomnia.

Other Non-pharmacological Approaches for Insomnia

Apart from CBT-I, there has been growing, albeit limited, research on complementary and alternative medicines (CAM) as a treatment for insomnia, such as mindfulness meditation, traditional Chinese medicine (TCM), Tai Chi, acupuncture, and acupressure. Indeed, CAM is the most preferred therapeutic approach selected by patients with insomnia, especially in Asian regions [140]. Among these strategies, mindfulness meditation has become another promising approach to treat insomnia in the past decade. Recently, the positive effects of mindfulness meditation on insomnia have been shown in two meta-analyses of RCTs [141, 142]. For example, Gong et al. found that mindfulness meditation significantly decreased total wake time ($d = -0.44$.) and improved sleep quality ($d = 0.68$) at post-treatment when compared with placebo or other treatments [141]. However, the results on the long-term efficacy of mindfulness mediation on insomnia were inconsistent [143–145]. For example, Wong et al. demonstrated the short-term benefits of mindfulness-based cognitive therapy (MBCT-I) on sleep in adults with chronic insomnia, but MBCT-I did not result in superior long-term treatment effects (at 8-month follow up) when compared to sleep education with exercise group [145]. In contrast, Ong et al.'s study demonstrated a long-lasting effect of mindfulness mediation in reducing insomnia symptoms. However, the study might be limited by a lack of adequate active control

Table 1 Summary of non-pharmacological treatment for management of insomnia

Insomnia treatment	Intervention component	Delivery format	Age group	Clinical population/insomnia subtypes	Future direction
CBT-I	• Psychoeducation • Sleep hygiene • Sleep restriction • Stimulus control • Relaxation exercise • Cognitive restructure	• Face-to-face individual/group • Guided/unguided ■ Website ■ Mobile App ■ Telephone consultation ■ Booklet ■ Video-based ■ Email-based	• Mainly focused on adults and elderly • Emerging evidence in youths • Limited application in children	• Chronic insomnia • Insomnia comorbid with psychiatric or medical illnesses • Insomnia with objective short sleep duration (?less effective)	• Increase the accessibility by modified brief session and digital means • Develop potential phenotype-specific insomnia treatment
Combination approach	• CBT-I + pharmacological treatment with different sequence • CBT-I + other psychological intervention (e.g., anxiety management)	• Mainly face to face individual/group format	• Adults • Elderly	• Mainly targeting chronic insomnia, insomnia comorbid with psychiatric illnesses	• Understand the best algorithm in treating insomnia • Personalized approach with consideration of patient's characteristics
Other non-pharmacological approach	• Mindfulness • Tai chi	• Mainly face to face individual/group format	• Adults • Elderly	• Mainly targeting chronic insomnia, insomnia comorbid with psychiatric illnesses	• Conduct RCTs to evaluate the treatment efficacy in different clinical populations

CBT-I cognitive behavioral therapy for insomnia, *RCT* randomized controlled trial

arm [144]. These contradictory findings indicate the need for further research on the effects of mindfulness meditation for insomnia with more rigorous study design, larger sample size, and longer-term follow up.

The herbal medications include both TCM and western herbs. There is some positive evidence supporting herbal treatment in relieving insomnia symptoms, both as monotherapy and adjunctive treatment [146, 147]. However, the specific effect of TCM for insomnia has not yet been determined owing to the heterogeneity in dosages and compositions of herbal medicine [148]. Similarly, although several reviews reported the positive effects of acupuncture and acupressure in improving sleep quality in insomnia patients, the existing studies are limited by poor study quality, small sample size, and heterogeneous methodology [149, 150]. In addition, Tai Chi, a low intensity exercise with the inclusion of meditation component, remains as another area of active research, particularly among older adults. There has been some initial evidence suggesting the positive effect of various forms of Tai Chi in improving sleep quality [151]. A recent study reported that Tai Chi has comparable effect to CBT-I in breast cancer survivors [152]. However, such a comparative effect was not observed among elderly with chronic and primary insomnia [153].

Conclusion

In summary, CBT-I is the most widely studied non-pharmacological treatment for insomnia, with strong evidence supporting its efficacy across different populations, including those with insomnia comorbid with psychiatric or medical problems. Different formats of CBT-I were found to produce significant sleep improvements across different age groups and clinical populations. There is also promising evidence regarding the concomitant improvement in functional outcomes, especially in the context of depression, anxiety, and pain, indicating that CBT-I could be an effective adjunctive treatment for patients with psychiatric and medical comorbidities. Additional research effort is warranted to further investigate the treatment mechanisms, the efficacy of different sequential treatment approaches when combining medication and CBT-I, and the algorithms of personalizing insomnia treatment that aim to maximize the long-term treatment gains, as well as the efficacy of alternative non-pharmacological interventions such as mindfulness adaptation and Tai Chi (Table 1) .

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