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Complete List of Authors:	Spiegelhalder, Kai; University Medical Center Freiburg, Psychiatry and Psychotherapy Baumeister, Harald; Universitat Ulm, Institut of Psychology and Education, Department of Clinical Psychology and Psychotherapy; Al-Kamaly, Abdulwahab; Medical Center - University of Freiburg Bader, Martina; Ulm University Bauereiss, Natalie; Ulm University Benz, Fee; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Braun, Lina; Ulm University, Clinical Psychology and Psychotherapy Buntrock, Claudia; Friedrich-Alexander-Universitat Erlangen-Nurnberg, Clinical Psychology and Psychotherapy Burkhardt, Maike; BARMER Cuijpers, Pim; VU University Amsterdam, Department of Clinical Psychology Domschke, Katharina; University of Freiburg, Center for Basics in Neuromodulation, Faculty of Medicine Dülsen, Patrick; Ulm University Franke, Marvin; GET.ON Institut für Online Gesundheitstrainings GmbH Frase, Lukas; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Heber, Elena; GET.ON Institut für Online Gesundheitstrainings GmbH Helm, Kathrin; Medical Center – University of Freiburg Jentsch, Terry; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Johann, Anna; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Küchler, Ann-Marie; Ulm University, Clinical Psychology and Psychotherapy Kuhn, Michael; BARMER Lehr, Dirk; Leuphana University Lueneburg, Department of Health Psychology and Applied Biological Psychology Maun, Andy; University of Freiburg, Division of General Practice, Faculty of Medicine, Medical Center Morin, Charles M.; Universite Laval Faculte de medecine, Moshagen , Morten ; Ulm University, Richter, Kneginja; Klinikum Nurnberg, University Clinic for Psychiatry and Psychotherapy; University Goce Delcev, , Faculty for medical sciences

	Schiel, Julian; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Simon, Laura; Ulm University Spille, Lukas; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Weeß, Hans-Günter; Pfalzklinikum Klingenmünster Riemann, Dieter; Freiburg University Hospital, Ebert, David; Technical University of Munich, Department for Sport and Health Sciences, Chair for Psychology and Digital Mental Health Care
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Spiegelhalder K[1*], Baumeister H[2*], Al-Kamaly A[3], Bader M[4], Bauereiß N[2], Benz F[1], Braun L[2], Buntrock C[5], Burkhardt M[6], Cuijpers P[7], Domschke K[1], Dülsen P[2], Franke M[5,8], Frase L[1], Heber E[8], Helm K[3], Jentsch T[1], Johann AF[1,9], Küchler AM[2], Kuhn M[6], Lehr D[10], Maun A[3], Morin CM[11], Moshagen M[4], Richter K[12,13], Schiel JE[1], Simon L[2], Spille L[1], Weeß HG[14], Riemann D[1*], Ebert DD[8,15*]

1 Department of Psychiatry and Psychotherapy, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
2 Department of Clinical Psychology and Psychotherapy, Institute of Psychology and Education, Ulm University, Ulm, Germany
3 Department of Medicine, Institute of General Practice/ Family Medicine, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
4 Department of Psychological Research Methods, Institute of Psychology and Education, Ulm University, Ulm, Germany
5 Department of Clinical Psychology and Psychotherapy, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany
6 BARMER, Schwäbisch-Gmünd, BARMER
7 Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health research institute, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
8 GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand "HelloBetter"), Hamburg, Germany
9 Medical Psychology and Medical Sociology, Faculty of Medicine, University of Freiburg, Germany
10 Department of Health Psychology and Applied Biological Psychology, Institute of Psychology, Leuphana University of Lueneburg, Lueneburg, Germany.
11 École de psychologie, Université Laval, Québec, Québec, Canada.
12 University Clinic for Psychiatry and Psychotherapy, Paracelsus Medical University, Nuremberg, Germany
13 Faculty for Social Work, Technical University Nuremberg Georg Simon Ohm, Nuremberg, Germany
14 Interdisciplinary Center of Sleep, Pfalzklinikum, Klinikum für Psychiatrie und Neurologie AdöR, Klingenmünster, Germany.
15 Department of Sport and Health Sciences, Technical University of Munich, Munich, Germany.

* These authors contributed equally (Spiegelhalder, Baumeister, Riemann, Ebert)

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Address for correspondence:
Kai Spiegelhalder, MD PhD
Department of Psychiatry and Psychotherapy
Medical Center – University of Freiburg
Hauptstraße 5, 79104 Freiburg, Germany
Tel: +49 761 270 69780
Fax: +49 761 270 66190
Email: Kai.Spiegelhalder@uniklinik-freiburg.de

Conflict of interest statement

H. Baumeister received consultancy fees, reimbursement of congress attendance and travel costs as well as payments for lectures from Psychotherapy and Psychiatry Associations as well as Psychotherapy Training Institutes in the context of E-Mental-Health topics. He has been the beneficiary of study support (third-party funding) from several public funding organizations. M. Burkhardt and M. Kuhn are employees of BARMER. K. Domschke is a member of the Janssen Pharmaceuticals Inc. “Steering Committee Neuroscience”. M. Franke, E. Heber, D. Lehr and D. D. Ebert are stakeholders of the GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand “HelloBetter”), which aims to implement scientific findings related to digital health interventions into routine care. HelloBetter distributes the digital intervention for insomnia that is used in this study. C. M. Morin received research grant from Canopy Health, Eisai, Idorsia, and Lallemand Health Solutions; he served as consultant to Eisai, Idorsia, Pear Therapeutics, Sunovion and Weight Watchers, and received royalties from Mapi Research Trust. D. D. Ebert has served as a consultant to/on the scientific advisory boards of Sanofi, Novartis, Minddistrict, Lantern, Schoen Kliniken, Ideamed, German health insurance companies (BARMER, Techniker Krankenkasse) and a number of federal chambers for psychotherapy. None of the other authors declare any conflict of interest.

Abstract

Introduction: It is unclear how internet-delivered cognitive behavioural therapy for insomnia (CBT-I) can be integrated into healthcare systems, and little is known about the optimal level of therapist guidance. The aim of this study is to investigate three different versions of a stepped care model for insomnia (IG1, IG2, IG3) versus treatment-as-usual (TAU). IG1, IG2, and IG3 rely on treatment by general practitioners (GPs) in the entry level and differ in the amount of therapist guidance in internet-delivered CBT-I.

Methods and analysis: In this randomised controlled trial, 4,268 patients meeting ICD-10 criteria for insomnia will be recruited. The study will use cluster randomisation of GPs with an allocation ratio of 3:3:3:1 (IG1, IG2, IG3, TAU). In step 1 of the stepped care model, GPs will deliver psychoeducational treatment; in step 2, an internet-delivered CBT-I program will be used; in step 3, GPs will refer patients to specialised treatment. Outcomes will be collected at baseline, and 4 weeks, 12 weeks and 6 months after baseline assessment. The primary outcome is insomnia severity at 6 months. An economic evaluation will be conducted and qualitative interviews will be used to explore barriers and facilitators of the stepped care model.

Ethics and dissemination: The study protocol was approved by the Ethics Committee of the Medical Center – University of Freiburg. The results of the study will be published irrespective of the outcome.

Registration details: The study has been registered in the German Clinical Trials Register (https://www.drks.de/drks_web/; DRKS00021503).

Strength and limitations of the study

- This randomised controlled trial will recruit 4,268 patients and will be the largest clinical trial on insomnia.
- This trial will investigate three different versions of a stepped care model for insomnia which rely on treatment by general practitioners in the entry level and differ in the amount of therapist guidance in internet-delivered CBT-I.
- The primary outcome is insomnia severity. An economic evaluation will be conducted and qualitative interviews will be used to explore barriers and facilitators of the stepped care model.
- Patients with insomnia will not be blind to treatment allocation in this trial.

1. Introduction

Insomnia disorder is characterised by difficulties initiating and/or maintaining sleep resulting in significant daytime dysfunction.[1] In Western industrialised countries, 5-10% of the general population[2] and 20% of primary care patients[3] suffer from the disorder. Insomnia is associated with a reduced quality of life,[4] and is a risk factor for other mental disorders, in particular depression and anxiety disorders,[5] as well as for cardiovascular diseases.[6,7]

Clinical guidelines recommend cognitive behavioural therapy for insomnia (CBT-I) as first-line treatment.[8 9] CBT-I is a multi-component intervention consisting of psychoeducation, relaxation therapy, sleep restriction therapy, stimulus control therapy, and cognitive therapy. However, only a small proportion of patients with insomnia has access to this treatment. For example, data from BARMER, a large German public health insurance, indicate that around 1.6% of the insured persons received a diagnosis of insomnia in 2017, but only 10% of these patients received a psychotherapeutic treatment.[10] Assuming a prevalence of insomnia of 5.7% in Germany,[11] this suggests that only 2.8% of all insomnia patients in Germany receive psychotherapeutic treatment. Since cognitive-behavioural therapy is not the only form of psychotherapy reimbursed by German health insurances and the focus of the psychotherapeutic treatment may, in many patients, be a comorbid disorder rather than insomnia, the assumption that 1% of all insomnia patients receive CBT-I might already be a very optimistic estimation. Instead, many insomnia patients are treated with benzodiazepine receptor agonists or sedating antidepressants on a long-term basis,[12] which is potentially harmful and not recommended by clinical guidelines.[8 9] This situation is unfortunate both from a clinical and from a health-economic perspective. Insomnia is associated with estimated annual costs of about 5,900 Euros per person in Germany due to absenteeism and presenteeism.[13] Thus, given its prevalence, a reasonable estimate of the indirect costs of insomnia in Germany is 25 billion Euros per year. This number is broadly in line with previously published socioeconomic data from the United States[14] and Canada.[15]

The dissemination of CBT-I is a major healthcare challenge, and internet-delivered psychotherapy has been suggested as a possible mean to lower the treatment gap.[16] Compared to face-to-face treatment, main advantages of internet-delivered CBT-I are convenience, increased accessibility, and potentially lower costs. In particular, internet interventions are easily accessible anytime and anywhere. Patients do not incur travelling expenses; they can work at their own pace; they may provide more honest answers in the privacy of their own home; and barriers related to the stigma of mental disorders may be reduced.[17] Hence, offering internet-delivered CBT-I might increase the utilisation of psychotherapy in undertreated populations. Meta-analyses suggest that internet-delivered CBT-I is highly effective in comparison to waitlist control conditions,[18 19] and that the effects appear to be comparable in size to those of face-to-face CBT-I.[20] In addition, follow-up data of up to 3 years demonstrate a high long-term effectiveness of online CBT-I.[21 22]

However, at least two questions with a high degree of healthcare relevance remain to be answered. First, it is unclear how internet-delivered CBT-I can be effectively integrated into existing healthcare systems that rely on general practitioners (GPs) to take the lead in coordinating patient care. Previous research has shown that the implementation of CBT-I techniques in primary care is challenging but promising.[23 24] In line with a stepped care approach to the treatment of insomnia,[25] GPs may serve as the entry level of a multistep model that offers more intense support for those with more complicated complaints in a cost-effective way. Although conceptually appealing, there are very few studies investigating such stepped care models for insomnia,[26-28] and none of them included active treatment provided by GPs. Second, little is known about the optimal level of therapist guidance in the context of internet-delivered CBT-I. While it is generally thought that human support has positive effects on adherence and efficacy in online mental health interventions,[29] many studies in the insomnia field have successfully implemented online interventions without any human support/ guidance (e.g.,[16 22 30 31]). One study has directly compared an online intervention for insomnia with and without guidance via email and found a superior efficacy in the guided

group.[32] However, there is limited knowledge about who needs and who does not need guidance and how this translates into cost-effectiveness estimates.

The central objective of the present study is to improve the quality and efficiency of healthcare for patients with insomnia. In addition, it is intended to improve interdisciplinary and intersectoral cooperation between GPs, psychotherapists and medical specialists working in outpatient and inpatient settings. Three different versions of a stepped care model (intervention group 1, IG1; intervention group 2, IG2; intervention group 3, IG3) that differ in the amount of therapist guidance that is provided in the internet-delivered intervention in step 2 will be compared with treatment-as-usual (TAU) in, to the best of our knowledge, the largest clinical trial to date on insomnia (see Fig. 1). At step 1, participating GPs will provide a brief psychoeducational treatment; at step 2, patients will receive an internet intervention based on CBT-I; and at step 3, patients will be referred to specialised medical face-to-face treatment. Patients who are unresponsive to the treatment at one step will proceed to the next step of the model. The primary research question is the effectiveness of the interventions. We will also investigate differential treatment outcomes in four subgroups of patients: 1) insomnia without any comorbidity; 2) insomnia with mental comorbidity; 3) insomnia with somatic comorbidity; 4) insomnia with mental and somatic comorbidity. In addition, an economic evaluation will be carried out and qualitative interviews will be conducted to explore barriers and facilitators of the stepped care model. In case of a positive evaluation, it is intended to include the stepped care model in the guidelines of the Federal Joint Committee, the highest decision-making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany.

(please insert Figure 1 here)

2. Methods

2.1. Study design

The study is a four-armed pragmatic parallel-group cluster-randomised controlled trial investigating three different versions of a stepped care model for insomnia versus TAU. The unit of randomisation will be the participating GPs to avoid treatment diffusion. Primary and secondary outcomes as well as moderating and mediating variables and intervention-related variables will be assessed online by patient self-report using LimeSurvey (https://www.limesurvey.org/). Online assessments will take place at baseline (T0) and after 4 (T1) and 12 (T2) weeks, as well as 6 months after baseline (T3; see Fig. 2 for trial design). Informed consent will also be given online. The trial might be continued with further annual follow-up assessments after 1-5 years in case of patients´ informed consent and dependent on follow-up assessment resources beyond the funded 6 months follow-up.

The study has been registered in the German Clinical Trials Register (https://www.drks.de/drks_web/; DRKS00021503) and will be conducted in accordance with the Declaration of Helsinki. The study protocol was approved by both the Ethics Committee of the Medical Center – University of Freiburg and the Ethics Committee of the State Chamber of Physicians ('Landesärztekammer Baden-Württemberg'). In addition, the data protection officers of the Medical Center – University of Freiburg and Ulm University have approved the formal data protection concept of this study.

The study will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) Statement 2010 and the extensions for reporting pragmatic trials, noninferiority trials, cluster randomised trials, multi-arm parallel group trials and trials on psychological interventions.[33-38] This trial protocol was created according to SPIRIT guidelines.[39]

(please insert Figure 2 here)

2.2. Participants

Overall, 4,268 patients are planned to be recruited. The inclusion criteria are: a) age ≥ 18 years; and b) ICD-10 diagnosis of non-organic insomnia (F51.0) or insomnia (G47.0). Exclusion criteria are: a) untreated sleep apnoea syndrome (ICD-10: G47.3); b) untreated restless legs syndrome or periodic leg movement disorder (ICD-10: G25.8); c) untreated hyperthyroidism (ICD-10: E05.9); d) ongoing psychotherapy for insomnia; e) conditions that may be aggravated by CBT-I (bipolar disorder, ICD-10: F31.x; epilepsy, ICD-10: G40.x); e) conditions that pose a serious threat to treatment adherence (e.g., organic, including symptomatic, mental disorders (ICD-10: F00-F09); mental and behavioural disorders due to psychoactive substance use (ICD-10: F10-F19); schizophrenia, schizotypal and delusional disorders (ICD-10: F20-F29)); f) acute suicidality.

Up to 320 GPs from Bavaria and Baden-Wuerttemberg, who participate in this study, will recruit eligible patients during consultations. In addition, online, print and broadcast media advertisements as well as postal mailings by the BARMER to potential patients will be used to recruit insomnia patients from all over Germany. These patients will be referred to a group of GPs that use telehealth consultations for checking inclusion and exclusion criteria, delivering step 1 of the stepped care model and guiding patients through the stepped care model. All GPs will receive remuneration for each participating patient (up to 158.25€ depending on the number of consultations). In addition to receiving free access to the stepped care model or TAU, participants will receive payment at completion of online assessments T1 (15€), T2 (15€), and T3 (20€) to increase adherence.

2.3. Randomisation and allocation concealment

This study will use cluster randomisation of GPs with an allocation ratio of 3:3:3:1 (IG1:IG2:IG3:TAU). Randomisation will be performed by authors MB and MM (Ulm University) who are not otherwise involved in the trial and therefore blinded to all processes

of the study. Population-density stratified permuted block randomisation (nine strata based on population density and average level of income, one stratum for GPs that exclusively employ telehealth consultations) will be employed with varying block sizes concealed to the investigators to minimise selection bias. GPs from community practices will be randomised into the same trial arm. The GPs are instructed to conceal group allocation until the baseline assessment is completed by the patient.

2.4. Blinding

Blinding of patients and healthcare providers is not feasible. However, screenings and baseline assessments will be performed before patients are informed about treatment assignment to avoid contamination with anticipated treatment effects. In case of non-completion of assessments participants will receive fully automated standardised reminders. Data analysts are blinded with respect to group allocation and outcomes.

2.5. Intervention

The stepped care model that will be tested in the current study is presented in Figure 1.

2.5.1. Step 1

In step 1 of the stepped care model, the responsible GP will deliver a brief standardised psychoeducational treatment after being trained by sleep medicine specialists of the Department of Psychiatry and Psychotherapy of the Medical Center – University of Freiburg and by primary care physicians of the Department of Medicine, Division of General Practice, of the Medical Center – University of Freiburg. The treatment includes the following psychoeducational recommendations: a) avoid alcohol as a hypnotic; b) avoid clock-watching at night; c) avoid afternoon caffeine use; d) exercise regularly. In addition, the following

stimulus control instructions will be given by the GPs: a) use the bed only for sleep and sexual activity; b) get out of bed when unable to sleep; c) do not nap during the day. GPs can also consult a psychiatrist of the Department of Psychiatry and Psychotherapy of the Medical Center – University of Freiburg whenever they feel that discontinuation of hypnotic medication would be appropriate. After four weeks, patients will be given the opportunity to access step 2 of the stepped care model. Importantly, for each patient, GPs can decide to skip step 1 of the stepped care model if they do not expect a substantial impact on insomnia severity.

2.5.2. Step 2

At step 2 of the stepped care model, the GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand "HelloBetter") will provide an internet intervention based on CBT-I with an accompanying mobile sleep diary app. The intervention was initially developed at Leuphana University Lüneburg by the team of author DL and was positively evaluated in three randomised controlled trials.[40-42] Since the intervention was initially designed for workers, it has been adapted and technically updated for the current study by HelloBetter to meet the needs of all potential patients. Treatment content is based on CBT-I manuals and includes psychoeducation, relaxation therapy, sleep restriction therapy, stimulus control therapy, and cognitive interventions targeting rumination and worry. Delivery is structured into eight sessions, lasting approximately 45-60 min each.

All patients receive an initial and a final consultation with one of a team of e-coaches of HelloBetter, who are trained and supervised psychologists. The consultations will be conducted by telephone, or, if this is not possible, by in-platform messages. In addition to the initial and final consultation, patients randomised to the 'standard' version of the intervention (IG1) receive written feedback and support by the responsible e-coach after each session. E-coaches are instructed to spend, on average, 25 min per session for writing this feedback. Patients randomised to the 'flex' version of the intervention (IG2) receive written on-demand

support by the responsible e-coach. Patients randomised to the 'basic' version of the intervention (IG3) do not receive additional human guidance.

The treatment platform operates according to the ISO 27000 and NEN 7510 standards. All data is securely stored on ISO 27000-certified servers and transmitted via HTTPS with SSL certificates (AES-256 and SHA-1, 2048-bit RSA). Unauthorised access to the platform is not possible.

2.5.3. Step 3

In step 3 of the stepped care model, non-responders will be referred by their GPs to specialised medical treatment. The decision about this referral lies with the responsible GP and is based on clinical judgement of response. However, the responsible e-coach of HelloBetter will make a recommendation to the GP about whether and by whom the treatment should be continued after step 2. As a rule of thumb, GPs are recommended to refer patients with an ISI score ≥ 15 and a comorbid mental health syndrome to a psychiatrist and/or a psychotherapist in step 3, and all other patients with an ISI score ≥ 15 to a sleep medicine specialist.

2.6. Safety protocol

During the screening procedure, GPs exclude patients with acute suicidality. Suicidal ideation will also be screened by the e-coaches of HelloBetter at their initial consultations, and at T0, T1, T2, and T3 using QIDS-SR16 and NEQ (see paragraph on measures for details). Reports of current suicidal ideation in the interview, a score ≥ 1 on the suicide item of the QIDS-SR16 (item 12; 0 = "I do not think of suicide or death.", 1 = "I feel that life is empty or wonder if it's worth living.", 2 ="I think of suicide or death several times a week for several minutes", 3 = "I think of suicide or death several times a day in some detail, or I have made

specific plans for suicide or have actually tried to take my life"), or the answer „yes" to item 10 of the NEQ ("I got thoughts that it would be better if I did not exist anymore and that I should take my own life") will result in a standardised safety protocol. In particular, participants will receive an information document with detailed information on available health services and the advice to consult their GP. The wording of the online information document is adapted in emphasis, depending on the severity of the indicated suicidality.

2.7. Measures

Table 1 presents an overview of measures that are assessed in this trial.

(please insert Table 1 here)

2.7.1. Primary outcome measure

The primary outcome will be insomnia severity at T3, six months after the baseline assessment. Insomnia severity will be assessed with the Insomnia Severity Index (ISI[43]). The ISI is composed of seven 5-point Likert scale items (0-4 points; total score range: 0-28 points) probing perceived severity of insomnia symptoms during the preceding two weeks. Several studies have shown good internal consistency of the ISI with Cronbach's Alpha ranging from 0.70 to 0.90.[43-45]

2.7.2. Secondary outcome measures

Sleep quality will be assessed using the Pittsburgh Sleep Quality Index (PSQI[46]), a 19-item self-report measure covering different aspects of sleep quality. The total score of the PSQI ranges from 0 to 21, internal consistency was found to be 0.80.[47] Quality of life will be assessed with the AQoL-8D,[48] an instrument composed of 35 items that measure eight

dimensions (independent living, pain, senses, mental health, happiness, coping, relationships, self-worth). The AQoL-8D generates patient preference–based utilities on a scale of 0 (death) to 1 (perfect health), using the time-trade-off method,[48] which will be used to estimate quality-adjusted life years (QALYs) based on the area-under-the-curve (AUC) method. The AQoL-8D has been reported to have excellent internal consistency with a Cronbach's Alpha of 0.96.[48] Depressive symptoms will be measured using the 16-item Quick Inventory of Depressive Symptoms in the self-report format (QIDS-SR16[49]). The total score of the QIDS-SR16 ranges from 0 to 27, internal consistency was reported to be good (Cronbach's Alpha = 0.86).[50] Incident depression will be assessed in patients without a depression diagnosis at T0 and defined using a cut-off score of ≥13 on the QIDS-SR16.[51] Anxiety symptoms will be assessed with the 7-item General Anxiety Disorder 7 questionnaire (GAD-7[52]; total score 0-21; Cronbach's Alpha = 0.89[53]). Somatic symptoms will be measured using the 8-item Somatic Symptom Scale 8 (SSS-8[54]; total score 0-32; Cronbach's Alpha = 0.81). For the health-economic evaluation, health-care utilisation, patient and family expenditures and productivity losses due to absence from work or reduced efficiency during paid and unpaid work will be established with the Trimbos/iMTA questionnaire for costs associated with psychiatric illness (TiC-P), a retrospective self-report questionnaire covering the previous three months.[55-57] A list of unit cost prices will be used to compute health care costs on a per-participant basis.[58] Test-retest reliability has previously been shown to be satisfactory.[56]

2.7.3. Intervention-related variables

At T2 after 12 weeks, the 12-item Working Alliance Inventory for guided Internet interventions (WAI-I[59]) and the 12-item Technological Alliance Inventory (TAI-OT) will be administered in all patients of the intervention groups (IG1, IG2, IG3) who entered step 2 of the stepped care model (internet-delivered CBT-I). The WAI-I and the TAI-OT will be used to assess the therapeutic alliance between patient and e-coach and the technological alliance between

patient and e-coach and the technological alliance between client and the internet-based intervention, respectively. The WAI-I score ranges from 12 to 60 and the questionnaire has excellent internal consistency with a Cronbach's Alpha of 0.93.[59] The TAI-OT is a new self-report questionnaire developed by Labpsitec at Jaume I University in Castellón, Spain (Labpsitec (http://www.labpsitec.uji.es/eng/index.php) and measures the degree to which the internet-based intervention is perceived as being helpful in achieving therapeutic goals. The TAI-OT score ranges from 12 to 84. Patients in all conditions will receive the 8-item Client Satisfaction Questionnaire (CSQ-8[60 61]; total score 8-32), which is characterised by excellent internal consistency with a Cronbachs's Alpha of 0.93.[60] In addition, the 20-item Negative Effects Questionnaire (NEQ[62]) will be used in all patients. The NEQ measures the frequency, with a total score ranging from 0 to 20, and impact, with a total score ranging from 0 to 80, of possible negative effects during treatment. Its internal consistency was found to be excellent with a Cronbach's Alpha of 0.95.[62] Moreover, an additional self-developed 24-item Questionnaire on adverse effects of CBT-I will be used. For adverse events reported in the NEQ and the additional self-developed 24-item questionnaire, patients who entered step 2 of the stepped care model will be asked if they attribute the adverse events to the behavioural components of CBT-I. A self-developed Dropout Questionnaire based on the Health Action Process Approach (HAPA[63]) will be used at T2 to identify dropout reasons in participants not completing at least 80% of the internet-delivered intervention. For a comprehensive evaluation of the implementation of the stepped care model a battery of self-developed self-report items will be used in all patients to assess the usage of and adherence to treatment components across the steps.

2.7.4. Potential treatment moderators and mediators

At T0, demographic variables (e.g., age, gender), depressive and anxiety symptoms, as well as IT knowledge will be documented as potential moderators of treatment effectiveness. In addition, the baseline values of the following variables will be assessed as potential

moderators: the 10-item Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-10[64 65]; Cronbach's Alpha = 0.69), the 16-item Pre-Sleep Arousal Scale (PSAS[66 67]; Cronbach's Alpha = 0.80-0.94), the 10-item Brief Fatigue Inventory (BFI[68]; Cronbach's Alpha = 0.96), the 10-item Perceived Stress Scale (PSS[69]; Cronbach's Alpha = 0.78), the 13-item Sleep Hygiene Index (SHI[70]; Cronbach's Alpha = 0.66), and the 18-item short version of the Cognitive Emotion Regulation Questionnaire (CERQ-short[71]; Cronbach's Alpha = 0.68-0.81). In addition, mediation analyses will be conducted using some of the constructs described in this section (DBAS-10, PSAS, PSS, SHI, CERQ) as well as two intervention-related variables described above (WAI-I, TAI-OT).

2.7.5. Other data

Medical record data (e.g., ICD-10 diagnosis codes, treatment) will be provided by the GPs to enable allocation of patients to the four subgroups. In cases of missing medical record data, group allocation will be based on self-reported mental and somatic comorbidities. Sleep diary data will be assessed in step 2 of the stepped care model and will be used to evaluate treatment adherence, e.g., adherence to personalised sleep restriction recommendations. Additionally, usage data from the treatment platform will be used to assess adherence to the internet-delivered intervention. Secondary data from BARMER will be used to assess the validity of the TiC-P. In addition, qualitative interviews will be conducted with a subgroup of patients, GPs and e-coaches to assess their experience of positive and negative aspects of the stepped care model. Trained interviewers will explore acceptance, usage behaviour, barriers, and facilitators as well as side-effects of the stepped care model. The sample size and composition will be planned to consider the different intervention groups and gain sufficient theoretical data saturation. All subgroups will be represented in the interviews.

2.8. Sample size calculation

There is no universally accepted minimally important difference for the treatment of insomnia. Hence, this issue has been discussed among the clinicians involved in the current trial who are nationally and internationally leading experts in the field of insomnia research. Most clinicians agreed that 1.5 or more points on the ISI (exhibiting a common standard deviation of 6.0 points) are a reasonable minimally important difference corresponding to a minimally important effect size of d = 0.25. Based on previous research, it is assumed that all intervention groups (IG1, IG2, IG3) exhibit a considerably larger difference to the TAU group of at least d = 0.50 (e.g., [24]). Because of this, for ethical reasons and to reduce costs, the GPs are randomised with an allocation ratio of 3:3:3:1 (IG1, IG2, IG3, TAU), which ensures sufficient power for both differences between any IG and TAU (of at least d = 0.35) as well for differences between IGs (of at least d = 0.25). Based on 320 GPs with a median recruitment rate of n = 9 ± 14 patients, an ICC of 0.02, a correlation of the outcome at T3 with the corresponding baseline assessment of r = 0.5, d = 0.25, an α of 0.05 and (1-β) of 80%, the required sample size is n = 1,067 for each of the four subgroups of patients (IGs: n = 320 each; TAU: n = 107). Thus, a total sample size of N = 4,268 (IGs: n = 1,280 each; TAU: n = 428) is required. Sampling procedures for the qualitative interviews follow theoretical data saturation principles.[72 73]

2.9. Statistical analysis

Descriptive statistics of recruitment and dropout as well as baseline characteristics for each group will be provided. The primary effectiveness analysis will be conducted according to the intention-to-treat principle based on all patients with their original treatment allocation. Additionally, per-protocol analyses based on the data of patients who completed a substantial proportion of the internet intervention (i.e., 80% of the modules) will be conducted. Missing data will be handled via multiple imputation, using a multilevel imputation model to account for clustering. The effect of group allocation (IG1, IG2, IG3, TAU) on the

primary endpoint ISI at T3 (6 months after baseline) will be tested within a linear mixed model with corresponding 95% confidence intervals. All models will include the responsible GP as a clustering variable. Clinical significance as well as reliable reduction in insomnia severity will be determined using Number Needed to Treat (NNT) analyses[74] as well as the Reliable Change Index (RCI) by Jacobson & Truax[75]. Based on the RCI, participants will be categorised into responders and non-responders, and the proportion of responders will be compared between study groups (again accounting for clustering). Secondary outcomes will be analysed analogously to the primary outcome, using random effect regression models as appropriate for the respective type of data. Potential onset and remission of incident depression will be compared between study groups based on incidence rate ratios (IRR) using multilevel Poisson regression. No interim analysis is planned for effectiveness or futility. Exploratory moderator analyses will be used to investigate whether pre-treatment patient characteristics are associated with differential treatment effectiveness. Potential moderators include sociodemographic (e.g., age) and clinical (e.g., insomnia severity) variables. Exploratory mediator analyses will be employed to examine potential mechanisms of change. Among potential mediators are sleep-related (e. g. dysfunctional beliefs and attitudes about sleep) and intervention-related variables (e. g. working alliance).

The economic evaluation will be performed from the societal and public health care perspective. Two multilevel models (MLMs) will be specified, one for costs and one for effects, which take into account the hierarchical structure of the data. MLMs will be combined with cluster bootstrapping, which is recommended for resampling clustered data.[76] Across the four study groups, mean costs and QALYs will be compared to assess if any of the treatments are less effective and more expensive than the other treatments. If so, incremental cost-effectiveness ratios (ICERs) will not be estimated in relation to that treatment.[77] Otherwise, ICERs will be estimated by calculating the difference in costs between two treatment options divided by the difference in effectiveness of these two treatment options. We will bootstrap seemingly unrelated regression equation (SURE) models to generate 5,000 simulations of cost and effect pairs while allowing for correlated

residuals of the cost and effect equations and adjusting for potential confounders.[78] The joint uncertainty surrounding costs and effects will be summarised using cost-effectiveness acceptability curves (CEACs) based on a net benefit regression framework.[79] CEACs show the probability of an intervention being cost effective in comparison with the alternatives for a range of different willingness-to-pay thresholds. For patients insured by BARMER, the validity of the TiC-P will be assessed with secondary data from the health insurance.

Qualitative interviews of patients, GPs and e-coaches will be used to assess their experience of positive and negative aspects of the stepped care model. The interviews will be recorded, transcribed, and analysed based on qualitative content analysis. An inductive-deductive approach will be applied along the interview guide.

2.10. Patient and public involvement

No patient involvement. Public representatives approved the trial objectives and design as part of the application to the Innovationsfonds of the German Federal Joint Committee

3. Discussion

Insomnia is a common, costly and impairing sleep disorder. According to clinical guidelines, the first-line therapy is CBT-I, however, only few patients with insomnia have access to this treatment. Internet-delivered CBT-I has the potential to disseminate the recommended treatment to a larger number of patients. This study will determine whether a stepped care model for insomnia that includes psychoeducational treatment by GPs, internet-delivered CBT-I and specialised medical treatment, improves insomnia severity as well as psychological and physical well-being.

Authors statement: K. Spiegelhalder, D. D. Ebert, H. Baumeister, and D. Riemann conceived the project, have overall responsibility for the trial design and treatment design and drafted the trial protocol. C. Buntrock, M. Burkhardt, E. Heber, M. Kuhn, A. Maun, and M. Moshagen contributed to trial design. A. Al-Kamaly, M. Franke, L. Frase, E. Heber, K. Helm, D. Lehr, and A. Maun contributed to treatment design. H. Baumeister, M. Bader, N. Bauereiß, L. Braun, P. Dülsen, A. M. Küchler, M. Moshagen, and L. Simon are responsible for statistical analysis. C. Buntrock is responsible for economic analysis. All authors provided critical review on the trial protocol and approved the final manuscript.

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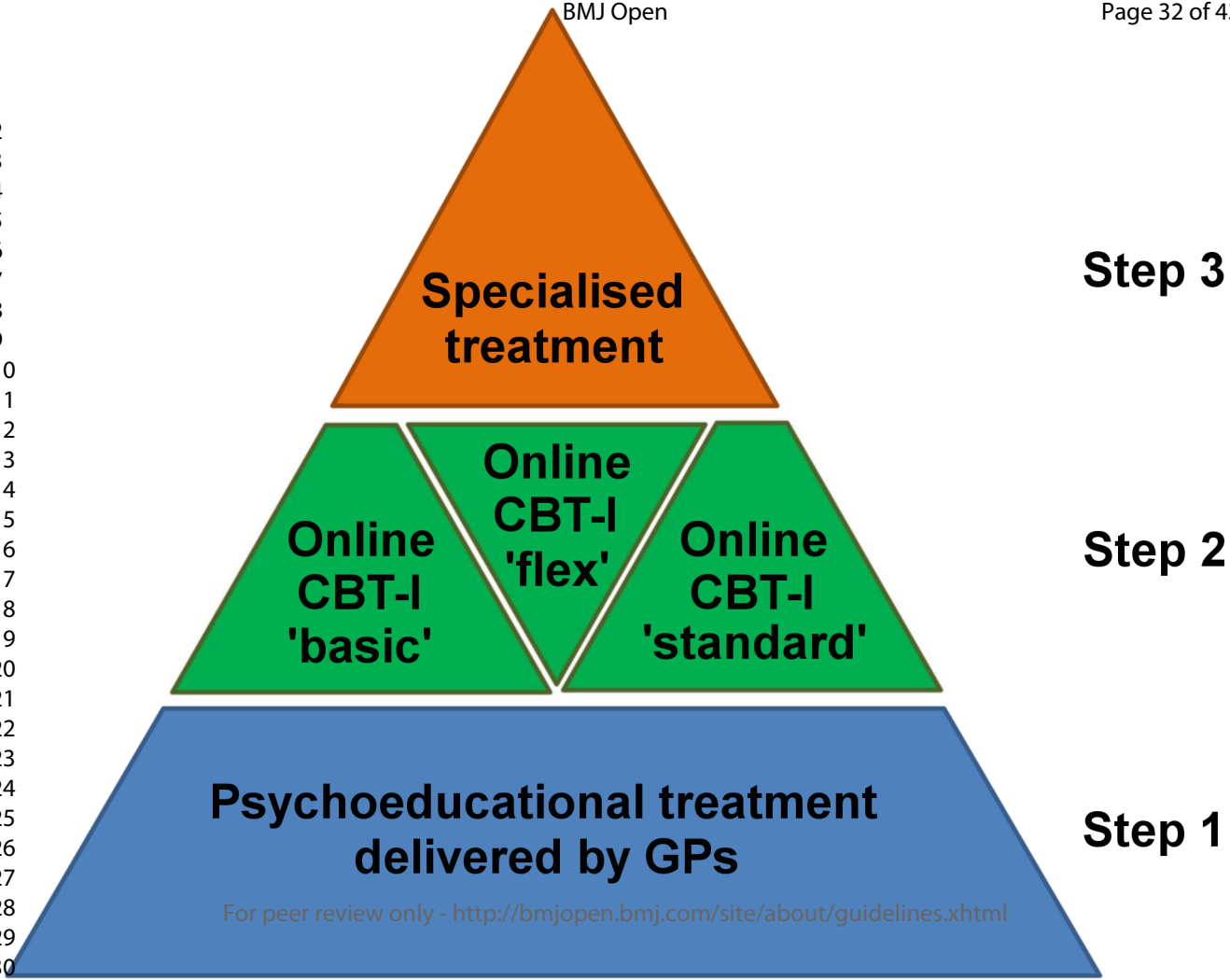
Figure Legends

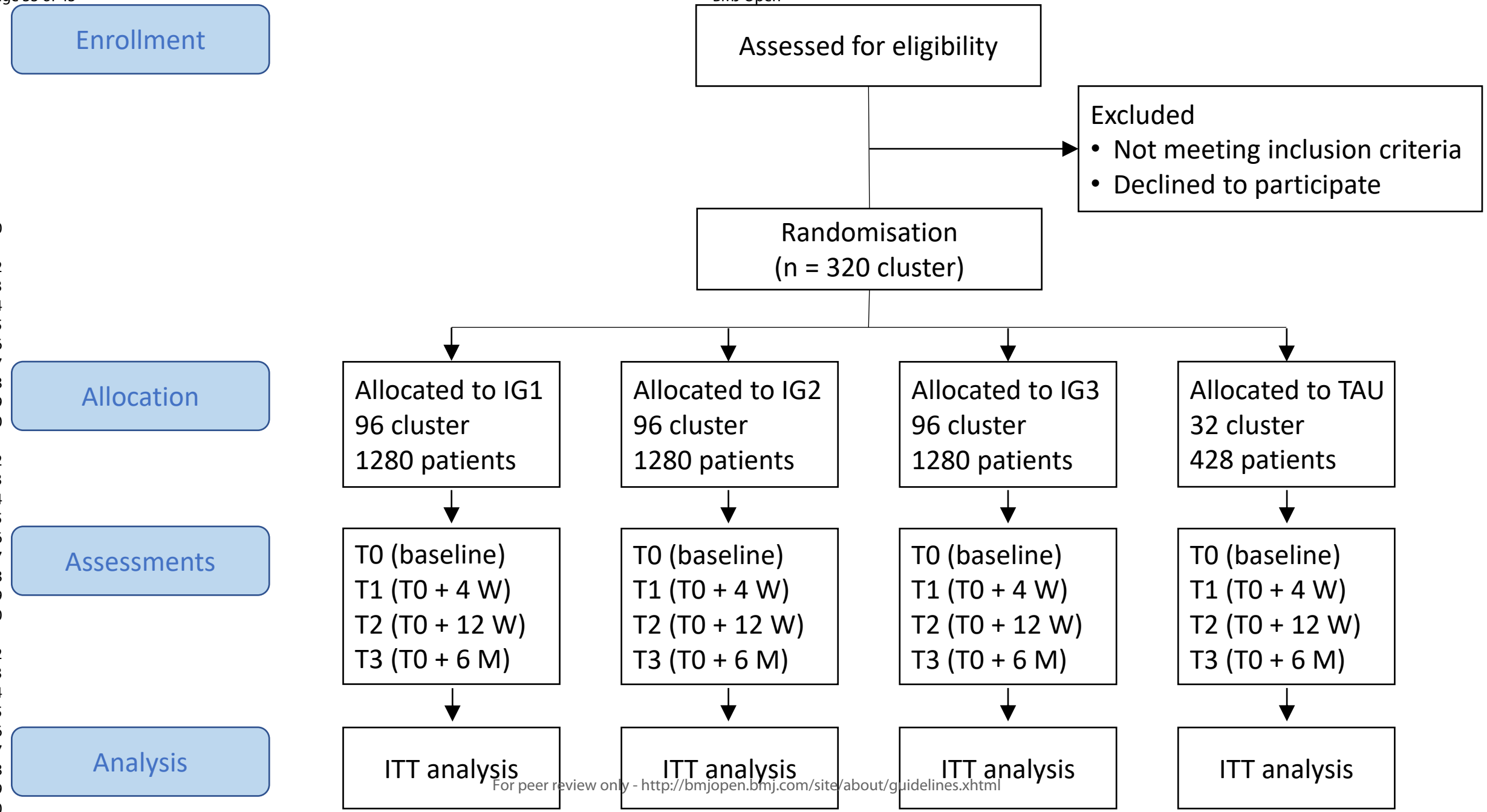
Figure 1: Stepped care model for insomnia that will be tested in the current trial. CBT-I: cognitive-behavioural treatment for insomnia; GPs: general practitioners.

Figure 2: IG1: intervention group 1 ('standard' version of step 2 of the stepped care model); IG2: intervention group 2 ('flex' version of step 2 of the stepped care model); IG3: intervention group 3 ('basic' version of step 2 of the stepped care model); TAU: treatment-as-usual; W: weeks; M: months; ITT: intention-to-treat.

Table 1: Overview of the assessments. [1] The ISI at T3 (6 months after T0) is the primary outcome of this trial; [2] only in patients of the intervention groups (IG1, IG2, IG3) who entered step 2 of the stepped care model; [3] only in patients of the intervention groups (IG1, IG2, IG3) not completing at least 80% of the internet-delivered intervention. ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; AQoL-8D: Assessment of Quality of Life instrument; QIDS-SR16: Quick Inventory of Depressive Symptoms in the self-report format; GAD-7: General Anxiety Disorder 7 questionnaire; SSS-8: Somatic Symptom Scale 8; TiC-P: Trimbos/iMTA questionnaire for costs associated with psychiatric illness; DBAS-10: Dysfunctional Beliefs and Attitudes about Sleep Scale; PSAS: Pre-Sleep Arousal Scale; BFI: Brief Fatigue Inventory; PSS: Perceived Stress Scale; SHI: Sleep Hygiene Index; CERQ-short: Cognitive Emotion Regulation Questionnaire; WAI-I: Working Alliance Inventory for guided Internet interventions; TAI-OT: Technological Alliance Inventory; CSQ-8: Client Satisfaction Questionnaire; NEQ: Negative Effects Questionnaire.

Activity/Assessment	**T-1**	**T0**	**T1**	**T2**	**T3**
	Pre-study	Baseline (week 0)	4 weeks after T0	12 weeks after T0	6 months after T0
Eligibility screen	X				
Informed consent	X				
Primary outcome					
Insomnia severity (ISI)		X	X	X	X[1]
Secondary outcomes					
Sleep quality (PSQI)		X	X	X	X
Quality of life (AQoL-8D)		X	X	X	X
Depressive symptoms (QIDS-SR16)		X	X	X	X
Anxiety symptoms (GAD-7)		X	X	X	X
Somatic symptoms (SSS-8)		X	X	X	X
Costs (TiC-P)		X		X	X
Potential treatment moderators and mediators					
Dysfunctional beliefs and attitudes about sleep (DBAS-10)		X	X	X	X
Pre-sleep arousal (PSAS)		X	X	X	X
Fatigue (BFI)		X	X	X	X
Stress (PSS)		X	X	X	X
Sleep hygiene behaviour (SHI)		X	X	X	X
Emotion regulation (CERQ-short)		X	X	X	X
Intervention-related variables					
Alliance (WAI-I)				X[2]	
Technological alliance (TAI-OT)				X[2]	
Client satisfaction (CSQ-8)					X
Adverse events and negative effects (NEQ, Questionnaire on adverse effects of CBT-I)				X	X
Dropout Questionnaire				X[3]	





Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet	3

		registered, name of intended registry	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	1-30
Funding	#4	Sources and types of financial, material, and other support	20
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the	8

		trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6-7
Objectives	#7	Specific objectives or hypotheses	7
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	8
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data	9

		will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10-12
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12-13
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15,17
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9,11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical	13-16

		relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10-12, 30
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is	9-10

		unavailable to those who enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9-10
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a – Participants will be unblinded after allocation
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a	13-16

		description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9-10
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	8,12
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-18
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	18-19
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg,	18

		multiple imputation)	
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a – no interim analyses
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics	#24	Plans for seeking research ethics committee /	3

approval		institutional review board (REC / IRB) approval	
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	2
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care,	12

trial care		and for compensation to those who suffer harm from trial participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	3
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	20
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Materials are available in German only but can be submitted on request
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

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Comparative effectiveness of three versions of a stepped care model for insomnia differing in the amount of therapist support in internet-delivered treatment – study protocol for a pragmatic cluster randomised controlled trial (GET Sleep)

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Complete List of Authors:	Spiegelhalder, Kai; Medical Center-University of Freiburg, Psychiatry and Psychotherapy Baumeister, Harald; Universitat Ulm, Institut of Psychology and Education, Department of Clinical Psychology and Psychotherapy; Al-Kamaly, Abdulwahab; Medical Center - University of Freiburg Bader, Martina; Ulm University Bauereiss, Natalie; Ulm University Benz, Fee; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Braun, Lina; Ulm University, Clinical Psychology and Psychotherapy Buntrock, Claudia; Friedrich-Alexander-Universitat Erlangen-Nurnberg, Clinical Psychology and Psychotherapy Burkhardt, Maike; BARMER Cuijpers, Pim; VU University Amsterdam, Department of Clinical Psychology Domschke, Katharina; University of Freiburg, Center for Basics in Neuromodulation, Faculty of Medicine Dülsen, Patrick; Ulm University Franke, Marvin; GET.ON Institut für Online Gesundheitstrainings GmbH Frase, Lukas; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Heber, Elena; GET.ON Institut für Online Gesundheitstrainings GmbH Helm, Kathrin; Medical Center – University of Freiburg Jentsch, Terry; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Johann, Anna; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Küchler, Ann-Marie; Ulm University, Clinical Psychology and Psychotherapy Kuhn, Michael; BARMER Lehr, Dirk; Leuphana University Lueneburg, Department of Health Psychology and Applied Biological Psychology Maun, Andy; University of Freiburg, Division of General Practice, Faculty of Medicine, Medical Center Morin, Charles M.; Universite Laval Faculte de medecine, Moshagen , Morten ; Ulm University, Richter, Kneginja; Klinikum Nurnberg, University Clinic for Psychiatry and Psychotherapy; University Goce Delcev, , Faculty for medical

	sciences Schiel, Julian; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Simon, Laura; Ulm University Spille, Lukas; Freiburg University Hospital Clinic of Psychiatry and Psychotherapy Weeß, Hans-Günter; Pfalzklinikum Klingenmünster Riemann, Dieter; Freiburg University Hospital, Ebert, David; Technical University of Munich, Department for Sport and Health Sciences, Chair for Psychology and Digital Mental Health Care
Primary Subject Heading:	General practice / Family practice
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Comparative effectiveness of three versions of a stepped care model for insomnia differing in the amount of therapist support in internet-delivered treatment – study protocol for a pragmatic cluster randomised controlled trial (GET Sleep)

Spiegelhalder K[1*], Baumeister H[2*], Al-Kamaly A[3], Bader M[4], Bauereiß N[2], Benz F[1], Braun L[2], Buntrock C[5], Burkhardt M[6], Cuijpers P[7], Domschke K[1], Dülsen P[2], Franke M[5,8], Frase L[1], Heber E[8], Helm K[3], Jentsch T[1], Johann AF[1,9], Küchler AM[2], Kuhn M[6], Lehr D[10], Maun A[3], Morin CM[11], Moshagen M[4], Richter K[12,13], Schiel JE[1], Simon L[2], Spille L[1], Weeß HG[14], Riemann D[1*], Ebert DD[8,15*]

[1] Department of Psychiatry and Psychotherapy, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
[2] Department of Clinical Psychology and Psychotherapy, Institute of Psychology and Education, Ulm University, Ulm, Germany
[3] Department of Medicine, Institute of General Practice/ Family Medicine, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
[4] Department of Psychological Research Methods, Institute of Psychology and Education, Ulm University, Ulm, Germany
[5] Department of Clinical Psychology and Psychotherapy, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany
[6] BARMER, Schwäbisch-Gmünd, BARMER
[7] Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health research institute, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
[8] GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand "HelloBetter"), Hamburg, Germany
[9] Medical Psychology and Medical Sociology, Faculty of Medicine, University of Freiburg, Germany
[10] Department of Health Psychology and Applied Biological Psychology, Institute of Psychology, Leuphana University of Lueneburg, Lueneburg, Germany.
[11] École de psychologie, Université Laval, Québec, Québec, Canada.
[12] University Clinic for Psychiatry and Psychotherapy, Paracelsus Medical University, Nuremberg, Germany
[13] Faculty for Social Work, Technical University Nuremberg Georg Simon Ohm, Nuremberg, Germany
[14] Interdisciplinary Center of Sleep, Pfalzklinikum, Klinikum für Psychiatrie und Neurologie AdöR, Klingenmünster, Germany.
[15] Department of Sport and Health Sciences, Technical University of Munich, Munich, Germany.

* These authors contributed equally (Spiegelhalder, Baumeister, Riemann, Ebert)

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Address for correspondence:
Kai Spiegelhalder, MD PhD
Department of Psychiatry and Psychotherapy
Medical Center – University of Freiburg
Hauptstraße 5, 79104 Freiburg, Germany
Tel: +49 761 270 69780
Fax: +49 761 270 66190
Email: Kai.Spiegelhalder@uniklinik-freiburg.de

Conflict of interest statement

H. Baumeister received consultancy fees, reimbursement of congress attendance and travel costs as well as payments for lectures from Psychotherapy and Psychiatry Associations as well as Psychotherapy Training Institutes in the context of E-Mental-Health topics. He has been the beneficiary of study support (third-party funding) from several public funding organizations. M. Burkhardt and M. Kuhn are employees of BARMER. K. Domschke is a member of the Janssen Pharmaceuticals Inc. “Steering Committee Neuroscience”. M. Franke, E. Heber, D. Lehr and D. D. Ebert are stakeholders of the GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand “HelloBetter”), which aims to implement scientific findings related to digital health interventions into routine care. HelloBetter distributes the digital intervention for insomnia that is used in this study. C. M. Morin received research grant from Canopy Health, Eisai, Idorsia, and Lallemand Health Solutions; he served as consultant to Eisai, Idorsia, Pear Therapeutics, Sunovion and Weight Watchers, and received royalties from Mapi Research Trust. D. D. Ebert has served as a consultant to/on the scientific advisory boards of Sanofi, Novartis, Minddistrict, Lantern, Schoen Kliniken, Ideamed, German health insurance companies (BARMER, Techniker Krankenkasse) and a number of federal chambers for psychotherapy. None of the other authors declare any conflict of interest.

Abstract

Introduction: It is unclear how internet-delivered cognitive behavioural therapy for insomnia (CBT-I) can be integrated into healthcare systems, and little is known about the optimal level of therapist guidance. The aim of this study is to investigate three different versions of a stepped care model for insomnia (IG1, IG2, IG3) versus treatment-as-usual (TAU). IG1, IG2, and IG3 rely on treatment by general practitioners (GPs) in the entry level and differ in the amount of guidance by e-coaches in internet-delivered CBT-I.

Methods and analysis: In this randomised controlled trial, 4,268 patients meeting ICD-10 criteria for insomnia will be recruited. The study will use cluster randomisation of GPs with an allocation ratio of 3:3:3:1 (IG1, IG2, IG3, TAU). In step 1 of the stepped care model, GPs will deliver psychoeducational treatment; in step 2, an internet-delivered CBT-I program will be used; in step 3, GPs will refer patients to specialised treatment. Outcomes will be collected at baseline, and 4 weeks, 12 weeks and 6 months after baseline assessment. The primary outcome is insomnia severity at 6 months. An economic evaluation will be conducted and qualitative interviews will be used to explore barriers and facilitators of the stepped care model.

Ethics and dissemination: The study protocol was approved by the Ethics Committee of the Medical Center – University of Freiburg. The results of the study will be published irrespective of the outcome.

Registration details: The study has been registered in the German Clinical Trials Register (https://www.drks.de/drks_web/; DRKS00021503).

Strengths and limitations of the study

- This randomised controlled trial will recruit 4,268 patients and will be the largest clinical trial on insomnia.
- This trial will investigate three different versions of a stepped care model for insomnia which rely on treatment by general practitioners in the entry level and differ in the amount of guidance by e-coaches in internet-delivered CBT-I.
- The primary outcome is insomnia severity. An economic evaluation will be conducted and qualitative interviews will be used to explore barriers and facilitators of the stepped care model.
- Patients with insomnia will not be blind to treatment allocation in this trial.

1. Introduction

Insomnia disorder is characterised by difficulties initiating and/or maintaining sleep resulting in significant daytime dysfunction.[1] In Western industrialised countries, 5-10% of the general population[2] and 20% of primary care patients[3] suffer from the disorder. Insomnia is associated with a reduced quality of life,[4] and is a risk factor for other mental disorders, in particular depression and anxiety disorders,[5] as well as for cardiovascular diseases.[6,7]

Clinical guidelines recommend cognitive behavioural therapy for insomnia (CBT-I) as first-line treatment.[8 9] CBT-I is a multi-component intervention consisting of psychoeducation, relaxation therapy, sleep restriction therapy, stimulus control therapy, and cognitive therapy. However, only a small proportion of patients with insomnia has access to this treatment. For example, data from BARMER, a large German public health insurance, indicate that around 1.6% of the insured persons received a diagnosis of insomnia in 2017, but only 10% of these patients received a psychotherapeutic treatment.[10] Assuming a prevalence of insomnia of 5.7% in Germany,[11] this suggests that only 2.8% of all insomnia patients in Germany receive psychotherapeutic treatment. Since cognitive-behavioural therapy is not the only form of psychotherapy reimbursed by German health insurances and the focus of the psychotherapeutic treatment may, in many patients, be a comorbid disorder rather than insomnia, the assumption that 1% of all insomnia patients receive CBT-I might already be a very optimistic estimation. Instead, many insomnia patients are treated with benzodiazepine receptor agonists or sedating antidepressants on a long-term basis,[12] which is potentially harmful and not recommended by clinical guidelines.[8 9] This situation is unfortunate both from a clinical and from a health-economic perspective. Insomnia is associated with estimated annual costs of about 5,900 Euros per person in Germany due to absenteeism and presenteeism.[13] Thus, given its prevalence, a reasonable estimate of the indirect costs of insomnia in Germany is 25 billion Euros per year. This number is broadly in line with previously published socioeconomic data from the United States[14] and Canada.[15]

The dissemination of CBT-I is a major healthcare challenge, and internet-delivered psychotherapy has been suggested as a possible mean to lower the treatment gap.[16] Compared to face-to-face treatment, main advantages of internet-delivered CBT-I are convenience, increased accessibility, and potentially lower costs. In particular, internet interventions are easily accessible anytime and anywhere. Patients do not incur travelling expenses; they can work at their own pace; they may provide more honest answers in the privacy of their own home; and barriers related to the stigma of mental disorders may be reduced.[17] Hence, offering internet-delivered CBT-I might increase the utilisation of psychotherapy in undertreated populations. Meta-analyses suggest that internet-delivered CBT-I is highly effective in comparison to waitlist control conditions,[18 19] and that the effects appear to be comparable in size to those of face-to-face CBT-I.[20] In addition, follow-up data of up to 3 years demonstrate a high long-term effectiveness of online CBT-I.[21 22]

However, at least two questions with a high degree of healthcare relevance remain to be answered. First, it is unclear how internet-delivered CBT-I can be effectively integrated into existing healthcare systems that rely on general practitioners (GPs) to take the lead in coordinating patient care. Previous research has shown that the implementation of CBT-I techniques in primary care is challenging but promising.[23 24] In line with a stepped care approach to the treatment of insomnia,[25] GPs may serve as the entry level of a multistep model that offers more intense support for those with more complicated complaints in a cost-effective way. Although conceptually appealing, there are very few studies investigating such stepped care models for insomnia,[26-28] and none of them included active treatment provided by GPs. Second, little is known about the optimal level of therapist guidance in the context of internet-delivered CBT-I. While it is generally thought that human support has positive effects on adherence and efficacy in online mental health interventions,[29] many studies in the insomnia field have successfully implemented online interventions without any human support/ guidance (e.g.,[16 22 30 31]). One study has directly compared an online intervention for insomnia with and without guidance via email and found a superior efficacy in the guided group.[32] However, there

is limited knowledge about who needs and who does not need guidance and how this translates into cost-effectiveness estimates.

The central objective of the present study is to improve the quality and efficiency of healthcare for patients with insomnia. In addition, it is intended to improve interdisciplinary and intersectoral cooperation between GPs, psychotherapists and medical specialists working in outpatient and inpatient settings. Three different versions of a stepped care model (intervention group 1, IG1; intervention group 2, IG2; intervention group 3, IG3) that differ in the amount of guidance that is provided by e-coaches in the internet-delivered intervention in step 2 will be compared with treatment-as-usual (TAU) in, to the best of our knowledge, the largest clinical trial to date on insomnia (see Fig. 1). At step 1, participating GPs will provide a brief psychoeducational treatment; at step 2, patients will receive an internet intervention based on CBT-I; and at step 3, patients will be referred to specialised medical face-to-face treatment. Patients who are unresponsive to the treatment at one step will proceed to the next step of the model. The primary research question is the effectiveness of the interventions. We will also investigate differential treatment outcomes in four subgroups of patients: 1) insomnia without any comorbidity; 2) insomnia with mental comorbidity; 3) insomnia with somatic comorbidity; 4) insomnia with mental and somatic comorbidity. In addition, an economic evaluation will be carried out and qualitative interviews will be conducted to explore barriers and facilitators of the stepped care model. In case of a positive evaluation, it is intended to include the stepped care model in the guidelines of the Federal Joint Committee, the highest decision-making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany.

(please insert Figure 1 here)

2. Methods

2.1. Study design

The study is a four-armed pragmatic parallel-group cluster-randomised controlled trial investigating three different versions of a stepped care model for insomnia versus TAU. The unit of randomisation will be the participating GPs to avoid treatment diffusion. Primary and secondary outcomes as well as moderating and mediating variables and intervention-related variables will be assessed online by patient self-report using LimeSurvey (https://www.limesurvey.org/). Online assessments will take place at baseline (T0) and after 4 (T1) and 12 (T2) weeks, as well as 6 months after baseline (T3; see Fig. 2 for trial design). Informed consent will also be given online. The trial might be continued with further annual follow-up assessments after 1-5 years in case of patients´ informed consent and dependent on follow-up assessment resources beyond the funded 6 months follow-up. The trial started recruitment of patients in October 2020 and will continue recruiting until September 2022.

The study will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) Statement 2010 and the extensions for reporting pragmatic trials, cluster randomised trials, multi-arm parallel group trials and trials on psychological interventions.[33-37] This trial protocol was created according to SPIRIT guidelines.[38]

(please insert Figure 2 here)

2.2. Participants

Overall, 4,268 patients are planned to be recruited. The inclusion criteria are: a) age ≥ 18 years; and b) ICD-10 diagnosis of non-organic insomnia (F51.0) or insomnia (G47.0). Exclusion criteria are: a) untreated sleep apnoea syndrome (ICD-10: G47.3); b) untreated restless legs syndrome or periodic leg movement disorder (ICD-10: G25.8); c) untreated

hyperthyroidism (ICD-10: E05.9); d) ongoing psychotherapy for insomnia; e) conditions that may be aggravated by CBT-I (bipolar disorder, ICD-10: F31.x; epilepsy, ICD-10: G40.x); e) conditions that pose a serious threat to treatment adherence (e.g., organic, including symptomatic, mental disorders (ICD-10: F00-F09); mental and behavioural disorders due to psychoactive substance use (ICD-10: F10-F19); schizophrenia, schizotypal and delusional disorders (ICD-10: F20-F29)); f) acute suicidality.

Up to 320 GPs from Bavaria and Baden-Wuerttemberg, who participate in this study, will recruit eligible patients during consultations and check inclusion and exclusion criteria. In addition, online, print and broadcast media advertisements as well as postal mailings by the BARMER to potential patients will be used to recruit insomnia patients from all over Germany. These patients will be referred to a group of GPs that use telehealth consultations for checking inclusion and exclusion criteria, delivering step 1 of the stepped care model and guiding patients through the stepped care model. All GPs will receive remuneration for each participating patient (up to 158.25€ depending on the number of consultations). In addition to receiving free access to the stepped care model or TAU, participants will receive payment after the completion of online assessments T1 (15€), T2 (15€), and T3 (20€) to increase adherence.

2.3. Randomisation and allocation concealment

This study will use cluster randomisation of GPs with an allocation ratio of 3:3:3:1 (IG1:IG2:IG3:TAU). Randomisation will be performed by authors MB and MM (Ulm University) who are not otherwise involved in the trial and therefore blinded to all processes of the study. Population-density stratified permuted block randomisation (nine strata based on population density and average level of income, one stratum for GPs that exclusively employ telehealth consultations) will be employed with varying block sizes concealed to the investigators to minimise selection bias. GPs from community practices will be randomised into the same trial arm. The GPs are instructed to conceal group allocation until the baseline assessment is completed by the patient.

2.4. Blinding

Blinding of patients and healthcare providers is not feasible. However, screenings and baseline assessments will be performed before patients are informed about treatment assignment to avoid contamination with anticipated treatment effects. In case of non-completion of assessments participants will receive fully automated standardised reminders.

2.5. Intervention

The stepped care model that will be tested in the current study is presented in Figure 1.

2.5.1. Step 1

In step 1 of the stepped care model, the responsible GP will deliver a brief standardised psychoeducational treatment after being trained by sleep medicine specialists of the Department of Psychiatry and Psychotherapy of the Medical Center – University of Freiburg and by primary care physicians of the Department of Medicine, Division of General Practice, of the Medical Center – University of Freiburg. The treatment includes the following psychoeducational recommendations: a) avoid alcohol as a hypnotic; b) avoid clock-watching at night; c) avoid afternoon caffeine use; d) exercise regularly. In addition, the following stimulus control instructions will be given by the GPs: a) use the bed only for sleep and sexual activity; b) get out of bed when unable to sleep; c) do not nap during the day. Of note, the GPs do not use standardised leaflets that summarise the psychoeducational recommendations. GPs can also consult a psychiatrist of the Department of Psychiatry and Psychotherapy of the Medical Center – University of Freiburg whenever they feel that discontinuation of hypnotic medication would be appropriate. After four weeks, all patients in the intervention groups will receive an email with a link providing the opportunity to access step 2 of the stepped care

model without further consultation of the GPs. Importantly, for each patient, GPs can decide to skip step 1 of the stepped care model if they do not expect a substantial impact on insomnia severity.

2.5.2. Step 2

At step 2 of the stepped care model, the GET.ON Institut für Online Gesundheitstrainings GmbH (operating under the registered brand "HelloBetter") will provide an internet intervention based on CBT-I with an accompanying mobile sleep diary app. The intervention was initially developed at Leuphana University Lüneburg by the team of author DL and was positively evaluated in three randomised controlled trials.[39-41] Since the intervention was initially designed for workers, it has been adapted and technically updated for the current study by HelloBetter to meet the needs of all potential patients. Treatment content is based on CBT-I manuals and includes psychoeducation, relaxation therapy, sleep restriction therapy, stimulus control therapy, and cognitive interventions targeting rumination and worry. Delivery is structured into eight sessions, lasting approximately 45-60 min each. Participants are instructed to complete one session per week resulting in an overall duration of eight weeks. However, participants are allowed to work through the sessions faster or slower accounting for interindividual differences in the therapeutic process.

Patients of the three IGs receive an initial and a final consultation (each about 20 min) with one of a team of e-coaches of HelloBetter, who are trained and supervised psychologists. The consultations will be conducted by telephone, or, if this is not possible, by in-platform messages. In addition to the initial and final consultation, patients randomised to the 'standard' version of the intervention (IG1) receive written feedback and support by the responsible e-coach after each session. E-coaches are instructed to spend, on average, 25 min per session for writing this feedback. Patients randomised to the 'flex' version of the intervention (IG2) receive written on-demand support by the responsible e-coach. Patients randomised to the 'basic' version of the intervention (IG3) do not receive additional human guidance.

The treatment platform operates according to the ISO 27000 and NEN 7510 standards. All data is securely stored on ISO 27000-certified servers and transmitted via HTTPS with SSL certificates (AES-256 and SHA-1, 2048-bit RSA). Industry-standard measures have been taken to ensure robust security for the platform.

2.5.3. Step 3

In step 3 of the stepped care model, non-responders will be referred by their GPs to specialised medical treatment. The decision about this referral lies with the responsible GP and is based on clinical judgement of response. However, the responsible e-coach of HelloBetter will send a report to the GP summarising step 2 treatment process and outcome. This includes a post-treatment ISI score based on an ISI that participants fill in on the treatment platform outside the research process, and a recommendation about whether and by whom the treatment should be continued after step 2. As a rule of thumb, GPs are recommended to refer patients with an ISI score ≥ 15 and a comorbid mental health syndrome to a psychiatrist and/or a psychotherapist in step 3, and all other patients with an ISI score ≥ 15 to a medical doctor that is a board-certified sleep medicine specialist.

2.6. Treatment-as-usual

In the TAU group, GPs are instructed to provide their routine clinical care for insomnia. This may or may not include non-pharmacological or pharmacological treatment by the GPs or referrals to specialised medical treatment. The GPs in the TAU group will not receive the specific training that is described in section 2.5.1. and will not be able to refer patients to the internet intervention described in section 2.5.2. All health care provisions in the TAU group will be retrospectively monitored with the Trimbos/iMTA questionnaire (TIC-P; see section 2.8.2.). Using these data, an accurate description of TAU can be provided.

2.7. Safety protocol

During the screening procedure, GPs exclude patients with acute suicidality. Suicidal ideation will also be screened by the e-coaches of HelloBetter at their initial consultations, and at T0, T1, T2, and T3 using QIDS-SR16 and NEQ (see paragraph on measures for details). Reports of current suicidal ideation in the interview, a score ≥ 1 on the suicide item of the QIDS-SR16 (item 12; 0 = "I do not think of suicide or death.", 1 = "I feel that life is empty or wonder if it's worth living.", 2 ="I think of suicide or death several times a week for several minutes", 3 = "I think of suicide or death several times a day in some detail, or I have made specific plans for suicide or have actually tried to take my life"), or the answer „yes" to item 10 of the NEQ ("I got thoughts that it would be better if I did not exist anymore and that I should take my own life") will result in a standardised safety protocol. In particular, participants will receive an information document with detailed information on available health services and the advice to consult their GP. The wording of the online information document is adapted in emphasis, depending on the severity of the indicated suicidality.

2.8. Measures

Table 1 presents an overview of measures that are assessed in this trial.

(please insert Table 1 here)

2.8.1. Primary outcome measure

The primary outcome will be insomnia severity at T3, six months after the baseline assessment. Insomnia severity will be assessed with the Insomnia Severity Index (ISI[42]). The ISI is composed of seven 5-point Likert scale items (0-4 points; total score range: 0-28 points)

probing perceived severity of insomnia symptoms during the preceding two weeks. Several studies have shown good internal consistency of the ISI with Cronbach's Alpha ranging from 0.70 to 0.90.[42-44]

2.8.2. Secondary outcome measures

Sleep quality will be assessed using the Pittsburgh Sleep Quality Index (PSQI[45]), a 19-item self-report measure covering different aspects of sleep quality. The total score of the PSQI ranges from 0 to 21, internal consistency was found to be 0.80.[46] Quality of life will be assessed with the AQoL-8D,[47] an instrument composed of 35 items that measure eight dimensions (independent living, pain, senses, mental health, happiness, coping, relationships, self-worth). The AQoL-8D generates patient preference–based utilities on a scale of 0 (death) to 1 (perfect health), using the time-trade-off method,[47] which will be used to estimate quality-adjusted life years (QALYs) based on the area-under-the-curve (AUC) method. The AQoL-8D has been reported to have excellent internal consistency with a Cronbach's Alpha of 0.96.[47] Depressive symptoms will be measured using the 16-item Quick Inventory of Depressive Symptoms in the self-report format (QIDS-SR16[48]). The total score of the QIDS-SR16 ranges from 0 to 27, internal consistency was reported to be good (Cronbach's Alpha = 0.86).[49] Incident depression will be assessed in patients without a depression diagnosis at T0 and defined using a cut-off score of ≥13 on the QIDS-SR16.[50] Anxiety symptoms will be assessed with the 7-item General Anxiety Disorder 7 questionnaire (GAD-7[51]; total score 0-21; Cronbach's Alpha = 0.89[52]). Somatic symptoms will be measured using the 8-item Somatic Symptom Scale 8 (SSS-8[53]; total score 0-32; Cronbach's Alpha = 0.81). For the health-economic evaluation, health-care utilisation, patient and family expenditures and productivity losses due to absence from work or reduced efficiency during paid and unpaid work will be established with the Trimbos/iMTA questionnaire for costs associated with psychiatric illness (TiC-P), a retrospective self-report questionnaire covering the previous three months.[54-56] A list of unit cost prices will be used to

compute health care costs on a per-participant basis.[57] Test-retest reliability has previously been shown to be satisfactory.[55]

2.8.3. Intervention-related variables

At T2 after 12 weeks, the 12-item Working Alliance Inventory for guided Internet interventions (WAI-I[58]) and the 12-item Technological Alliance Inventory (TAI-OT) will be administered in all patients of the intervention groups (IG1, IG2, IG3) who entered step 2 of the stepped care model (internet-delivered CBT-I). The WAI-I and the TAI-OT will be used to assess the therapeutic alliance between patient and e-coach and the technological alliance between patient and e-coach and the technological alliance between client and the internet-based intervention, respectively. The WAI-I score ranges from 12 to 60 and the questionnaire has excellent internal consistency with a Cronbach's Alpha of 0.93.[58] The TAI-OT is a new self-report questionnaire developed by Labpsitec at Jaume I University in Castellón, Spain (Labpsitec (http://www.labpsitec.uji.es/eng/index.php) and measures the degree to which the internet-based intervention is perceived as being helpful in achieving therapeutic goals. The TAI-OT score ranges from 12 to 84. Patients in all conditions will receive the 8-item Client Satisfaction Questionnaire (CSQ-8[59 60]; total score 8-32), which is characterised by excellent internal consistency with a Cronbachs's Alpha of 0.93.[59] In addition, the 20-item Negative Effects Questionnaire (NEQ[61]) will be used in all patients. The NEQ measures the frequency, with a total score ranging from 0 to 20, and impact, with a total score ranging from 0 to 80, of possible negative effects during treatment. Its internal consistency was found to be excellent with a Cronbach's Alpha of 0.95.[61] Moreover, an additional self-developed 24-item Questionnaire on adverse effects of CBT-I will be used. For adverse events reported in the NEQ and the additional self-developed 24-item questionnaire, patients who entered step 2 of the stepped care model will be asked if they attribute the adverse events to the behavioural components of CBT-I. A self-developed Dropout Questionnaire based on the Health Action Process Approach (HAPA[62]) will be used to identify dropout reasons in participants not

completing at least 80% of the internet-delivered intervention. For a comprehensive evaluation of the implementation of the stepped care model a battery of self-developed self-report items will be used in all patients to assess the usage of and adherence to treatment components across the steps.

2.8.4. Potential treatment moderators and mediators

At T0, demographic variables (e.g., age, gender), depressive and anxiety symptoms, as well as IT knowledge will be documented as potential moderators of treatment effectiveness. In addition, the baseline values of the following variables will be assessed as potential moderators: the 10-item Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-10[63 64]; Cronbach's Alpha = 0.69), the 16-item Pre-Sleep Arousal Scale (PSAS[65 66]; Cronbach's Alpha = 0.80-0.94), the 10-item Brief Fatigue Inventory (BFI[67]; Cronbach's Alpha = 0.96), the 10-item Perceived Stress Scale (PSS[68]; Cronbach's Alpha = 0.78), the 13-item Sleep Hygiene Index (SHI[69]; Cronbach's Alpha = 0.66), and the 18-item short version of the Cognitive Emotion Regulation Questionnaire (CERQ-short[70]; Cronbach's Alpha = 0.68-0.81). In addition, mediation analyses will be conducted using some of the constructs described in this section (DBAS-10, PSAS, PSS, SHI, CERQ) as well as two intervention-related variables described above (WAI-I, TAI-OT).

2.8.5. Other data

Medical record data (e.g., ICD-10 diagnosis codes, treatment) will be provided by the GPs to enable allocation of patients to the four subgroups. In cases of missing medical record data, group allocation will be based on self-reported mental and somatic comorbidities. Sleep diary data will be assessed in step 2 of the stepped care model and will be used to evaluate treatment adherence, e.g., adherence to personalised sleep restriction recommendations. Additionally, usage data from the treatment platform will be used to assess adherence to the

internet-delivered intervention. Secondary data from BARMER will be used to assess the validity of the TiC-P. In addition, qualitative interviews will be conducted with a subgroup of patients, GPs and e-coaches to assess their experience of positive and negative aspects of the stepped care model. Trained interviewers will explore acceptance, perceived effectiveness, usage behaviour, barriers, facilitators, transferability into routine care as well as side-effects of the stepped care model using semi-standardised interview guides. The sample size and composition will be planned to consider the different intervention groups and gain sufficient theoretical data saturation. All subgroups will be represented in the interviews.

2.9. Sample size calculation

There is no universally accepted minimally important difference for the treatment of insomnia. Hence, this issue has been discussed among the clinicians involved in the current trial who are nationally and internationally leading experts in the field of insomnia research. Most clinicians agreed that 1.5 or more points on the ISI (exhibiting a common standard deviation of 6.0 points) are a reasonable minimally important difference corresponding to a minimally important effect size of d = 0.25. Based on previous research, it is assumed that all intervention groups (IG1, IG2, IG3) exhibit a considerably larger difference to the TAU group of at least d = 0.50 (e.g., [24]). Because of this, for ethical reasons and to reduce costs, the sample size calculation is based on the comparisons between the IGs, and the GPs are randomised with an allocation ratio of 3:3:3:1 (IG1, IG2, IG3, TAU), which ensures sufficient power for both differences between any IG and TAU (of at least d = 0.35) as well for differences between IGs (of at least d = 0.25). Based on 320 GPs with a median recruitment rate of n = 9 ± 14 patients, an ICC of 0.02 (see [71] for comparison), a correlation of the outcome at T3 with the corresponding baseline assessment of r = 0.5, d = 0.25, an α of 0.05 and (1-β) of 80%, the required sample size is n = 1,067 for each of the four subgroups of patients (IGs: n = 320 each; TAU: n = 107). Thus, a total sample size of N = 4,268 (IGs: n = 1,280 each; TAU: n = 428) is

required. Sampling procedures for the qualitative interviews follow theoretical data saturation principles.[72 73]

2.10. Statistical and qualitative analysis

2.10.1. Effectiveness

Descriptive statistics of recruitment and dropout as well as baseline characteristics for each group will be provided. The primary effectiveness analysis will be conducted according to the intention-to-treat principle based on all patients with their original treatment allocation. Additionally, per-protocol analyses based on the data of patients who completed a substantial proportion of the internet intervention (i.e., 80% of the modules) will be conducted. Missing data will be handled via multiple imputation, using a multilevel imputation model to account for clustering. The effect of group allocation (IG1, IG2, IG3, TAU) on the primary endpoint ISI at T3 (6 months after baseline) will be tested using pairwise group comparisons based on linear mixed models with corresponding 95% confidence intervals. These analyses will be conducted separately for each subgroup of patients. The alpha level will be adjusted using the Bonferroni-Holm procedure. All models will include the responsible GP as a clustering variable as well as baseline insomnia severity, age, and gender as covariates. Clinical significance will be determined using Number Needed to Treat (NNT) analyses[74]. Additionally, reliable reduction in insomnia severity will be calculated with the Reliable Change Index (RCI) by Jacobson & Truax.[75] For calculating the RCI, a pre-specified Cronbach's alpha of 0.92 will be used, based on a validation study in 410 primary care patients.[76] Based on the RCI, participants will be categorised into responders and non-responders, and the proportion of responders will be compared between study groups (again accounting for clustering). Secondary outcomes will be analysed analogously to the primary outcome, using random effect regression models as appropriate for the respective type of data. Potential onset and remission of incident depression will be compared between study groups based on incidence rate ratios (IRR) using multilevel Poisson regression. No interim analysis is planned for effectiveness or futility.

Exploratory moderator analyses will be used to investigate whether pre-treatment patient characteristics are associated with differential treatment effectiveness. Potential moderators include sociodemographic (e.g., age) and clinical (e.g., insomnia severity) variables. Exploratory mediator analyses will be employed to examine potential mechanisms of change. Among potential mediators are sleep-related (e. g. dysfunctional beliefs and attitudes about sleep) and intervention-related variables (e. g. working alliance).

2.10.2. Economic evaluation

The economic evaluation will be performed from the societal and public health care perspective. Two multilevel models (MLMs) will be specified, one for costs and one for effects, which take into account the hierarchical structure of the data. MLMs will be combined with cluster bootstrapping, which is recommended for resampling clustered data.[77] Across the four study groups, mean costs and QALYs will be compared to assess if any of the treatments are less effective and more expensive than the other treatments. If so, incremental cost-effectiveness ratios (ICERs) will not be estimated in relation to that treatment.[78] Otherwise, ICERs will be estimated by calculating the difference in costs between two treatment options divided by the difference in effectiveness of these two treatment options. We will bootstrap seemingly unrelated regression equation (SURE) models to generate 5,000 simulations of cost and effect pairs while allowing for correlated residuals of the cost and effect equations and adjusting for potential confounders.[79] The joint uncertainty surrounding costs and effects will be summarised using cost-effectiveness acceptability curves (CEACs) based on a net benefit regression framework.[80] CEACs show the probability of an intervention being cost effective in comparison with the alternatives for a range of different willingness-to-pay thresholds. For patients insured by BARMER, the validity of the TiC-P will be assessed with secondary data from the health insurance.

2.10.3. Qualitative interviews

Qualitative interviews of patients, GPs and e-coaches will be used to assess barriers and supporting factors of the stepped care model. The sample size will be determined according to the principle of theoretical saturation. Thus, data collection will continue until no further insights can be gained from additional interviews.[81 82] Following the principles of theoretical sampling, for the stakeholder group patients, cases will be deliberately selected based on the following criteria: remitters/non-remitters; male/female; lower/higher age; intervention-adherers (defined as completing more than 80% of the intervention within 12 weeks)/non-adherers. Additionally, care will be taken to include participants from all three IGs and the TAU group. Given the limited number of GPs and e-coaches, all participants of these stakeholder groups will be invited to the interviews.

For each stakeholder group, a semi-structured interview schedule will be prepared. The content of the interview schedules will be primarily based on the dimensions of the Hierarchical Model of Health Service Quality (i.e., interpersonal quality, technical quality, environmental quality, administrative quality)[83] and will be supplemented by other relevant dimensions (e.g., therapeutic alliance, adverse effects). The questions aim at exploring acceptance, perceived effectiveness, usage behaviour, barriers, facilitators, and transferability into routine care as well as adverse effects. Interviews will be 60-90 min long and will be conducted by trained and supervised psychologists. Recordings will be transcribed according to the rules for computer-assisted evaluation.[84] Following the principles of qualitative content analysis by Kuckartz,[84] text units will be systematised and classified following an inductive-deductive approach. The data analysis will be carried out using MAXQDA, a software for the analysis of qualitative data.[85]

2.11. Patient and public involvement

Representatives of patient groups were not formally involved in the design of this study but will be involved in the discussion and dissemination of results. In addition, patients were involved

in user-experience and usability testing of the platform for the internet intervention in order to ensure that the interface is user-friendly and adaptive to factors related to age, gender, and education. Public representatives approved the trial objectives and design as part of the application to the Innovationsfonds of the German Federal Joint Committee

2.12. Ethics and dissemination

The study has been registered in the German Clinical Trials Register (https://www.drks.de/drks_web/; DRKS00021503) and will be conducted in accordance with the Declaration of Helsinki. The study protocol was approved by both the Ethics Committee of the Medical Center – University of Freiburg and the Ethics Committee of the State Chamber of Physicians ('Landesärztekammer Baden-Württemberg'). In addition, the data protection officers of the Medical Center – University of Freiburg and Ulm University have approved the formal data protection concept of this study. The results of the study will be published irrespective of the outcome.

3. Discussion

Insomnia is a common, costly and impairing sleep disorder. According to clinical guidelines, the first-line therapy is CBT-I, however, only few patients with insomnia have access to this treatment. Internet-delivered CBT-I has the potential to disseminate the recommended treatment to a larger number of patients. This study will determine whether a stepped care model for insomnia that includes psychoeducational treatment by GPs, internet-delivered CBT-I and specialised medical treatment, improves insomnia severity as well as psychological and physical well-being.

Authors statement: K. Spiegelhalder, D. D. Ebert, H. Baumeister, and D. Riemann conceived the project, have overall responsibility for the trial design and treatment design and drafted the trial protocol. C. Buntrock, M. Burkhardt, E. Heber, M. Kuhn, A. Maun, and M. Moshagen contributed to trial design. A. Al-Kamaly, M. Franke, L. Frase, E. Heber, K. Helm, D. Lehr, and A. Maun contributed to treatment design. H. Baumeister, M. Bader, N. Bauereiß, L. Braun, P. Dülsen, A. M. Küchler, M. Moshagen, and L. Simon are responsible for statistical analysis. C. Buntrock is responsible for economic analysis. All authors provided critical review on the trial protocol and approved the final manuscript.

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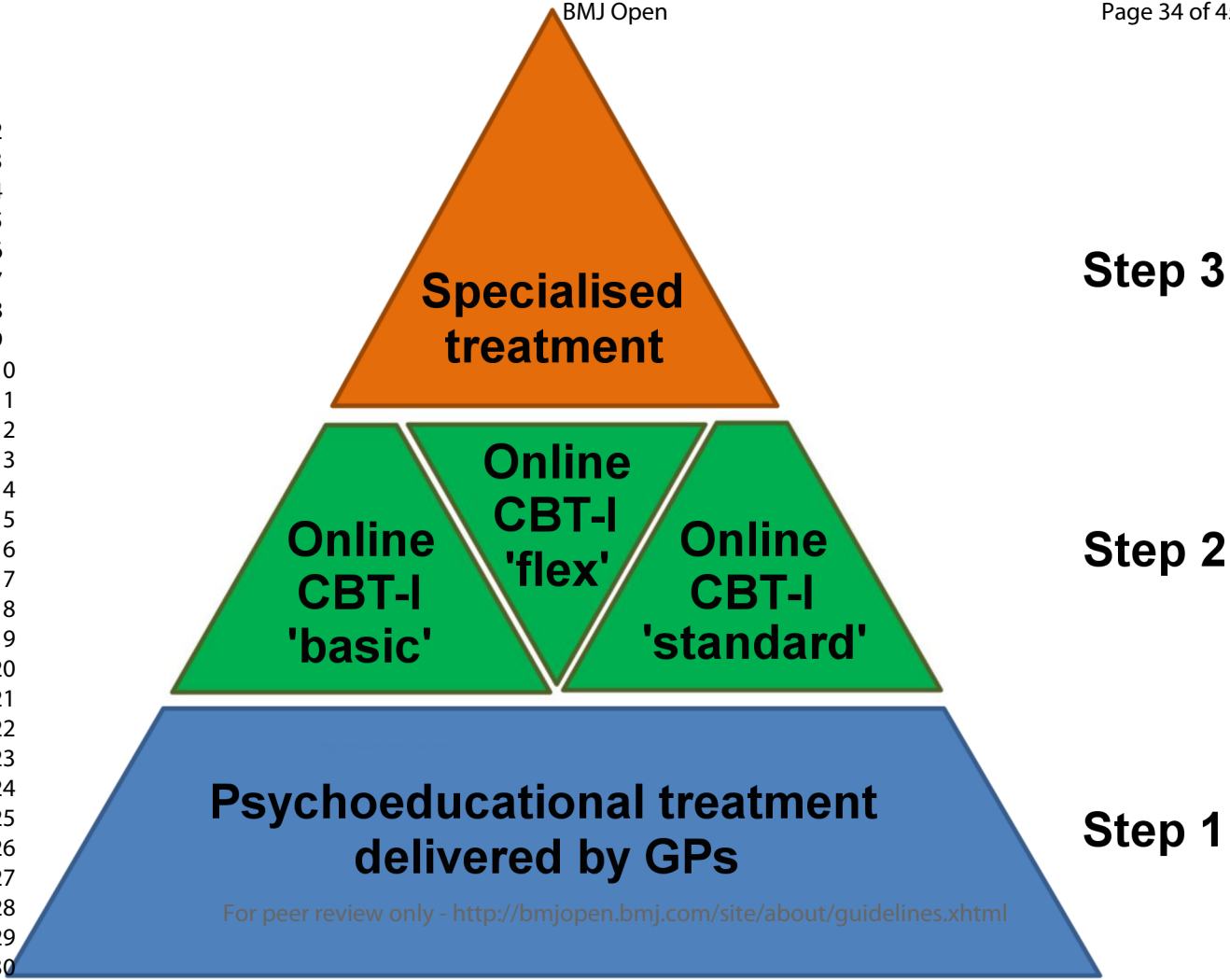
Figure Legends

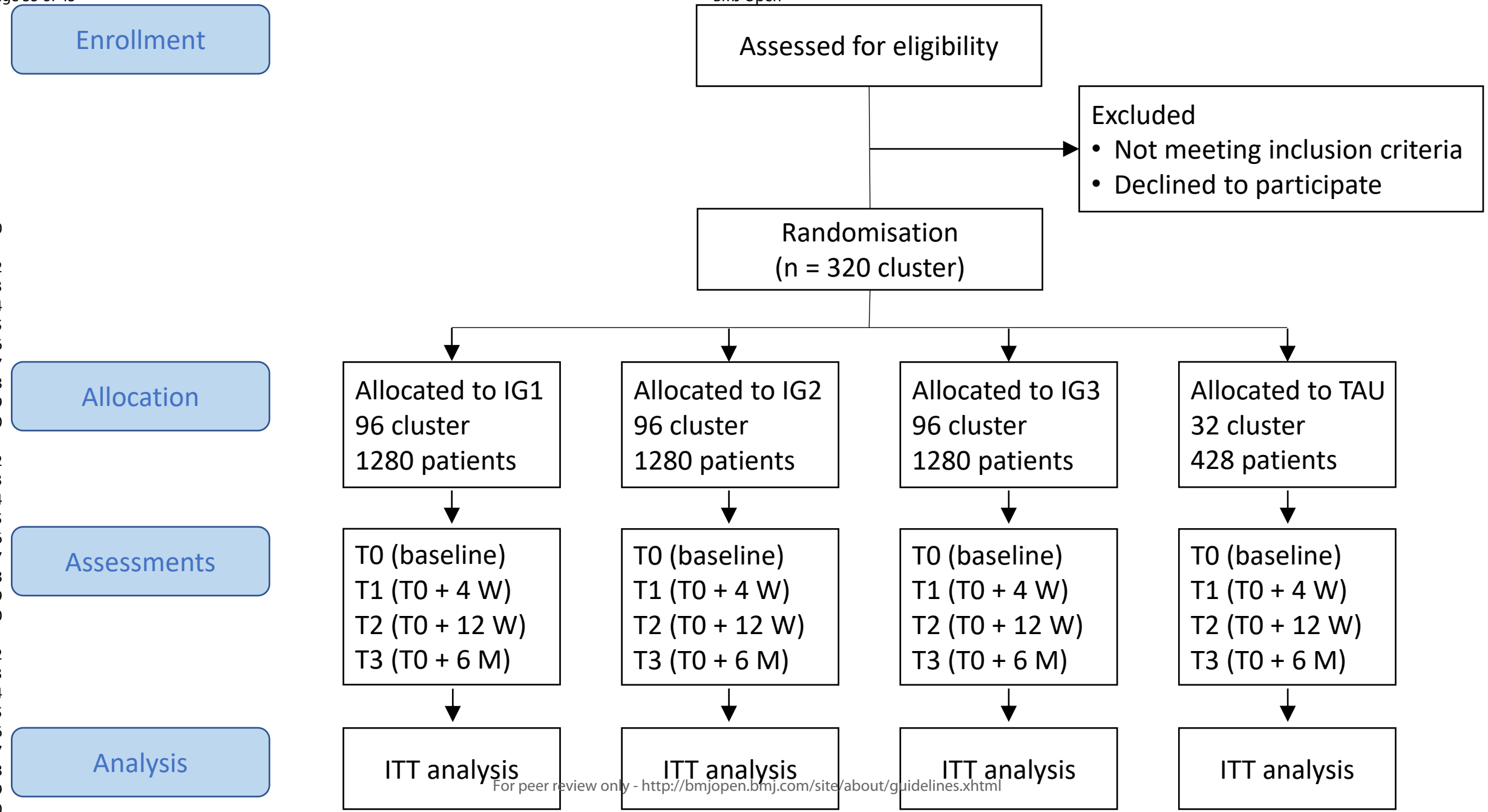
Figure 1: Stepped care model for insomnia that will be tested in the current trial. CBT-I: cognitive-behavioural treatment for insomnia; GPs: general practitioners.

Figure 2: IG1: intervention group 1 ('standard' version of step 2 of the stepped care model); IG2: intervention group 2 ('flex' version of step 2 of the stepped care model); IG3: intervention group 3 ('basic' version of step 2 of the stepped care model); TAU: treatment-as-usual; W: weeks; M: months; ITT: intention-to-treat.

Table 1: Overview of the assessments. [1] The ISI at T3 (6 months after T0) is the primary outcome of this trial; [2] only in patients of the intervention groups (IG1, IG2, IG3) who entered step 2 of the stepped care model; [3] only in patients of the intervention groups (IG1, IG2, IG3) not completing at least 80% of the internet-delivered intervention. ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; AQoL-8D: Assessment of Quality of Life instrument; QIDS-SR16: Quick Inventory of Depressive Symptoms in the self-report format; GAD-7: General Anxiety Disorder 7 questionnaire; SSS-8: Somatic Symptom Scale 8; TiC-P: Trimbos/iMTA questionnaire for costs associated with psychiatric illness; DBAS-10: Dysfunctional Beliefs and Attitudes about Sleep Scale; PSAS: Pre-Sleep Arousal Scale; BFI: Brief Fatigue Inventory; PSS: Perceived Stress Scale; SHI: Sleep Hygiene Index; CERQ-short: Cognitive Emotion Regulation Questionnaire; WAI-I: Working Alliance Inventory for guided Internet interventions; TAI-OT: Technological Alliance Inventory; CSQ-8: Client Satisfaction Questionnaire; NEQ: Negative Effects Questionnaire.

Activity/Assessment	**T-1**	**T0**	**T1**	**T2**	**T3**
	Pre-study	Baseline (week 0)	4 weeks after T0	12 weeks after T0	6 months after T0
Eligibility screen	X				
Informed consent	X				
Primary outcome					
Insomnia severity (ISI)		X	X	X	X[1]
Secondary outcomes					
Sleep quality (PSQI)		X	X	X	X
Quality of life (AQoL-8D)		X	X	X	X
Depressive symptoms (QIDS-SR16)		X	X	X	X
Anxiety symptoms (GAD-7)		X	X	X	X
Somatic symptoms (SSS-8)		X	X	X	X
Costs (TiC-P)		X		X	X
Potential treatment moderators and mediators					
Dysfunctional beliefs and attitudes about sleep (DBAS-10)		X	X	X	X
Pre-sleep arousal (PSAS)		X	X	X	X
Fatigue (BFI)		X	X	X	X
Stress (PSS)		X	X	X	X
Sleep hygiene behaviour (SHI)		X	X	X	X
Emotion regulation (CERQ-short)		X	X	X	X
Intervention-related variables					
Alliance (WAI-I)				X[2]	
Technological alliance (TAI-OT)				X[2]	
Client satisfaction (CSQ-8)					X
Adverse events and negative effects (NEQ, Questionnaire on adverse effects of CBT-I)				X	X
Dropout Questionnaire				X[3]	





Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet	3

		registered, name of intended registry	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	1-30
Funding	#4	Sources and types of financial, material, and other support	20
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the	8

		trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6-7
Objectives	#7	Specific objectives or hypotheses	7
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	8
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data	9

		will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10-12
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12-13
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15,17
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9,11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical	13-16

		relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10-12, 30
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is	9-10

		unavailable to those who enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9-10
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a – Participants will be unblinded after allocation
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a	13-16

		description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9-10
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	8,12
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-18
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	18-19
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg,	18

		multiple imputation)	
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a – no interim analyses
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics	#24	Plans for seeking research ethics committee /	3

approval		institutional review board (REC / IRB) approval	
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	2
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care,	12

trial care		and for compensation to those who suffer harm from trial participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	3
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	20
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Materials are available in German only but can be submitted on request
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a