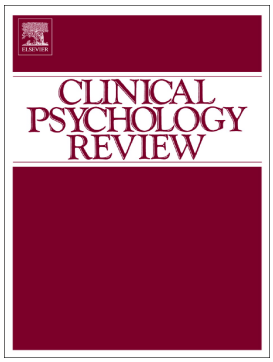

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The efficacy of cognitive and behavior therapies for insomnia on daytime symptoms: A systematic review and network meta-analysis

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Abstract

Insomnia disorder, defined by nocturnal and daytime symptoms, is highly prevalent worldwide and is associated with the onset of mental illness. Although daytime symptoms are often the reason insomnia patients seek help, it is not clear whether recommended treatment is effective on daytime symptoms. We aimed to investigate the efficacy of cognitive and behavior therapies for insomnia (CBT-I) on all daytime symptoms explored in the literature using both direct and indirect data. 86 studies (15578 participants) met inclusion criteria. Results showed significant effects of CBT-I administered face-to-face individually, in group and different self-help settings on depressive symptoms, anxiety, daytime sleepiness, fatigue, quality of life, daytime and social functioning and mental state, with Cohen's d's ranging from -0.52 and 0.81. Our results suggest that CBT-I is effective in the treatment of daytime symptoms, albeit with predominantly small to moderate effects compared to far stronger effects on the core symptoms of insomnia. Effects may be biased for depressive and anxiety symptoms, since many included studies excluded patients with severe levels of these complaints. Further, small to moderate effects may reflect that CBT-I, by improving nighttime symptoms, has a positive effect on daytime symptoms, but it does not target the daytime symptoms directly. Future studies may benefit from adding therapeutic techniques that address daytime symptoms more directly.

Keywords: network meta-analysis, insomnia disorder, cognitive behavior therapy, daytime symptoms

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Insomnia disorder is a highly prevalent disorder worldwide and belongs to the most common complaints in medical practice (Morin et al., 2015). Prevalence data show that 30-35% of the population report acute or recurrent insomnia symptoms while approximately 10% suffer from its chronic form (Ohayon, 2002). Insomnia disorder is associated with a wide range of negative outcomes including reduced quality of life (Kyle, Morgan, & Espie, 2010; LeBlanc et al., 2007; Léger et al., 2012), an increased risk for developing cardiovascular diseases (Sofi et al., 2014) as well as psychiatric disorders, especially depression and anxiety disorders (Baglioni et al., 2011, Hertenstein et al., 2019). Besides these associated negative outcomes for the individual patient, insomnia disorder is also linked with high societal costs, e.g. through increased utilization of health services, decreased workplace productivity and absenteeism at work (Léger & Bayon, 2010; Wickwire, Shaya, & Scharf, 2016). Thus, the treatment of insomnia disorder seems to be highly important. Cognitive-behavioral therapy for insomnia (CBT-I) is recommended as the first-line treatment for this disorder (Qaseem et al., 2016; Riemann et al.; 2017). Nevertheless, it is not clear whether CBT-I is effective on daytime symptoms which, however, are often the main reason insomnia patients seek help (Morin, Leblanc, Daley, Gregoire, & Merette, 2006). The present systematic review and network meta-analysis aims at filling this gap by integrating all available information from randomized controlled trials that investigated the efficacy of cognitive and behavioral therapies for insomnia on daytime symptoms.

The definition of insomnia disorder

Insomnia disorder is acknowledged as a 24-hour-disorder specifying that it consists of both nocturnal and daytime symptoms. More specifically, it is defined by a subjective report of having difficulties in initiating or maintaining sleep or early morning awakening occurring

at least three times per week over a period of at least three months. In addition, sleep difficulties must be accompanied by significant distress or impairment in daytime functioning (DSM-5, APA, 2013). While the DSM-5 provides a precise definition considering frequency, intensity and duration criteria for nocturnal symptoms, clear definitions and diagnostic criteria for daytime symptoms are missing. Compared to previous editions of DSM, DSM-5 lists the main daytime complaints associated with insomnia disorder including fatigue, decreased energy, sleepiness, mood disturbance and reduced cognitive functions, such as impaired attention, concentration and memory. Since daytime impairment is often the reason leading insomnia patients to seek treatment (Morin et al., 2006), the efficacy of insomnia treatment to address diurnal symptoms is of utmost importance.

The association between insomnia, daytime dysfunction and mental health

Since sleep occupies up to one third of the human life span, it may belong to the most important psychophysiological processes for brain function and mental health (Harvey, Murray, Chandler, & Soehner, 2011; Regier, Kuhl, Narrow, & Kupfer, 2012). Research has shown that insomnia disorder is highly comorbid with a broad range of other psychiatric disorders (Smith, Huang, & Manber, 2005). In the last years, clinical and research interest in psychopathology put emphasis on a better understanding of psychophysiological mechanisms shared between disorders, highlighting transdiagnostic and dimensional processes. Sleep disturbances in general as well as insomnia disorder have been suggested to be such a transdiagnostic process (Harvey, 2008, 2009; Riemann, Krone, Wulff. & Nissen, 2020). This argument is based on results showing that insomnia is related to the onset and maintenance of several psychiatric disorders and that CBT-I in the treatment of insomnia patients with another psychiatric comorbidity is effective not only in reducing insomnia, but also symptoms of the comorbid disorder. Harvey (2009) proposes a bidirectional relationship between sleep dysfunction and daytime symptoms/processes of psychiatric disorders

interacting in a vicious cycle and maintaining each other. She suggests that daytime symptoms like mood disturbance or distress interfere with sleep and conversely, sleep disturbances contribute to symptoms during the next day. Also, it seems reasonable to effectively treat sleep difficulties as well as daytime symptoms before they may become psychopathologic. Correspondingly, the treatment of insomnia disorder as a possible transdiagnostic factor might be important in terms of preventing psychiatric disorders (Johann, Baglioni, Hertenstein, Riemann, & Spiegelhalder, 2015; Riemann et al., 2020).

The first-line treatment of insomnia disorder

Cognitive-behavioral therapies for insomnia (CBT-I) are at present the gold standard in the treatment of the disorder (Qaseem et al. 2016; Riemann et al., 2017). This psychological treatment is considered to be superior to pharmacotherapy, especially in the long-term (Morin et al., 1999; Perlis, Jungquist, Smith, Posner, 2005). CBT-I is a multi-component treatment including behavioral techniques, relaxation, and cognitive therapy. The individual components include:

Sleep restriction. Sleep restriction therapy is a behavioral method where bedtime is restricted during the night drawing on data from a sleep diary in order to consolidate sleep (Spielman, Saskin, & Thorpy, 1987).

Stimulus control therapy. This component comprises a set of behavioral instructions to establish a stable sleep-wake rhythm and to reinforce the association between bed and sleep (i.e. going to bed only when tired and leaving the bed when unable to sleep; using the bed only for sleep; arising at the same time every morning; no daytime napping) (Bootzin, 1972).

Cognitive therapy. Cognitive therapy includes a set of strategies dealing with dysfunctional sleep-related beliefs and aiming to reduce or prevent excessive worrying about insomnia and the daytime consequences (Espie & Morin, 2004)

Sleep hygiene/psychoeducation. This component usually includes basic information about sleep and the 'sleep hygiene rules' about health practices (e.g. substance use, clockwatching) and environmental factors (e.g. temperature, noise) that promote or disturb sleep (Stepanski & Wyatt, 2003).

Relaxation. Relaxation therapy includes techniques for physical (e.g. progressive muscle relaxation, autogenic training) and mental relaxation (e.g. imagery training, meditation). (Morin, 2004)

The efficacy of CBT-I in the treatment of insomnia with and without mental and somatic comorbidity is supported by several meta-analyses of randomized controlled trials (Ballesio et al., 2018; Geiger-Brown et al., 2015; Ho et al., 2015; Ho, Chan, Lo, & Leung, 2020; Johnson et al., 2016; Koffel, Koffel, & Gehrman, 2015; Mitchell, Bisdounis, Ballesio, Omlin, & Kyle, 2019; Morin, Culbert, & Schwartz, 1994; Okajima, Komada, & Inoue, 2011; Pallesen, Nordhus, & Kvale, 1998; Seyffert et al., 2016; Trauer, Qian, Doyle, Rajaratnam, & Cunnington, 2015; van Straten & Cuijpers, 2009; Wu, Appleman, Salazar, & Ong, 2015; Ye et al., 2016; Zachariae, Lyby, Ritterband, & O'Toole, 2016). However, previous meta-analyses mainly focused on the improvement of nocturnal symptoms and only few on daytime symptoms. Van Straten and Cuijpers (2009), Ho et al. (2015, 2020), Ye et al. (2015) and Seyffert et al. (2016) conducted systematic reviews and meta-analyses on the efficacy of self-help CBT-I compared to waiting list on symptoms of anxiety and depression. They found small effects on anxiety and small to medium effects on depressive symptoms. The meta-analysis of Koffel et al. (2015) examined the efficacy of group CBT-I compared to a control condition on depressive symptoms and found no significant effects between the groups. Ballesio et al. (2018) conducted a systematic review and network meta-analysis about the efficacy of CBT-I on depressive and fatigue symptoms. Results showed small effects for

individual face-to-face CBT-I on depressive but not on fatigue symptoms, with high heterogeneity between studies.

However, there are several limitations to these systematic reviews. On the one hand, the focus was primarily on depressive symptoms and to a lower level on anxiety and fatigue symptoms. Daytime symptoms of insomnia, instead, include a much larger variety of complaints, such as sleepiness, quality of life or cognitive impairment. On the other hand, most previous reviews have been limited to pairwise comparisons using traditional meta-analysis. Therefore, they could not compare different therapeutic settings, like individual therapy, group treatment or different self-help settings (internet/booklet). The only exception is the work of Ballesio et al. (2018) who conducted a network meta-analysis, but also with some important limitations. For instance, their literature search extended a previous systematic review by Kyle et al. (2015) considering only three literature databases. Furthermore, they only included studies where sleep restriction was part of the therapy and their focus was limited to two daytime symptoms.

Network meta-analysis

Systematic reviews are of utmost importance in order to develop and implement evidence-based clinical guidelines and practice. In order to make informed decisions, clinicians must have knowledge about which of a number of existing treatments is the best for a patient with a given medical condition. However, traditional meta-analyses are able to investigate the efficacy of only one intervention compared to only one control condition. Hence, they only partially yield the necessary information for clinicians since in general there are more than two therapeutic options available (Tonin, Rotta, Mendes, & Pontarolo, 2017). Network meta-analysis, on the other hand, enters all arms of all studies of a given medical condition into a single model. The arms or interventions are entered irrespective of whether the original studies used one of them as control condition. By following the network of

reported comparisons ("edges"), direct and indirect evidence is used to obtain consensus estimates of treatment differences and associated errors. Through indirect evidence, network meta-analysis is able to estimate effects for all comparisons, even those not directly compared in any randomized controlled trial. For the explanation of the concept of indirect evidence, assume a network with three interventions A, B and C. Some studies provide information on the direct comparison of A and C (AC) and other studies provide direct evidence on the comparison of B and C (BC). Taken together, those studies provide indirect evidence for the comparison of A to B from the difference AC-BC. If direct evidence is also available, it is reconciled with the indirect evidence (Schwarzer, Carpenter, & Rücker, 2015).

Study aim

Although insomnia patients mainly suffer from the negative impact the disorder has on their daytime functioning, a precise definition of daytime symptoms is lacking and there is no sufficient knowledge about the efficacy of the first-line treatment on these diverse symptoms.

The present systematic review aims at filling this gap by evaluating the efficacy of cognitive and behavioral therapies for insomnia on all daytime symptoms and thus, to move the clinical focus closer to patients' complaints and needs. The network meta-analytic approach allows a combination of direct and indirect evidence and a differentiation between different therapeutic settings. The effective treatment of both nocturnal and daytime symptoms of insomnia can possibly prevent a wide range of negative outcomes for individual patients and for society. Knowledge about the strengths and also limitations of the first-line treatment is important for clinical practice and future research and may lead to adaptations and modifications of the treatment.

Methods

The study protocol of this systematic review and network meta-analysis was reviewed and approved for funding from the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF, FKZ: 01KG1703, https://www.gesundheitsforschung-bmbf.de/de/die-wirksamkeit-von-kognitiven-und-behavioralen-therapien-fur-insomnie-hinsichtlich-7185.php). It was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses (PRISMA-NMA) guidelines (Hutton et al., 2015) which is an extension of the original PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009) specialized for reporting systematic reviews incorporating network meta-analyses.

Search strategy

Potential studies were identified via literature search using PubMed, PsycINFO, PsycARTICLES, MEDLINE, CINAHL and Web of Science. These databases were searched from 1987, which is the publication date of DSM-III-R, until 2nd March 2020. The key search terms were: ((cognitive therapy [Title/Abstract] OR cognitive behavio* therapy [Title/Abstract] OR behavio* therapy [Title/Abstract]) AND (insomnia [Title/Abstract] OR sleep initiation [Title/Abstract] OR sleep maintenance [Title/Abstract])). Further, special issues including abstracts presented at the conferences of the European Sleep Research Society (ESRS) from 2010 to 2018 were screened in order to identify potentially eligible unpublished literature. In addition, references of all studies that were included after screening of full texts were manually searched.

Study selection

After screening of abstracts, full texts were examined to determine whether they met inclusion criteria. The present systematic review and network meta-analysis only included randomized controlled trials written in English, German, Italian, Spanish and French. Eligible

studies contained patients of any age with insomnia disorder, either in absence or in presence of other mental or somatic conditions. Insomnia disorder must be diagnosed according to DSM-5 (APA, 2013), DSM-IV-TR (APA, 2000), DSM-IV (APA, 1994), DSM-III-R (APA, 1987) or consistent criteria. Only studies including at least one arm with cognitive or behavioral therapy for insomnia disorder (CBT-I) were included. CBT-I could be administered face-to-face individually, in group treatment and different self-help settings (booklet/internet) with or without therapist support. Furthermore, insomnia therapy had to incorporate at least sleep restriction therapy, stimulus control therapy or cognitive therapy. Study arms combining CBT-I with other therapies, for example pharmacological treatment, were excluded. Studies were selected only if no CBT-I component (apart from sleep hygiene and relaxation) was included in the condition that was compared to CBT-I. Moreover, only those studies measuring daytime symptoms through standardized instruments were considered. Screening of abstracts and examination of full texts were conducted by the first and second authors (FB and TK) who discussed each study together. Any discrepancies were resolved by voting of a third author (CB). In cases of any remaining uncertainties, the studies were comprehensively discussed together with a larger group of co-authors (BF, DR, AFJ, CB, FB, TK) and decision was made by consensus.

Data extraction

For each study, data on a number of socio-demographic, clinical and treatment variables were collected. Descriptive data included a) age and sex of interventions, b) diagnostic tool according to which participants met the definition of insomnia disorder, c) inclusion criterion for duration of insomnia disorder, d) information about mental and somatic comorbidities, e) medication intake, f) treatment setting (e.g. face-to-face therapy, group therapy, etc.), g) treatment duration, h) kind of therapist, i) components of the experimental condition, j) type of control intervention and k) follow-up periods.

During data extraction, 19 classes of interventions were identified (see table 1).

Table 1

Interventions identified in the network

CBT-I interventions	other interventions
CBT-I face-to-face individually	waiting list
BT-I face-to-face individually	treatment as usual
CBT-I group	active contact control
BT-I group	sleep hygiene
CBT-I self-help (internet)	pharmacological interventions for insomnia or other condition
CBT-I self-help (internet) with therapist support	pharmacological placebo
BT-I self-help (internet) with therapist support	psychological placebo
CT-I self-help (internet) with therapist support	behavioral and psychological interventions for insomnia (e.g. stress management, mindfulness, relaxation, exercise)
CBT-I self-help (booklet)	psychological intervention for other condition
CBT-I self-help (booklet) with therapist support	

Outcome measures were classified into ten subgroups of daytime symptoms: 1.) depression, 2.) anxiety/worry, 3.) daytime sleepiness, 4.) fatigue, 5.) quality of life, 6.) daytime and social functioning, 7.) physical functioning, 8.) mental state (this outcome comprises mental functioning, mental well-being and mood), 9.) stress, 10.) cognitive functions.

Since those studies investigating the efficacy of cognitive and behavioral therapies for insomnia on cognitive functions focused on different aspects of these functions using incommensurable instruments, this outcome is not included in the network meta-analysis.

Means and standard deviations of corresponding standardized test instruments were extracted. When those data were not available in the articles, means and standard deviations were calculated from other indexes or, if not possible, authors were contacted.

Assessment of risk of bias

Risk of bias was assessed using the Cochranes Collaborations Tool (Higgins et al., 2011). In this tool six domains are assessed with a judgement of high, low or unclear risk.

Selection bias. This domain refers to systematic differences between baseline characteristics and covers two parts: 1) Did the investigators use a random sequence generation process? 2) Could intervention allocations have been foreseen in advance of enrolment?

Performance bias. This domain judges whether participants and personnel were blinded.

Detection bias. This domain refers to whether outcome assessors are aware of intervention assignments.

Attrition bias. This domain refers to systematic differences between groups in withdrawals from a study. Amount, nature, or handling of incomplete outcome data are evaluated.

Reporting bias. This domain refers to selective outcome reporting.

Other bias. This domain covers other sources of bias, e.g. differences in baseline characteristics despite of the use of a random sequence generation process.

Because blinding therapists and patients is often not possible in psychotherapy studies, an additional category “risk of bias not judged” was used in the assessment of performance and detection bias.

The first and the second author (FB, TK) as well as the third and the fourth author (AB, VB) conducted the risk of bias assessment together. Any discrepancies were resolved by consensus discussion.

Statistical analyses

Analyses were planned for funding application to the German Regional Ministry for Education and Research (Bundesministerium für Bildung und Forschung, BMBF, FKZ: 01KG1703, https://www.gesundheitsforschung-bmbf.de/de/die-wirksamkeit-von-kognitiven-und-behavioralen-therapien-fur-insomnie-hinsichtlich-7185.php). The plan was structured together with a biostatistician with excellent expertise in network meta-analyses (GR). Since the included studies measured daytime symptoms with a variety of different instruments, effect sizes were calculated as standardized mean differences (Cohen's d) from baseline to post-treatment assessment. We referred to data of participants who completed the post-treatment assessment. Meta-analytic calculations were performed with the open statistical software environment R (R Core Team, 2019). A frequentist network meta-analysis was performed using the R-package "netmeta" (Rücker et al., 2019; Schwarzer et al., 2015). All classes of interventions were compared against waiting list because this was the most commonly used control group. A random-effects model was employed because of expected considerable heterogeneity between studies (e.g. comorbidities, different treatment variables, etc.).

To test network heterogeneity, Cochran's Q and Higgin's I^2 were calculated. Cochran's Q is computed as a weighted sum of squared differences between single study effects and the pooled effect across studies. Significant values indicate a high level of heterogeneity between studies that needs to be further investigated. Higgin's I^2 calculates the variability in effect estimates that is due to between-study heterogeneity rather than due to chance. Low percentages of I^2 are indicative of low heterogeneity while percentages over 75% represent considerable levels of heterogeneity (Higgins & Thompson, 2002).

To assess the geometry of the network, function netgraph() of "netmeta" was used. This function allows a graphical representation of the comparisons included in the network. An example is shown in figure 1.

Please insert here figure 1

Figure 1. Network graph for the outcome "depression". The network graph consists of nodes that represent the interventions and edges that represent direct evidence, i.e. interventions that are directly compared in at least one study. The width of those lines is based on sample size for those comparisons. Finally, shadows indicate multi-arm studies.

Net heat plots (Krahn, Binder, & König, 2014) were plotted to investigate potential sources of heterogeneity.

When possible, sensitivity analyses were conducted by splitting the network into subgroups in order to further investigate potential sources of heterogeneity and to precise clinical recommendations.

Results

Figure 2 illustrates the search flow. A total of 5480 studies were identified by pasting the key words in the databases PubMed, PsycINFO, PsycARTICLES, MEDLINE, CINAHL and Web of Science. After removing the duplicates and screening of abstracts 348 studies remained and the corresponding full texts were evaluated. Examining references within the full texts and searching for eligible unpublished studies identified one additional article. Finally, 86 studies met inclusion criteria and were included in the qualitative synthesis. 81 studies were entered in the network meta-analysis. One study examined the efficacy of CBT-I on cognitive functions exclusively and for this outcome no network meta-analysis was performed. For the remaining four studies, no quantitative data of daytime symptoms were available and authors either didn't have the data anymore or didn't answer to our request.

Reasons for excluding studies are reported in figure 2. Detailed information on reasons for exclusion all potential full-texts can be found in the supplemental material (Table S1).

Please insert here figure 2

Figure 2. Search flow. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and MetaAnalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Study characteristics

A summary of included studies is shown in table A1 in appendix. The total sample included 15578 participants at baseline and 10686 participants at post-treatment assessment. 41 studies investigated a specific sample of insomnia patients, e.g. insomnia patients with a comorbid disorder. 45 studies investigated insomnia patients without a particular comorbidity. In 23 studies, abstinence of sleep medication before begin of the study was demanded. 19 Studies required sleep medication to be stable while 44 did not document such a requirement.

Eight studies administered BT-I, six of them through individual therapy, one through group therapy and one through self-help (internet) with therapist support. One study investigated the efficacy of CT-I delivered through self-help setting (internet) with therapist support. CBT-I was administered individually face-to-face in 27 trials, in group setting in 28 trials and in self-help setting in 29 trials. Taking a closer look at the self-help setting, 22 studies conducted internet-based CBT-I while seven of them additionally offered support by a therapist. Seven studies conducted self-help therapy administered through a booklet, three of them offered additional therapist support.

With respect to the control conditions, the majority of studies used waiting list (n = 23). Sleep hygiene was chosen as control condition in 19 trials, active contact control in twelve trials, treatment as usual (TAU) in 14 trials, psychological placebo in nine trials and

pharmacological placebo in three trials. Other interventions that were compared to CBT-I comprised pharmacological interventions (five trials), other behavioral and psychological interventions for insomnia (eleven trials) and CBT for other conditions (three trials: CBT for generalized anxiety disorder, CBT for pain, CBT for depression).

Eight studies including 3114 participants at baseline and 1806 participants at posttreatment investigated the efficacy of CBT-I on cognitive functions. Since these studies used different instruments measuring different aspects of cognitive functions, no meta-analytical comparison was performed on them. A summary of their results can be found in table A2 (appendix).

Instruments for daytime outcomes included in the network meta-analysis are summarized in table A3 (appendix).

Network meta-analysis

63 studies measured depressive symptoms, while 59 of those provided quantitative data and therefore could be included in the network meta-analysis. In total, 9008 participants were investigated with respect to this outcome. The network consisted of 17 interventions and was based on 83 pairwise comparisons. Figure 3a shows the forest plot presenting the effects of all available classes compared with waiting list. Results showed significant mean effects of group CBT-I (d = -0.41, 95% CI: [-0.64; -0.17]), CBT-I administered individually face-to-face (d = -0.37, 95% CI: [-0.62; -0.12]), and in different self-help settings (internet: d = -0.35, 95% CI: [-0.59; -0.12]; internet + therapist support: d = -0.36, 95% CI: [-0.62; -0.11]) with small effect sizes. All other interventions did not show significant effects compared to waiting list. Cochran's Q and Higgins I^2 tests revealed high heterogeneity between studies (Q = 327.71, df = 55, $p < 0.0001$, $I^2 = 83.2\%$). The net heat plot with detailed information on sources of heterogeneity can be found in appendix (see figure A4).

Please insert here figure 3

Figure 3. Forest plots of all outcomes. Effects of all available classes are compared with waiting list.

47 studies measured anxiety/worry symptoms as outcome measure. Of those, 44 studies including 7305 participants (16 interventions/58 pairwise comparisons) indicated quantitative data for network meta-analytical calculations. Results (see forest plot in figure 3b) showed significant mean effects of CBT-I administered individually face-to-face (d = -0.31, 95% CI: [-0.61; -0.01]), in group setting (d = -0.37, 95% CI: [-0.64; -0.11]) and in different self-help settings with small effect sizes (internet: d = -0.32, 95% CI: [-0.57; -0.08]; internet + therapist support: d = -0.38, 95% CI: [-0.65; -0.11]). A large effect was found for CBT for other condition which consists of CBT for pain, depression and generalized anxiety disorder (d = -1.56, 95% CI: [-2.67; -0.45]). Cochran's Q and Higgins I^2 tests revealed high heterogeneity between studies (Q = 220.83, df = 36, p < 0.0001, I^2 = 83.7%). The net heat plot with detailed information on sources of heterogeneity can be found in appendix (see figure A5).

20 studies measured the efficacy of BT-I/CBT-I on daytime sleepiness, 18 studies investigating a total of 2193 participants (13 interventions/28 pairwise comparisons) could be included in the network meta-analysis. Results showed significant mean effects of individually delivered BT-I (d = -0.34, 95% CI: [-0.66; -0.03]) and CBT-I administered individually face-to-face, in group and internet self-help setting with small effect sizes (individual therapy: d = -0.43, 95% CI: [-0.70; -0.16]; group: d = -0.20, 95% CI: [-0.36; -0.04]; internet self-help: d = -0.38, 95% CI: [-0.66; -0.11]). Also, significant effects were shown for pharmacological intervention with a medium effect size (d = -0.57, 95% CI: [-1.00; -0.13]) and for behavioral and psychological intervention (d = -0.25, 95% CI: [-0.49; -

0.02] with a small effect size. Cochran's Q and Higgins I^2 tests revealed no heterogeneity between studies (Q = 7.83, df = 11, p = 0.7280, I^2 = 0%).

36 studies measured fatigue as outcome measure, 33 studies with 3736 participants (14 interventions/43 pairwise comparisons) were entered in the network meta-analysis. Significant mean effects with small effect sizes were found for CBT-I administered in group setting (d = -0.42, 95% CI: [-0.62; -0.21]) and different self-help settings (booklet + therapist support: d = -0.47, 95% CI: [-0.81; -0.13]; internet: d = -0.49, 95% CI: [-0.70; -0.28]; internet + therapist support: d = -0.30, 95% CI: [-0.57; -0.03]) as well as for other interventions like behavioral and psychological intervention (d = -0.42, 95% CI: [-0.73; 0.11]) and TAU (d = -0.26, 95% CI: [-0.50; -0.03]). Furthermore, results showed a significant mean effect for CBT-I individually face-to-face with a medium effect size (d = -0.52, 95% CI: [-0.77; -0.27]). Cochran's Q and Higgins I^2 tests revealed moderate heterogeneity between studies (Q = 58.69, df = 25, p = 0.0002, I^2 = 57.4%). Detailed information on sources of heterogeneity can be found in appendix (see figure A6).

Nine studies including 794 participants (11 interventions/11 pairwise comparisons) investigated the effects on overall quality of life. Results showed significant mean effects of group CBT-I (d = 0.43, 95% CI: [0.04; 0.81]) and different self-help settings (CBT-I booklet: d = 0.25, 95% CI: [0.07; 0.43]; CT-I internet + therapist support: d = 0.38, 95% CI: [0.14; 0.61]) with small effect sizes. Since the network consists of only eleven interventions and eleven comparisons, heterogeneity tests are not possible.

22 studies investigated the efficacy of cognitive and behavior therapies for insomnia on "daytime and social functioning", 20 studies investigating 4893 participants (18 interventions/30 pairwise comparisons) could be included in the network meta-analysis. Significant mean effects with medium effect sizes were found for BT-I delivered through group therapy (d = 0.60, 95% CI: [0.15; 1.04], through individual therapy (d = 0.53, 95% CI:

[0.12; 0.94]) and through self-help therapy (internet + therapist support) (d = 0.62, 95% CI: [0.36; 0.89]. Looking at CBT-I, significant mean effects with small effects were found for individual therapy (d = 0.48, 95% CI: [0.14; 0.82]) and self-help therapy (booklet + therapist support) (d = 0.48, 95% CI: [0.15; 0.82]). Medium effect sizes were found for group CBT-I (d = 0.50, 95% CI: [0.23; 0.77]) and online self-help CBT-I without support (d = 0.74, 95% CI: [0.41; 1.06]) and with support by a therapist (d = 0.62, 95% CI: [0.17; 1.08]). Large effects were shown for CT-I delivered in self-help setting (internet) accompanied by therapist support (d = 0.81, 95% CI: [0.53; 1.08]) and for pharmacological placebo (d = -1.40, 95% CI: [-1.97; -0.83]). Further, significant effects were found for TAU (d = 0.36, 95% CI: [0.04; 0.68]), sleep hygiene (d = 0.45, 95% CI: [0.12; 0.77]) and psychological placebo (d = 0.50, 95% CI: [0.15; 0.85]) with small to moderate effect sizes. Heterogeneity between studies can be considered as low (Q = 9.85, df = 8, p = 0.2758, I^2 = 18.8%).

11 studies including 1156 participants (11 interventions/17 pairwise comparisons) measured physical functioning as outcome measure. No significant effects were found. Cochran's Q and Higgins I^2 tests revealed no heterogeneity between studies (Q = 1.01, df = 4, p = 0.9077, I^2 = 0%).

24 studies measured "mental state" as outcome measure, 23 of them (4755 participants/13 interventions/33 pairwise comparisons) could be included in the network meta-analysis. Results showed significant mean effects of CBT-I administered in different self-help settings with small effect sizes (booklet + therapist support: d = 0.39, 95% CI: [0.01; 0.76]; internet: d = 0.31, 95% CI: [0.08; 0.54]; internet + therapist support: d = 0.32, 95% CI: [0.05; 0.59]). Heterogeneity between studies was moderate (Q = 28.64, df = 16, p = 0.0265, I^2 = 44.1%). Detailed information on sources of heterogeneity is available in appendix (figure A7).

Six studies investigating 585 participants (7 interventions/8 pairwise comparisons) measured stress. Since CBT-I was compared to four different conditions, they were lumped together as "control" because otherwise no consistent network could be created. No significant effects were found. Cochran's Q and Higgins I^2 tests revealed no heterogeneity between studies (Q = 0.25, df = 1, p = 0.6198, I^2 = 0%).

Subgroup analysis

Since the largest networks with most data were found for depressive and anxiety symptoms, they were considered most suitable for conducting subgroup analyses. Because heterogeneity was very high between studies, interpretation of results is limited. In order to reduce heterogeneity, we aimed at investigating the efficacy of CBT-I in a subgroup of studies that did not demand any comorbidities (e.g. cancer, depression) or specific conditions (e.g. pregnancy) in addition to insomnia disorder as inclusion criteria.

Depression

The subgroup comprised 30 studies investigating 6572 participants. The network consisted of 15 interventions and was based on 48 pairwise comparisons. Results indicated significant effects of individual CBT-I (d = -0.28, 95% CI: [-0.49; -0.08]), group CBT-I (d = -0.20, 95% CI: [-0.36; -0.04]) and different self-help settings (CBT-I booklet: d = -0.26, 95% CI: [-0.42; -0.10]; internet: d = -0.32, 95% CI: [-0.45; -0.19]; internet + therapist support: d = -0.25, 95% CI: [-0.40; -0.10]; BT-I internet + support: d = -0.45, 95% CI: [-0.75; -0.14]; CT-I internet + support: d = -0.49, 95% CI: [-0.79; -0.18]), with small to moderate effect sizes. Cochran's Q and Higgins I^2 tests revealed moderate heterogeneity between studies (Q = 42.63, df = 25, p = 0.0154, I^2 = 41.4%).

Anxiety/worry

The subgroup comprised 25 studies investigating 5448 participants (14 interventions/37 pairwise comparisons). Results showed significant effects of differently administered self-

help formats (CBT-I booklet: d = -0.21, 95% CI: [-0.39; -0.03]; CBT-I internet: d = -0.33, 95% CI: [-0.48; -0.18]; CBT-I internet + therapist support: d = -0.34, 95% CI: [-0.49; -0.18]; BT-I internet + therapist support: d = -0.39, 95% CI: [-0.72; -0.06]), with small effect sizes. Significant mean differences with medium effect sizes were found for individually administered CBT-I (d = -0.58, 95% CI: [-0.90; -0.26]) and active contact control (d = -0.52, 95% CI: [-0.96; -0.09]). Cochran's Q and Higgins I^2 tests revealed moderate heterogeneity between studies (Q = 32.94, df = 18, p = 0.0170, I^2 = 45.4%).

Risk of bias

Figure 4 shows an overview of the risk of bias across all included studies. Detailed information about the risk of bias assessment including the reasons for each judgement for all domains and all included studies is available upon request.

Please insert here figure 4

Figure 4. Overview of risk of bias results across all included studies. The ratings are illustrated in four colors: green indicates a low risk, yellow indicates an unclear risk and red indicates a high risk. Grey color means that risk of bias was not judged.

Many studies were rated as unclear, especially with respect to the randomization process and reporting bias. Therefore, many studies did not sufficiently describe their methods and for most of them no study protocol existed. The majority of studies was not judged with respect to performance and detection bias because in most psychotherapy studies blinding of participants and therapists is not possible. The percentage of "not judged risk" is lower for detection bias because in some cases participants could be blinded and outcome measures usually were questionnaires that were assessed by the participants themselves. The most problematic aspect in our sample of studies was study attrition. The highest amount of high risk was found in this domain and again, amount and handling of missing data was not sufficiently reported by 12% of studies. Taken together, no study was judged with "high risk"

in more than two risk of bias domains and therefore no study was excluded from the network meta-analysis. Due to the high percentage of unclear ratings risk of bias can be rated as moderate across all studies.

Discussion

To our knowledge, this is the first systematic review and network meta-analysis investigating the efficacy of cognitive and behavioral therapies for insomnia taking into consideration all daytime symptoms explored in the literature. Through the network meta-analytical approach, it was possible to compare the efficacy of different kinds of treatment settings (individual therapy, group therapy, different self-help settings). According to this work, ten subgroups of daytime symptoms can be differentiated: depressive symptoms, anxiety/worry symptoms, daytime sleepiness, fatigue, overall quality of life, daytime and social functioning, physical functioning, mental state, stress and cognitive impairment.

Efficacy of CBT-I on daytime symptoms

With respect to the quantitative synthesis, we found significant effects of cognitive and behavioral therapies for insomnia (CT-I/BT-I/CBT-I) on all daytime symptoms with small to medium effect sizes, except for physical functioning and stress.

Depression

Network meta-analytic results have shown significant effects of CBT-I administered through individual therapy, group therapy and internet self-help therapy (with and without additional support by a therapist) on depressive symptoms. Effect sizes were small and comparable suggesting that none of the specific treatment settings examined is superior. No other intervention reached statistical significance. Results should be interpreted with caution because of large heterogeneity between studies. However, results from a subgroup of studies

in a more homogenous population of insomnia patients revealed less heterogeneity between studies while showing similar results.

Anxiety/worry

Also with respect to anxiety/worry, significant effects were found for CBT-I delivered individually face-to-face, in group and internet self-help settings with small effect sizes. Again, none of the examined treatment setting was superior. The largest effect size was found for "CBT for other condition" which is not surprising since this intervention includes CBT for generalized anxiety disorder. Heterogeneity was found to be high indicating that results should be interpreted with caution. Subgroup analyses in the more homogeneous insomnia patient studies showed comparable effects, but a medium – instead of a small - effect of individual CBT-I.

Daytime sleepiness

Results showed significant results of individual BT/CBT-I, group CBT-I as well as internet self-help CBT-I on daytime sleepiness. Effect sizes were small with the smallest effect size for group CBT-I suggesting that individual and internet self-help treatment formats might be slightly superior in the treatment of daytime sleepiness.

Fatigue

Considering fatigue, the results of this network meta-analysis showed small to moderate effects for different CBT-I settings (individual face-to-face, group, different self-help formats) as well as for two other interventions, namely behavioral and psychological interventions and treatment as usual (TAU). Looking at the CBT-I settings, the largest effect size was found for individual therapy, followed closely by the two self-help settings internet CBT-I and booklet CBT-I with therapist support. Behavioral and psychological interventions, comprising acupuncture and tai chi, had a similar effect on fatigue as CBT-I.

Quality of life

Group CBT-I and different self-help settings showed significant effects on quality of life, with small effect sizes. Group setting and cognitive therapy administered through online self-help setting, but with additional therapist support, seem to be slightly superior over others. The highest effect size was found for individually delivered CBT-I, but did not reach statistical significance, probably due to smaller sample size.

Daytime and social functioning

With respect to daytime and social functioning, many CBT-I as well as other interventions showed significant effects, with small to high effect sizes. Hence, CBT-I seems to be effective in comparison to waiting list. However, in comparison to other interventions, CBT-I might be only slightly superior. The largest effect size in the favorable direction was found for self-help CT-I with additional support by a therapist, indicating that cognitive strategies might be helpful in the treatment of daytime and social functioning. The large negative effect for pharmacological placebo can be interpreted as a morphological artefact since this control intervention is connected to the network through a single three-arm study with large treatment differences to the active interventions (CBT-I individual and pharmacological intervention).

Mental state

Considering the outcome 'mental state', significant effects were found for CBT-I administered in different self-help settings. Effect sizes were small and similar between the different self-help formats.

Comparison to other meta-analyses of CBT-I on daytime symptoms

Our results are partly in accordance with previous qualitative and quantitative syntheses that have investigated the efficacy of cognitive and behavioral therapies for insomnia on daytime symptoms. Van Straten and Cuijpers (2009), Ho et al. (2015, 2020), Ye

et al. (2015) and Seyffert et al. (2016) investigated the efficacy of self-help CBT-I compared to waiting list on symptoms of depression and anxiety. In accordance with our results, they found small effects on anxiety. With respect to depressive symptoms, we found small effects of self-help CBT-I while they found small to medium effects. Like in our sample of studies, heterogeneity was found to be moderate to large for depressive symptoms, but low for anxiety symptoms while heterogeneity was high in our sample of studies. Investigating the efficacy of group CBT-I compared to a control group on depressive symptoms, Koffel et al. (2015) found no significant effects between the groups while we found a small effect. Ballesio et al. (2018) investigated the efficacy of CBT-I on depressive and fatigue symptoms using a network meta-analytical approach. Results showed small effects for individual face-to-face CBT-I on depressive but not on fatigue symptoms, with high heterogeneity between studies. In comparison to their results, we additionally found significant effects of group and self-help CBT-I on depressive symptoms and significant effects of differently administered CBT-I (individual, group, different self-help formats) on fatigue symptoms, with small to moderate effect sizes and high heterogeneity between studies.

Clinical implications

Taken together, this systematic review and network meta-analysis suggests that CBT-I, while developed to treat insomnia, is effective with respect to daytime symptoms in large heterogeneous patient groups. However, results indicate predominantly small to moderate effects. In comparison, systematic reviews evaluating the efficacy of CBT-I on self-report nocturnal symptoms and sleep parameters (e.g. sleep efficiency, total sleep time, sleep onset latency, wake after sleep onset) demonstrate good efficacy, with moderate to large effect sizes (e.g. Geiger-Brown et al., 2015; Johnson et al., 2016; Koffel et al., 2015; Morin et al., 1994; Okajima et al., 2011; Pallesen et al., 1998; Seyffert et al., 2016; Trauer et al., 2015; Van Straten et al., 2018; Wu et al., 2015; Zachariae et al., 2016). This could suggest that

CBT-I may not target the daytime symptoms directly but indirectly through improving nocturnal symptoms. In fact, the CBT-I protocol exists since more than 20 years (Morin, 1993) and there weren't significant modifications since that time. Hence, it might be appropriate to widen the existing treatment protocol by concepts or techniques from other therapies addressing daytime symptoms more directly, e.g. emotion regulation training, motivational elements, acceptance, behavioral activation and exercise etc. Adaptations of the treatment protocol in future studies might be promising, also due to the fact that many patients retain sleep disturbances after CBT-I (Harvey & Tang, 2003).

Transdiagnostic models highlighted insomnia as a possible process involved in the onset of several psychiatric disorders (Harvey, 2008, 2009) and thus, its importance in the psychiatric field. Consequently, successfully treating nocturnal and daytime symptoms of the disorder may have potential impact on preventing mental disorders. According to the results of the present work, CBT-I seems to be effective in reducing symptoms of depression and anxiety and improving mental functioning even though the effects were mainly small. However, it must be noted that most of the included studies investigated samples without severe baseline levels of depression or anxiety. Widening CBT-I by treatment elements that more directly target daytime symptoms like for instance motivational or emotional techniques might have the potential to reach greater improvements of symptoms of psychopathology.

Limitations and future directions

Some limitations of the present work should be addressed. For instance, some daytime symptoms as well as specific treatment comparisons have been less frequently investigated than others, i.e. many networks have unbalanced designs. Thus, quality of evidence differs and clinical conclusions are limited. For some outcomes (e.g. depression) the network is based on data from many studies and consists of many different interventions. For other outcomes (e.g. quality of life, physical functioning or stress) few data exists and

consequently, their networks are rather small. With regard to cognitive functions, no network meta-analytic calculations could be performed because instruments were difficult to compare. Furthermore, due to lack of data, some daytime instruments measuring slightly different constructs were summarized in particular categories. For instance, the outcome "daytime and social functioning" consists of instruments measuring social functioning, work performance and general daytime functioning. "Mental state" comprises instruments measuring mental well-being, mood and mental functioning. Altogether, more research is definitely necessary in order to strengthen the empirical evidence base on the efficacy of different administered CBT-I treatment settings on daytime symptoms and to formulate further clinical recommendations.

Another limitation of this work is that no analysis of follow-up data was conducted. It would be interesting to find out if effects remain stable or even increase after sleep parameters have stabilized. However, the included randomized controlled trials measured outcomes at varying follow-up times, e.g. 2, 3, 6 or 12 months which were difficult to summarize. Moreover, heterogeneity was moderate to high for some daytime symptoms which limits corresponding conclusions. Consequently, future clinical studies on insomnia treatment should put effort on establishing consistent study designs and procedures (e.g. use similar instruments, choose similar follow-up times, apply consistent inclusion criteria, etc.).

Furthermore, risk of bias results were not considered in our meta-analytic calculations, i.e. no study was excluded from the network meta-analysis due to the risk of bias assessment. This approach was based on the finding that for a lot of studies many bias domains were rated as unclear because no sufficient information was available to give a high or low risk judgement. This illustrates the necessity of high reporting quality of future individual studies in order to increase meaningfulness of future qualitative and quantitative syntheses.

Additionally, no further subgroup analyses were performed. Clearly, it would be interesting to gain insight into the efficacy of CBT-I in different populations (e.g. insomnia patients with only mental or somatic comorbidity, insomnia patients on or off sleep medication, etc.) in order to know which treatment is best for an individual patient with a given condition. Nevertheless, it was decided to conduct no further subgroup analyses because splitting networks leads to data loss and other parameters might not be equally distributed across different subgroups.

Finally, publication bias could not be analyzed. Indeed, it is still debated in the literature how to conduct publication bias analyses in the specific context of network meta-analyses. Funnel plots which are commonly used in traditional meta-analyses to assess publication bias are not recommended with regard to network meta-analyses where the direction of effects of small studies cannot be assumed (Chaimani et al., 2013). Most of our included trials were performed to test the efficacy of CBT-I on nocturnal symptoms, while daytime symptoms were observed as secondary outcomes. Therefore, we assume a minor risk of not publishing negative results.

Conclusion

This systematic review and network meta-analysis was the first attempt to summarize all available information from randomized controlled trials evaluating the efficacy of cognitive and behavioral therapies for insomnia on daytime symptoms. Until now, no precise definition for daytime symptoms exists. This work identified ten classes of daytime symptoms: depression, anxiety, daytime sleepiness, fatigue, quality of life, physical functioning, mental state, daytime and social functioning, stress and cognitive impairment. CBT-I was shown to be effective on a wide range of daytime symptoms with small to moderate effect sizes. In order to reach larger effects, future studies may add therapeutic techniques that directly address daytime symptoms, like for example motivational and

emotional elements. The treatment of nocturnal and daytime symptoms of insomnia disorder, e.g. through stepped care models (Espie, 2009; Vincent & Walsh, 2013) has the potential to prevent a wide range of negative outcomes for both, the individual patient and the society.

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Appendix A

Table A1

Study characteristics

Study	Insomnia definition according to	CBT-I Intervention	Inclusion of a comorbidty (insomnia + …)	Daytime instrument	N [Pre-Post]	Age [Years: Mean (SD)]	Sex [% Fem-ale]	Other study arms	N [Pre-Post]	Age [Years: Mean (SD)]	Sex [% Fem-ale]
Alessi et al. 2016	ICSD-2	CBT-I individual face-to-face CBT-I group		PHQ-9, SF-12-PCS, SF-12-MCS	54 - 52 52 - 45*	72.1 (7.9) 72.1 (7.9)	1.8 3.8	SH	53 - 53	72.4 (7.3)	1.9
Belleville et al. 2016	DSM-IV	CBT-I individual face-to-face	Generalized Anxiety Disorder	BAI, BDI	5 - 5	44.5 (10.09)	100	CBT for other condition (Generalized Anxiety Disorder)	5 - 5	44.5 (10.09)	100
Bergdahl et al. 2016	DSM-5	CBT-I group	Long-term hypnotic drug users	HADS-A, HADS-D, ESS	32 - 25	60.5 (9.4)	85.7	Behavioral and psychological intervention (Auricular Acupuncture)	27 - 25	60.5 (9.4)	87.5
Bergdahl et al. 2017	DSM-5	CBT-I group	Long-term hypnotic drug users	SF-12-PCS, SF-12-MCS	32 - 25	60.5 (9.4)	85.7	Behavioral and psychological intervention (Auricular Acupuncture)	27 - 25	60.5 (9.4)	87.5
Bjorvatn et al. 2011	DSM-IV	CBT-I self-help (booklet)		HADS-A, HADS-D	77 - 66	49.6 (14.5)	59.7	SH	78 - 61	50.3 (13.2)	56.4

Blom et al. 2015	DSM-5	CBT-I self help (internet) + therapist support	Major Depression	MADRS-S	22 - 21	46.1 (13.6)	35	CBT for other condition (iCBT Depression)	21 - 20	48.2 (11)	65
Bothelius et al. 2013	RDC	CBT-I group		HADS-A, HADS-D, ESS, FSS, SF-36-MCS	32* - 31	48.1 (13.2)	78	WL	34* - 33	53 (9.4)	94
Bruin et al. 2015	DSM-5	CBT-I self help (internet) + therapist support		ANT, AVLT, FT, PVT, CSRQ-DS, CSRQ - LoE, CSRQ-I	18 - 18	15.4 (1.4)	77.8	WL	14 - 14	16.6 (1.7)	85.7
Bruin et al. 2018	DSM-5	CBT-I self help (internet) + therapist support, CBT-I group		YSR (anxiety and affective subscales)	39 – 38 38 - 38	15.3 (1.4) 15.6 (1.7)	84.6 68.4	WL	39 - 39	15.9 (1.6)	71.8
Cassidy-Eagle et al. 2018	DSM-5	CBT-I group	older adults with mild cognitive impairment (MCI)	HVLT-R, Trail Making Test parts A/B, D-KEFS,	14 - 12	89.36 (4.6)	86	Placebo condition (psychological)	14 - 11	88.69 (4.87)	86
Chen et al. 2011	DSM-IV	CBT-I group	hemodialysis patients	BAI, BDI, FSS	37 - 37	57 (9)	54.1	SH	35 - 35	59 (11)	62.9
Chen et al. 2008	DSM-IV	CBT-I individual face-to-face	hemodialysis patients	FSS, PSQI-DD	13 - 13	51.9 (8.6)	38.5	SH	13 - 11	48.7 (14.6)	46.2

Cheng et al. 2019	DSM-5	CBT-I self help (internet)		QIDS	946 - 358	44.5 (15.8)	78	SH	439 - 300	45.7 (15.1)	80
Christensen et al. 2016	DSM-IV	CBT-I self-help (internet)	(subclinical- / mild-) Depression	GAD-7, PHQ-9, BTACT, WHODAS-12	574 - 248	42.51 (12.24)	45	Placebo condition (psychological)	575 - 333	42.95 (12.17)	74
Cortesi et al. 2012	Other	CBT-I individual face-to-face	Autism Spectrum Disorder	CSHQ	33 - 33	7.1 (0.7)	17	Pharmacological intervention	34 - 34	6.8 (0.9)	18
								Placebo condition (pharmacological)	32 - 32	6.3 (1.2)	16
Currie et al. 2004	DSM-IV	CBT-I individual face-to-face	Nonmalignant chronic pain of a musculoskeletal origin	BDI	20 - 16	43.3 (10.9)	30	Active Contact Control	20 - 17	43.3 (10.9)	30
		CBT-I self-help (booklet) + therapist support			20 - 15	43.3 (10.9)	30				
Currie et al. 2000	DSM-IV	CBT-I group	Recovering Alcoholics	BDI	32 - 31	45 (8)	55	Active Contact Control	28 - 26	45 (8)	55
Dirksen & Epstein 2008	DSM-IV, ICSD-R	CBT-I group	Breast cancer survivors	STAI-T, CES-D, POMS-F	34 - 34	57.2 (9.9)	100	SH	38 - 38	59.2 (10.7)	100
Edinger et al. 2005	DSM-III	CBT-I individual face-to-face	Fibromyalgia	SF-36-MCS	15* - 15*	50.1 (6.9)	94.4	Active Contact Control	9* - 9*	48.3 (9.1)	100
								SH	17* - 17*	46.5 (9.0)	94.4
Edinger et al. 2001	DSM-III	CBT-I individual face-to-face		BDI	25 - 23	55.8 (12.1)	44.0	Behavioral and psychological intervention (Progressive Muscle Relaxation Training)	25 - 23	54.5 (10.2)	44.0

								Placebo condition (psychological)	25 - 24	55.7 (9.5)	52.0
Edinger et al. 2007	DSM-IV	CBT-I individual face-to-face		STAI-T, BDI, POMS	23* - 21*	57.0 (10.2)	50.0	Active Contact Control	11* - 9	52.4 (7.3)	36.4
Epstein et al. 2012	Other	CBT-I group		STAI-T, GDS	41 - 39	67.22 (6.55)	65.9	WL	50 - 38	69.50 (8.34)	64.0
Espie et al. 2008	DSM-IV	CBT-I group	Cancer survivors	HADS-A, HADS-D, FSI-I	85 - 74	Median 60.5	69	TAU	43 - 41	Median 60.5	68
Espie et al. 2012	DSM-5	CBT-I self-help (internet)		DC	55 - 43	50.7 (13.8)	72.7	Placebo condition (psychological) TAU	55 - 41 54 - 47	47.3 (13.0) 49.1 (13.7)	76.4 70.4
Espie et al. 2014	DSM-5	CBT-I self-help (internet)		DASS-A, DASS-D, DASS-S	55 - 43	50.7 (13.8)	72.7	Placebo condition (psychological) TAU	55 - 41 54 - 47	47.3 (13.0) 49.1 (13.7)	76.4 70.4
Espie et al. 2007	DSM-IV, ICSD-R	CBT-I group		SF-36-EV, SF-36-SF, SF-36-PCS	107 - 76	54.4 (15.4)	67.3	TAU	94 - 67	54.1 (14.4)	69.1
Espie et al. 2019	DSM-5	CBT-I self-help (internet)		GAD-7, CFQ, ESS, PHQ-9, FFS, WEMWBS, WPAI, PROMIS-10, RAS	853 - 468	48.4 (13.9)	76.7	SH	858 - 517	47.7 (13.6)	78.7
Falloon et al. 2015	ICSD-2	BT-I individual face-to-face		GAD-7, PHQ-9, ESS, FFS	46 - 45	55.4 (12.7)	84.8	SH	51 - 50	51.8 (13.4)	70.6

Freeman et al. 2015	ISI Score ≥15	CBT-I individual face-to-face	Non-affective psychosis	MFI, EQ-5D-5L, WEMWBS	24* - 22	39.6 (11.6)	33.3	TAU	26 - 24	42.2 (13.5)	30.8
Freeman et al. 2017	DSM-5	CBT-I self-help (internet)		GAD-7, PHQ-9, WEMWBS, WSAS	1891 - 733	24.8 (7.7)	72	TAU	1864 - 1142	24.6 (7.6)	71
Garland et al. 2014	DSM-IV, ICSD-2, RDC	CBT-I group	Cancer survivors	POMS-SF, C-SOSI	40 - 40	58.73 (10.46)	80	Behavioral and psychological intervention (Mindfulness Based Stress Reduction)	32 - 32	60.33 (12.21)	62.5
Garland et al. 2019	DSM-5	CBT-I individual face-to-face	Cancer survivors	HADS-A, HADS-D, MFSI-SF, PROMIS-10 (PCS + MCS)	80 - 73	60.7 (12.0)	60	Behavioral and psychological intervention (Acupuncture)	80 - 75	62.3 (11.4)	53.8
Hagatun et al. 2018	DSM-5	CBT-I self-help (internet)		HADS, CFS	95 - 76	45.0 (12.4)	64	SH	86 - 65	44.8 (13.7)	71
Ho et al. 2014	DSM-IV	CBT-I self-help (internet)		DASS-A, DASS-D, MFI, SF-36-PCS, SF-36-MCS	104 - 60	38.6 (11.8)	67.3	WL	105 - 65	39.9 (12.7)	75.2
		CBT-I self-help (internet) + therapist support			103 - 58	36.9 (13.0)	70.9				
Horsch et al. 2017	DSM-5	CBT-I self-help (internet)		HADS-A, CES-D	74 - 45	39.0 (13.0)	61	WL	77 - 62	41.0 (13.9)	64
Hou et al. 2014	Other	BT-I group	Hemodialysis patients	PSQI-DD	51 - 51	54.5 (13.8)	60.8	TAU	47 - 47	52.4 (14.5)	53.2

Irwin et al. 2014	DSM-IV-TR/ICSD-2	CBT-I group		ESS, IDS-C, MFI	50 - 48	66.4 (6.1)	78	Behavioral and psychological intervention (Tai Chi Chih)	48 – 40	66.3 (7.4)	64.6
								SH	25 - 24	66.4 (7.7)	72
Irwin et al. 2017	DSM-5	CBT-I group	Breast cancer survivors	ESS, IDS-C, MFI	45 - 42	60.0 (9.3)	100	Behavioral and psychological intervention (Tai Chi Chih)	45 - 38	59.6 (7.9)	100
Jacobs et al. 2004	Other	CBT-I individual face-to-face		BDI, POMS-F	15-14	47.1 (8.1)	66.7	Pharmacological intervention	15-13	45.4 (9.3)	73.3
								Placebo condition (pharmacological)	15-14	46.6 (10.1)	73.3
Jansson-Frojmark et al. 2012	DSM-IV-TR	CBT-I individual face-to-face	Hearing impairment	HADS-A, HADS-D, WSAS	17 - 15	57.8 (6.6)	58.9	WL	15 - 15	53.6 (10.4)	66.6
Jernelov et al. 2012	RDC	CBT-I self-help (booklet)		SDS-DF, SD-PDR, CORE-OM, PSS	45 - 44	47.4 (13.3)	80	WL	44* - 39	45.4 (16)	90.9
		CBT-I self-help (booklet) + therapist support			44 - 43	50.8 (11.8)	75				
Jungquist et al. 2010	Other	CBT-I individual face-to-face	Nonmalignant chronic pain of a musculoskeletal origin	BDI	19 - 15	52 (9.9)	83.3	Active Contact Control	9 - 6	43 (10.7)	88.9

Kaldo et al. 2015	RDC	CBT-I self-help (internet) + therapist support		PSS	73 - 66	47.0 (15.2)	81	Behavioral and psychological intervention	75 - 60	49.0 (15.6)	76
Kaldo et al. 2020	RDC	CBT-I group		GP- CORE, SD-DF, SD-F	20 - 18	52.2 (10.7)	65	TAU	20 - 15	57.9 (10.8)	75
Kalmbach et al. 2019	DSM-5	CBT-I individual face-to-face, BT-I individual face-to-face	Postmenopausal women	BDI, PSWQ	52 – 42, 52 - 38	55.14 (5.06) 56.63 (4.95)	100	SH	50 - 42	57.34 (5.97)	100
Kalmbach et al. 2019	DSM-5	CBT-I individual face-to-face, BT-I individual face-to-face	Postmenopausal women	FSS, ESS, WPAI, SF-36 subscales	52 – 50, 52 - 50	55.32 (5.90) 56.76 (5.39)	100	SH	50 - 50	57.24 (5.55)	100
Lancee et al. 2012	DSM-IV	CBT-I self-help (booklet) CBT-I self-help (internet)		HADS-A, CES-D	203 - 175 214 - 165	51.2 (12.8) 52.2 (11.4)	74.4 68.7	WL	200 - 181	51.9 (12.2)	68.0
Lancee et al. 2015	DSM-5	CBT-I self-help (internet) + therapist support		HADS-A, CES-D	36 - 32	47.47 (14.37)	83.3	WL	27 - 22	49.98 (13.71)	74.1
Lancee et al. 2016	DSM-5	CBT-I individual face-to-face, CBT-I self-		HADS-A, CES-D	30 – 29, 30 -	38.5 (13.1) 41.2	73.3 86.7	WL	30 - 26	45.1 (13.7)	83.3

		help (internet) + therapist support			26	(14.1)					
Lopez et al. 2019	DSM-5	CBT-I self-help (internet)		BDI, ESS, STAI, CFS, EQ-5D	23 - 18	46.0 (8.15)	82.61	SH	23 - 20	45.0 (9.64)	65.22
Lovato et al. 2014	Other	CBT-I group		ESS, FFS, DFFS	86 - 78	64 (6.45)	50	WL	32 - 31	64 (6.45)	50
Manber et al. 2019	DSM-5	CBT-I individual face-to-face	Pregnant women	EPDS	89 - 71	33.4 (5.2)	100	Placebo condition (psychological)	90 - 63	32.6 (4.9)	100
Martínez et al. 2014	DSM-IV	CBT-I group	Fibromyalgia	SCL-90-R, MFI-GF, PSQI-DD	30 - 30	46.53 (8.31)	100	SH	29 - 27	48.66 (7.27)	100
Matthews et al. 2014	Other	CBT-I individual face-to-face	Breast cancer survivors	HADS-A, HADS-D, FFI, PFS	32 - 30	52.17 (6.86)	100	Placebo condition (psychological)	28 - 26	52.85 (7.75)	100
McCrae et al. 2018	DSM-5	BT-I individual face-to-face		STAI, BDI, GDS, neuro-psychological test battery	32 - 27	67.97 (5.97)	68.75	Active Contact Control	30 - 23	71.03 (9.06)	66.67
McGrath et al. 2017	Other	CBT-I self-help (internet)	Blood pressure 130-160 / <110 mmHg	BAI, BDI	54 - 54	58.3 (11.9)	62.7	TAU	67 - 67	59.7 (9.9)	59.7
Miró et al. 2011	DSM-IV	CBT-I group	Fibromyalgia	HADS-A, HADS-D, ANT-I	20 - 20	43.94 (6.06)	100	SH	20 - 20	50.20 (6.12)	100
Morgan et al. 2012	DSM-IV	CBT-I self-help (booklet) + therapist support	Chronic disease (osteoarthritis, heart disease, hypertension, diabetes, fibromyalgia, cancer, depression,	FSS	98 - 63	67.0 (7.9)	69.4	TAU	95 - 74	66.3 (6.9)	63.2

			COPD, parkinson)								
Morin et al. 1993	ICSD	CBT-I group		STAI, BDI, POMS	12 - 12	67.1 (5.3)	70.8	Active Contact Control	12 - 12	67.1 (5.3)	70.8
Norell-Clarke et al. 2015	DSISD	CBT-I group	(Subclinical- / mild-) Depression	BDI, WSAS	32 - 30	49.3 (12.5)	68.8	Behavioral and psychological intervention (Relaxation Training)	32 - 23	53.7 (12.4)	84.4
Omvik et al. 2008	DSM-IV	CBT-I individual face-to-face		STAI-T , BDI, SDA, VIG-CR, VIG-RT, QoLI, IIP, SF-36-PCS, SF-36-MCS	21* - 21*	59.74 (4.14)	47.8	Pharmacological intervention	18* - 18*	62.00 (6.52)	47.8
Pigeon et al. 2012	Other	CBT-I individual face-to-face	Nonmalignant chronic pain of a musculoskeletal origin	CES-D, ISS, MH	6 - 6	50.7 (8.3)	66.7	WL	5 - 5	50.7 (8.3)	66.7
								CBT for other condition (Pain)	4 - 4	50.7 (8.3)	66.7
Ritterband et al. 2012	DSM-IV	CBT-I self-help (internet)	Cancer survivors	HADS-A, HADS-D, MFSI, SF-12-PCS, SF-12-MCS	14 - 14	53.7 (10.8)	100	WL	14 - 14	59.6 (12.3)	71.4
Robabeh et al. 2015	DSM-IV	CBT-I individual face-to-face	Patients undergoing methadone maintenance therapy (MMT)	PSQI-DD	11 - 11	43.5 (8.3)	0	Placebo condition (psychological)	11 - 11	44.7 (7.8)	0
Rybarczyk et al. 2005	Other	CBT-I group	Coronary artery disease, Nonmalignant chronic pain of a	GDS, SF-36-PCS, SF-36-MCS	45* - 45*	70.1 (9.1)	60.9	Behavioral and psychological intervention (Stress Management and	43* - 43*	67.7 (7.9)	73.9

			musculoskeletal origin, Pulmonary disease					Wellness Training)			
Sadler et al. 2018	DSM-5	CBT-I group	Major Depression	GDS, GAI-SF, EQ-5D,	24 – 24	74.7 (7.1)	62.5	SH	23 - 22	72.3 (7.6)	52.2
Sandlund et al. 2018	DSM-IV	CBT-I group		MADRS-S, FSS, GHQ-12	82 - 72	55.0 (17.1)	71.1	TAU	71 - 60	54.0 (14.7)	74.7
Savard et al. 2005	DSM-IV, ICSD	CBT-I group	Breast cancer survivors	HADS-A, HADS-D, MFI, QLQ-C33 (global)	28 – 24	54.81 (7.01)	100	WL	30 - 30	53.37 (7.72)	100
Schlarb et al. 2016	ICSD-3	CBT-I group		ESS-C	86 - 71	8.1 (1.8)	47.3	WL	26 - 24	8.1 (1.8)	47.3
Schlarb et al. 2011	ICSD-2	CBT-I group		CSHQ	22 - 22	7.6	52.6	Active Contact Control	16 - 16	7.7	52.6
Smitherman et al. 2016	ICSD-3	BT-I individual face-to-face	Chronic migraine	GAD-7, PHQ-9, ESS	16 - 14	29.6 (13.4)	93.8	Behavioral and psychological intervention ("Lifestyle Modification")	15 - 13	32.1 (12.8)	86.7
Soeffing et al. 2008	ICSD-2	BT-I individual face-to-face	Hypnotic-dependent adults	STAI, GDS, ESS, FSS, IIS	20 - n.i.	63.5 (8.7)	60	Placebo condition (psychological)	27 - n.i.	64.82 (6.5)	66.7
Sunnhed et al. 2020	DSM-5	CT-I self-help (internet) + therapist support, BT-I self-help (internet) + therapist support		HADS-A, HADS-D, WSAS, BBQ	72 – 67	51.5 (12.5)	76.4	WL	74 - 74	54.2 (14.6)	73
					73 - 70	51.8 (14.5)	69.9				

Sweetman et al. 2019	ICSD-3	CBT-I individual face-to-face	obstructive sleep apnea	ESS, FFS, DASS-A, DASS-D, DASS-S	72 – 70	59.1 (9.9)	44.4	TAU	73 - 72	57.3 (9.9)	45.2
Talbot et al. 2014	RDC	CBT-I individual face-to-face	PTSD	BDI, ESS, WSAS	29 - 27	37.1 (10.4)	75.9	Active Contact Control	16 - 15	37.3 (11.0)	56.3
Taylor et al. 2014	DSM-5	CBT-I individual face-to-face		STAI, QIDS, ESS, MFI-GF, Q-LES-QSF, PSS	17 - 16	19.47 (1.66)	23.5	WL	17 - 13	19.94 (2.49)	58.8
Taylor et al. 2017	DSM-5	CBT-I individual face-to-face, CBT-I self-help (internet)		ESS	33 – 30 34 - 27	30.79 (6.42) 34.53 (7.73)	21 18	Active Contact Control	33 - 29	32.82 (8.11)	12
Taylor et al. 2018	DSM-5	CBT-I individual face-to-face		BAI, BDI, MFI, VR-12-PCS, VR-12-MCS	75 – 65	32.21 (7.18)	17	Active Contact Control	76 - 68	32.67 (7.97)	18
Thorndike et al. 2013	DSM-IV	CBT-I self-help (internet)		STPI-T, BDI, MFSI, SF-12-MCS	22 - 21	44.68 (10.61)	81.8	WL	23 - 22	45.05 (11.67)	72.7
Vallieres et al. 2005	DSM-IV	CBT-I individual face-to-face		PSWQ, BDI	6 - 6	41.6 (5.7)	58.8	Pharmacological intervention	6 - 5	41.6 (5.7)	58.8
van der Zweerde et al. 2019	DSM-5	CBT-I self-help (internet) + therapist support	Depressive symptoms	HADS-A, PHQ-9, FSS, DC	52 - 45	44.64 (13.12)	80.8	Active Contact Control	52 - 47	46.29 (15.07)	82.7

van der Zweerde et al. 2020	DSM-5	CBT-I self-help (internet) + therapist support	HADS-A, HADS-D, FSS, WSAS, DC	69 - 43	51.7 (15.77)	62	TAU	65 - 41	49.4 (16.01)	68
van Straten et al. 2014	DSM-IV	CBT-I self-help (internet) + therapist support	HADS-A, CES-D, EQ-5D-5L	59 - 49	48.7 (13.8)	59.3	WL	59 - 53	50.1 (11.9)	81.4
van Straten et al. 2009	Other	CBT-I self-help (booklet)	HADS-A, CES-D, EQ-5D-5L, SF-36-MCS	126 - 118	52.0	67	WL	121 - 115	52.0	64
Vincent et al. 2009	RDC	CBT-I self-help (internet)	MFI	59 - 40	n.i.	67.80	WL	59 - 39	n.i.	66.10
Wu et al. 2006	Other	CBT-I individual face-to-face	PSQI-DD	19 - 19	38 (12)	53.2	Pharmacological intervention	17 - 17	38 (12)	53.2
							Placebo condition (pharmacological)	17 - 17	38 (12)	53.2

Note. BT-I = Behavioral therapy for Insomnia, CBT-I = Cognitive behavioral therapy for Insomnia; N = Number of participants; n.i. = not indicated; SH = Sleep hygiene; TAU = Treatment as usual; WL = Waiting list; * = if different numbers for different outcome measures are indicated in the study, here the highest is shown; Abbreviations of daytime instruments and their meanings are listed in table 3.

Table A2

Studies evaluating the efficacy of CBT-I on cognitive functions

Study (Author, Year)	Sample N, Mean age ± SD, % Female	CBT-I compo-nents	Therapy delivery	Outcome measures	Cognitive domain investigated	Results (Baseline - Post-treatment)
de Bruin et al., 2015	Total N = 32, adolescents CBT-I: 18 (15.4±1.4; 77.8%) WL: 14 (16.6±1.7; 85.7%)	SH, CT, SR, SC, R	6 weekly sessions; self-help (internet) + therapist support; Certified sleep therapist	Five subtests of the Amsterdam Neuropsychological Tasks (ANT): baseline speed, feature identification, memory search letters, response organization arrows, and spatial temporal span; Auditory Verbal Learning Test (AVLT); Letter Fluency; Psychomotor Vigilance Task (PVT) (all objective measures)	Simple reaction time, visuospatial processing, selective attention and working memory, response inhibition and set-shifting, visuospatial working memory; declarative memory; aspects of language and executive functioning; sustained attention	CBT-I superior to control on visuospatial processing, selective attention and phonological working memory ($p < .05$). Trend towards improvements also in response inhibition and set shifting, letter fluency and sustained attention ($p < .01$)
Cassidy-Eagle et al., 2018	Total N = 28, older adults with mild cognitive impairment CBT-I: 14 (89.36±4.6, 86%) Placebo: 14 (88.69±4.87, 86%)	SH, CT, SR, SC, R	6 sessions; group therapy; clinical psychologist/board certified behavioral sleep medicine specialist	Neuropsychological assessment battery: Hopkins Verbal Learning Test (HVLT-R); Trail Making Test parts A/B; Delis Kaplan Executive Function System (D-KEFS) (objective measures)	Verbal learning and memory; attention and processing speed; executive functioning and task shifting; inhibition and switching	Results showed a significant effect of CBT-I on a key measure of executive functioning sub task of inhibition ($p < .02$) and a positive trend on the inhibition-switching task ($p < .08$) compared to placebo.
Christensen et al., 2016	Total N = 1149, internet users with depressive symptoms CBT-I: 574 (42.51±12.24;	SH, CT, SR, SC	6 sequential online modules (SHUTi); self-help (internet)	Brief Test of Adult Cognition by Telephone (BTACT) (objective measure)	Verbal memory (immediate and delayed), working memory span, verbal fluency, attention	Group by time interaction effects were non-significant for all task domains

	45%) Placebo (HealthWatch): 575 (42.95±12.17; 74%)				switching/reaction time, reasoning, speed of processing	(p > .05)
Espie et al., 2019	Total N = 1711, adults CBT-I: 853 (48.4±13.9; 76.7%) SH: 858 (47.7±13.6, 78.7%)	SH, CT, SR, SC, R	6 sessions (Sleepio); self-help (internet)	Cognitive Failures Questionnaire (CFQ) (self-report cognitive measure)	Subjective cognitive functioning	Significant difference in favor of dCBT-I, small effect size (p < .001, d = 26)
Matthews et al., 2014	Total N = 56, breast cancer survivors CBT-I: 30 (52.17±6.86; 100%) Placebo: 26 (52.85±7.75; 100%)	SH, CT, SR, SC	6 weekly sessions; individual face-to-face; Nurse	Attentional Function Index (AFI) (self-report cognitive measure)	Attention and working memory	A trend toward improvement in the cognitive functioning in the CBT-I group (p = .07, d = .56)
McCrae et al., 2018	Total N = 62, older adults BT-I: 32 (67.97±5.97, 68.75%) Active Contact Control: 30 (71.03±9.06, 66.67%)	SH, SC, SR, R	4 weekly sessions; individual face-to-face; predoctoral psychology students	Neuropsychological battery: Mini-Mental State Exam (MMSE); Vocabulary, Digit Symbol- Wechsler Intelligence Scale-III; Trailmaking Test A/B; Controlled Oral Word Association (COWA)-Semantic Verbal + Phonemic Fluency; Boston Naming Test (BNT); California Verbal Learning Test (CVLT-II); Rey-Osterreith Complex Figure Test (Rey-O); Logical Memory from Wechsler Memory Scale 3 (LM-WMS-III), (objective measures)	Overall cognitive functioning; attention, processing speed; language; memory; executive functioning	No change in performance on any of the neuropsychological outcomes.
Miró et al.,	Total N = 31, fibromyalgia	SH, CT,	6 weekly sessions;	Attentional Network	Alertness, orienting and	The CBT-I group showed

2011	patients CBT-I: 16 (43.94±6.06; 100%) SH: 15 (50.20±6.12; 100%)	SC, SR, R	group therapy (n = 5-6 patients); Psychologists, CBT-I experts	Test-Interactions (ANT-I) (objective measure)	executive functioning	a significantly greater improvement than the SH group in executive functioning ($p < .01$) and in alerting ($p < .01$), and a marginally significant larger reduction in overall RT.
Omvik et al., 2008	Total N = 45, older patients, 47.8 % Female CBT-I: 23 (59.74±4.14) Zopiclone: 22 (62.00±6.52)	SH, CT, SR, SC, R	6 weekly sessions; individual face-to-face; Clinical psychologist	Sleep diary (alertness) (self-report), Vigil 5.0 (objective measure)	Subjective alertness and vigilance	Subjective alertness: a significant interaction effect between the CBT-I and the Zopiclone group appeared ($p < .05$): subjective alertness improved more in the Zopiclone group than the CBT-I group from baseline to post-treatment Vigilance: Group by time interaction effects were non-significant for both reaction times and accuracy ($p >. 05$).

Note. CBT-I = Cognitive Behavioral Therapy for Insomnia; SH = Sleep Hygiene Education; CT = Cognitive Therapy; R = Relaxation; SC = Stimulus Control; SR = Sleep Restriction; WL = Waiting list

Table A3

Daytime instruments

Outcome	Scale	Number of studies
Depression	Beck Depression Inventory (BDI; Beck, 1961; Beck, Steer, Ball, & Ranieri, 1996)	19
	Depression Score of Hospital Anxiety and Depression Scale (HADS-D; Zigmond & Snaith, 1983)	12
	Centre for Epidemiologic Studies Depression Scale (CES-D; Eaton, Smith, Ybarra, Muntaner, & Tien, 2004)	8
	Patient Health Questionnaire-Depression Scale (PHQ-9; Kroenke, Spitzer, & Williams, 2001)	7
	Geriatric Depression Scale (GDS; Yesavage et al., 1982)	5
	Depression Score of Depression Anxiety Stress Scale (DASS-D; Henry & Crawford, 2005)	3
	Quick Inventory of Depressive Symptomatology (QIDS; Rush et al., 2003)	2
	Depression Subscale of Symptom Checklist-90-Revised (Derogatis & Unger, 2010)	1
	Self-Report of the Montgomery Asberg Depression Scale (MADRS-S; Montgomery & Asberg, 1979; Svanborg & Asberg, 1994)	2
	Subscale "Affective problems" of the Youth Self-Report (YSR, Achenbach, 1991)	1
	Inventory of Depressive Symptomatology, IDS-C (Rush et al., 1996)	2
	Edinburgh Postnatal Depression Scale (EPDS, Cox, Holden, & Sagovsky, 1987)	1
Anxiety/Worry	Anxiety Score of Hospital Anxiety and Depression Scale (HADS-A; Zigmond & Snaith, 1983)	19
	State-Trait Anxiety Inventory (STAI; Spielberger, 2010)	9
	Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988)	4
	Generalized Anxiety Disorder 7-item Scale (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006)	5
	Penn State Worry Questionnaire (PSWQ; Startup & Erickson, 2006)	2
	Anxiety Scale of Depression Anxiety Stress Scale (DASS-A; Henry & Crawford, 2005)	3
	Anxiety Subscale of SCL-90-R (Derogatis & Unger, 2010)	1
	Anxiety Subscale of State-Trait Personality Inventory (STPI-Trait only; Spielberger, 1995)	1
	Geriatric Anxiety Inventory-Short Form (GAI-SF, Byrne et al., 2011)	1
	Subscale "Anxiety problems" of the Youth Self-Report (YSR, Achenbach, 1991)	1
Daytime sleepiness	Epworth Sleepiness Scale (ESS; Johns, 1991)	17
	Children's Sleep Habit Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000)	2
	Epworth Sleepiness Scale for Children (ESS-C; Melendres, 2004)	1
	Sleepiness Subscale of Chronic Sleep Reduction Questionnaire (CSRQ-DS; Dewald, Short, Gradisar, Oort, & Meijer, 2012)	1

Fatigue	Fatigue Severity Scale (FSS; Krupp, 1989)	9
	Multidimensional Fatigue Inventory (MFI; Smets, Garssen, Bonke, & De Haes, 1995)	10
	Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF; Stein, Jacobsen, Blanchard, & Thors, 2004)	3
	Dimension "General Fatigue" of Multidimensional Fatigue Inventory (MFI-GF; Smets et al., 1995)	2
	Flinders Fatigue Scale (FFS; Gradisar et al., 2007)	5
	Piper Fatigue Scale (PPS; Piper et al., 1998)	1
	Fatigue/Inertia Subscale of Profile of Mood States (POMSF/I; McNair, Lorr, & Droppleman, 1992)	1
	Energy/Vitality Subscale of Short Form-36 Health Questionnaire (SF-36; Jenkinson, Layte, Wright, & Coulter, 1996)	1
	Daytime Fatigue Subscale of Sleep Diary (Morin, 1993)	2
	Interference Subscale of Fatigue Symptom Inventory (FSI; Hann et al., 1998)	1
	Loss of Energy Subscale of Chronic Sleep Reduction Questionnaire (CSRQ-LoE, Dewald et al., 2012)	1
	Chalder Fatigue Scale (CFS, Chalder, Berelowitz, Pawlikowska, et al., 1993)	2
Quality of life	Euroqol 5 Dimensions 5 Levels (EQ-5D; Brooks, 1996; Brooks, Rabin, & de Charro, 2003)	5
	Quality of Life Inventory (QoLI; Frisch, Cornell, Villanueva, & Retzlaff, 1992)	1
	Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-QSF; Endicott, Nee, Harrison, & Blumenthal, 1993)	1
	Global quality of life scale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30+3, Aaronson, Ahmedzai, & Bergman, 1993; Osoba, Aaronson, Zee, et al., 1997)	1
	Brunnsviken Brief Quality of Life (BBQ, Lindner et al., 2016)	1
Daytime and social functioning	Daytime Dysfunction Subscale of Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989)	5
	Work and Social Adjustment Scale (WSAS; Mundt, Marks, Shear, & Greist, 2002)	6
	Daytime Feeling and Functioning Scale (DFFS; Gradisar, Lack, Harris, Richards, Gallasch, Boundy, & Garrett, 2006)	1
	Social Functioning Subscale of Short Form-36 Health Questionnaire (SF-36; Jenkinson et al., 1996)	2
	Inventory of Interpersonal Problems (IIP; Alden, Wiggins, & Pincus, 1990)	1
	Positive Daytime Ratings Subscale of Sleep Diary (Morin, 1993)	1
	WHO Disability Assessment Scale (WHODAS; Epping-Jordan, & Ustun, 2000)	1
	Work Productivity and Activity Impairment questionnaire (WPAI,, Reilly, Zbrozek, & Dukes, 1993)	2
	Relationship Assessment Scale (RAS, Hendrick, Dicke, & Hendrick, 1998)	1
	Daytime Consequences of insomnia (DC, Espie et al., 2012)	3
Physical functioning	Physical Component Score of Short Form-36 Health Questionnaire (SF-36-PCS; Ware, Kosinski, & Keller, 1994)	5
	Physical Component Score of Short Form-12 Health Questionnaire (SF-12-PCS; Ware, Kosinski, & Keller, 1996)	3

	Physical health summary score of the Patient-Reported Outcomes Measurement Information System-Global Health Scale (PROMIS-10, Hays, Bjorner, Revicki, et al., 2009)	1
	Physical Component Summary of the Veterans RAND 12-Item Health Survey (VR-12, Kazis et al., 2006)	1
Mental state	Mental Component Score of Short Form-36 Health Questionnaire (SF-36-MCS; Ware et al., 1994)	7
	Mental Component Score of Short Form-12 Health Questionnaire (SF-12-MCS; Ware et al., 1996)	4
	Profile of Mood States (POMS; McNair et al., 1971)	2
	Profile of Mood States – Short Form (POMS-SF; Shacham, 1983)	1
	Clinical Outcomes in Routine Evaluation-Outcome Measure (CORE-OM; Evans et al., 2002)	1
	Warwick-Edinburgh Mental Well-being Scale (WEMWBS; Tennant et al., 2007)	3
	Irritation Subscale of Chronic Sleep Reduction Questionnaire (CSRQ; Dewald et al., 2012)	1
	Mental health summary score of the Patient-Reported Outcomes Measurement Information System-Global Health Scale (PROMIS-10, Hays, Bjorner, Revicki, et al., 2009)	1
	Mood item of the Consensus Sleep Diary (Carney et al., 2012)	1
	Mental Component Summary of the Veterans RAND 12-Item Health Survey (VR-12, Kazis et al., 2006)	1
	Clinical Outcomes in Routine Evaluation (GP-CORE, Evans et al., 2005)	1
Stress	Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983)	3
	Stress Subscale of Depression Anxiety Stress Scale (DASS-S; Henry & Crawford, 2005)	2
	Calgary Symptoms of Stress Inventory (C-SOSI; Carlson & Thomas, 2007)	1

Figure A4. Net heat plot of „depression“. The area of the grey squares indicates the contribution of pooled direct evidence of each single design in the column to each network estimate in the row. This tool also graphically represents changes in Cochran's Q statistic due to relaxing the consistency assumption for single designs in a matrix visualization. "Hot spots" of inconsistency are indicated by red colors while blue colors indicate consistency. The net heat plot suggests that the designs that are together responsible for the majority of between-design heterogeneity are the following ones: 1.) CBT-I group compared to sleep hygiene, 2.) CBT for other condition compared to CBT-I individual face-to-face, 3.) CBT for other condition compared to waiting list (designs 2. and 3. are designs involved in a three-arm study comparing CBT for other condition, CBT-I individual face-to-face and waiting list.) and 4.) CBT-I individual face-to-face compared to CBT-I self-help (internet) + therapist support (design from a three-arm study comparing CBT-I individual face-to-face, CBT-I self-help (internet) + therapist support and waiting list. Red color which is not on the top-left to bottom-right diagonal indicates that the evidence for the treatment comparison of a row from the design(s) in the corresponding column is inconsistent with the other evidence.

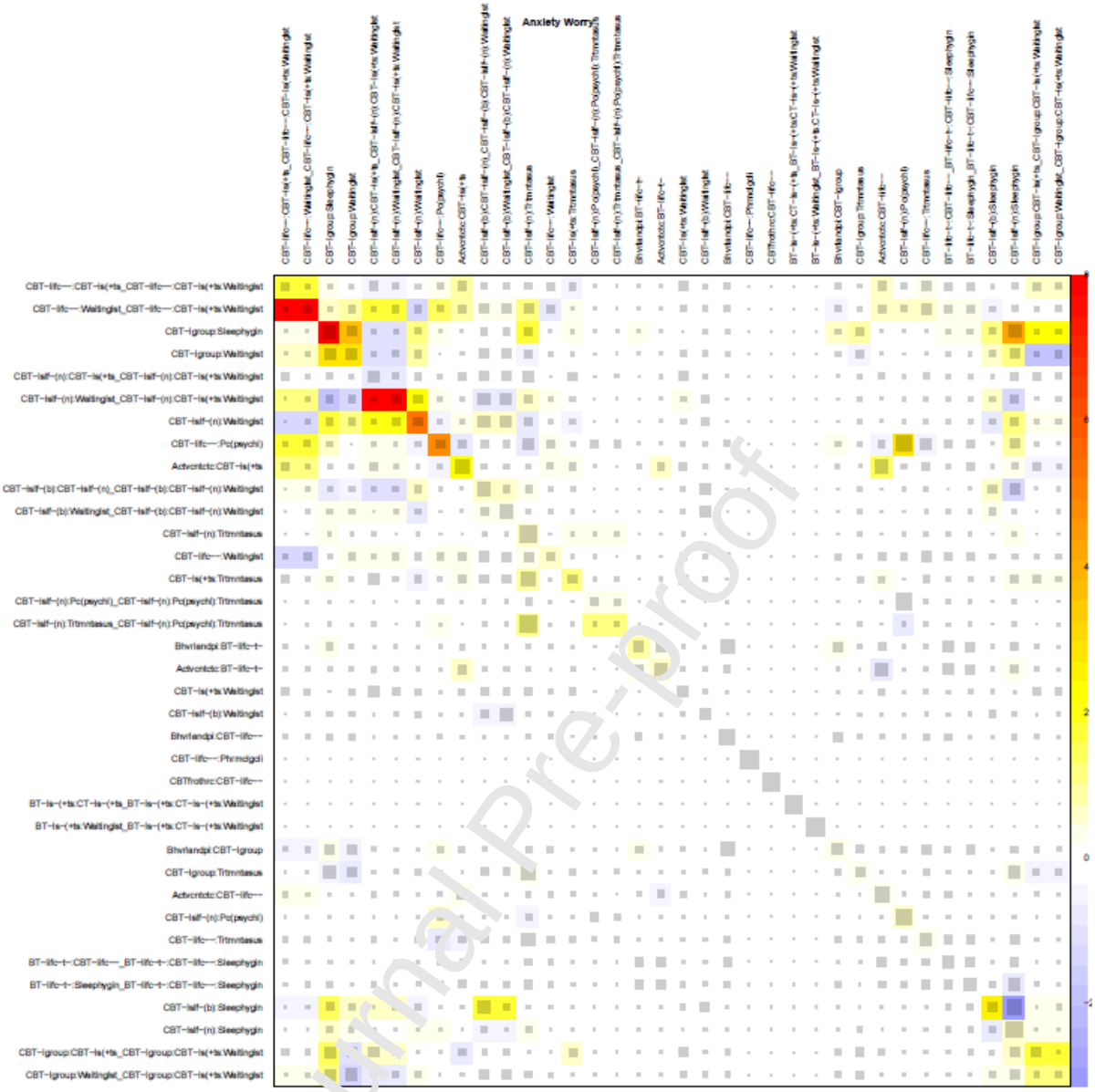

Figure A5. Net heat plot of "anxiety/worry". The net heat plot suggests that the designs that are together responsible for the majority of between-design heterogeneity are the following ones: 1.) CBT-I individual face-to-face compared to waiting list (from the three-arm study comparing CBT-I individual face-to-face, CBT-I self-help (internet) + therapist support and waiting list), 2.) CBT-I group compared to sleep hygiene, 3.) CBT-I self-help (internet) compared to waiting list (from the three-arm study comparing CBT-I self-help (internet), waiting list and CBT-I self-help (internet) + therapist support).

Figure A6. Net heat plot of "fatigue". According to the net heat plot the design "CBT-I self-help (internet) compared to waiting list" is responsible for the majority of between-design heterogeneity. This design is part of a three-arm study comparing CBT-I self-help (internet) with and without therapist support and waiting list. Furthermore, the net heat plot suggests that the evidence for the treatment comparison CBT-I self-help (internet) vs. waiting list (part of the mentioned three-arm study) from the design CBT-I self-help (internet) vs. CBT-I self-help (internet) + therapist support (design from the same three-arm study) is inconsistent with the other evidence.

Figure A7. Net heat plot of "mental state". The net heat plot suggests that the design that is responsible for the majority of between-design heterogeneity is the following one: CBT-I group compared to sleep hygiene (design from a three-arm study comparing CBT-I group, CBT-I individual face-to-face and sleep hygiene). Furthermore, the evidence for this treatment comparison from the designs "CBT-I group vs. CBT-I individual face-to-face" (design from the mentioned three-arm study), "CBT-I self-help (internet) vs. sleep hygiene" and "CBT-I self-help (internet) vs. TAU" is inconsistent with the other evidence.

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Contributors

Chiara Baglioni and Dieter Riemann had the idea for this study, contributed to study design and supervised with their clinical expertise. Fee Benz and Teresa Knoop conducted the literature search advised by Chiara Baglioni and Bernd Feige. Andrea Ballesio and Valeria Bacaro searched for unpublished literature. Fee Benz and Teresa Knoop conducted the abstract and full-text screening as well as the risk of bias assessment. Andrea Ballesio and Valeria Bacaro also conducted the risk of bias assessment independently, discrepancies were solved by consensus discussion with all authors. Data extraction was done by Fee Benz and Teresa Knoop. Bernd Feige and Fee Benz conducted the data analyses, Gerta Rücker contributed to the statistical analysis with her expertise in network meta-analysis. Fee Benz drafted the manuscript, and all authors contributed to and have approved the final manuscript.

Conflict of Interest

All authors declare that they have no conflicts of interest.

Highlights

- Ten subgroups of daytime symptoms were identified in the literature
- Cognitive and behavior therapies for insomnia are effective on daytime symptoms
- Effects are predominantly small to moderate compared to stronger effects on nocturnal symptoms
- CBT-I might benefit from adding techniques targeting more directly daytime symptoms