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Overcoming insomnia: protocol for a large-scale randomised controlled trial of online cognitive behaviour therapy for insomnia compared with online patient education about sleep

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ABSTRACT

Introduction Insomnia is a major public health concern. While cognitive behaviour therapy for insomnia (CBT-I) is acknowledged as the best available intervention, there are unanswered questions about its wider dissemination, socioeconomic benefits and its impact on health resource utilisation. The aim of this randomised controlled trial (RCT) is to investigate the effectiveness of a fully automated online version of CBT-I compared with online patient education about sleep (PE). Outcome measures comprise changes in symptoms of insomnia, time off work due to sick leave as well as medication and health resource utilisation. Also, we will examine (i) putative mediators of the effects of CBT-I on insomnia severity and (ii) selected potential psycho-bio-social moderators of the effects of the interventions.

Methods and analysis A parallel-group RCT will be conducted in a target sample of about 1500 adults recruited across Norway. Participants will complete an online screening and consent process. Those who meet eligibility criteria will be randomised to receive direct access to fully automated online CBT-I or to an online PE programme. The primary outcome is change in insomnia severity immediately postintervention; secondary outcomes are change in daytime functioning and other sleep measures postintervention and at 6-month and 24-month follow-up. Objective data from national registries will be obtained at two time points (1 year and 2 years post-treatment), allowing a mirror image study of preintervention and postintervention rates of sick leave, and of medication and healthcare utilisation by condition.

Ethics and dissemination The study protocol was approved by the Regional Committee for Medical and Health Research Ethics in South East Norway (2015/134). Findings from the RCT will be disseminated in peer-reviewed publications and conference presentations. Exploratory analyses of potential mediators and moderators will be reported separately. User-friendly outputs will be disseminated to patient advocacy and other relevant organisations.

Trial registration number NCT02558647; Pre-results.

Strengths and limitations of this study

► A large-scale, population-based trial with broad inclusion and lenient exclusion criteria and an extended follow-up period which may yield findings that are generalisable to real-world settings.

► National registers will offer objective data on the short-term and medium-term impact of cognitive behaviour therapy for insomnia on rates of sick leave, and medication and health resource utilisation.

► Adequate statistical power to detect small effects on insomnia severity associated with the interventions, and to analyse secondary outcomes such as preintervention and postintervention changes in sick leave, etc, and to undertake exploratory analyses of mediators and moderators.

► Many participants are self-referred or recruited by convenience sampling, which may introduce some self-selection biases.

► Reliance on online and self-report assessments is likely to lead to higher levels of sample attrition and/or incomplete and missing assessment data compared with studies that use face-to-face contact with therapists and researchers.

INTRODUCTION

Insomnia is characterised by a persistent inability to fall asleep, waking up during the night or too early in the morning and subsequent impairment in daytime functioning. It is the most commonly reported sleep problem, affecting 10%–12% of the population[1] and its prevalence has increased over the last decade.[2] Insomnia is now the second most frequent health complaint (after pain) and represents an independent risk factor for the development of a wide range of mental and somatic conditions and illnesses.[3] Furthermore, spontaneous improvement in

insomnia is uncommon.[4] Taken together, this demonstrates that chronic insomnia is a significant public health concern.

The daytime consequences of insomnia, such as fatigue, psychological distress, physical discomfort and lower work productivity[5] imply that insomnia impairs the quality of life of the individual,[6] and increases healthcare and medication utilisation.[7] Insomnia is further associated with increased rates of short-term and long-term sick leave, as well as permanent work disability.[8–12] Growing awareness of the broad range of health and occupational effects of chronic insomnia has led to recognition that treating insomnia could have benefits that extend beyond symptomatic remission to include societal and economic gains.[13] This is highlighted in a recent review by the *National Institutes of Health* and *the Sleep Research Society* which argued that, to realise the return on investment in sleep and circadian science, we need to accelerate the dissemination and implementation of research findings into clinical practice.[14] Furthermore, the report suggested that the highest priority in insomnia research is to identify costs and economic impacts of screening, diagnosing and treating insomnia across different systems (eg, healthcare, employment, etc).[14]

While there is a growing consensus that cognitive behaviour therapy for insomnia (CBT-I) should be the first-line treatment option for insomnia,[15 16] patients are however rarely offered such interventions even when they specifically present for medical assistance.[17] Furthermore, there are often long waiting times to commence CBT-I because of a shortage of trained therapists.[13 18] Arguably, the biggest current challenge to the dissemination of insomnia treatment is not a lack of empirical evidence for CBT-I, but lack of *access* to the intervention. Recently, this barrier has been partially overcome by delivering interventions via the internet.[19] An online adaptation of CBT-I that seems to be particularly promising in this respect is the Sleep Healthy Using The internet (SHUTi) program.[20] In a recent treatment trial, individuals with insomnia were randomised to receive either SHUTi or an online control condition. The researchers reported that 83% of participants allocated to SHUTi completed the intervention and 73% of them were in remission from insomnia at the 6 months follow-up assessment.[20] The short-term efficacy of SHUTi has been replicated in larger randomised controlled trials (RCTs) in the USA, Australia, Denmark and Norway, and findings suggest that online CBT-I has similar efficacy to CBT-I delivered in-person by a therapist.[21–24] The long-term effectiveness of SHUTi compared with a control intervention has been investigated in one study; this demonstrated that symptoms of depression, anxiety and insomnia decreased significantly more postintervention in the SHUTi group and remained significantly lower in the SHUTi group for >18 months compared with a control group.[25] A significant advantage of SHUTi or similar online CBT-I interventions is that, as the programs are fully automated, they can be delivered entirely online, hence there is no specific need for direct contact with a health professional, enabling timely, direct access to the intervention and widespread dissemination.

As online CBT-I is a relatively recent innovation, there are still important questions to address regarding its wider benefits. For example, little is known about the effects of the intervention in large-scale studies, and/or in self-referred or convenience samples recruited cross-nationally and in samples completing the programme without any clinician input or researcher support. Also, data are sparse on the durability of the effects of online CBT-I in the medium-to-longer-term (ie, beyond 12–18 months).[19] In addition, there is limited knowledge regarding its impact on basic health resource utilisation (beyond medication use alone), such as frequency of outpatient appointments, etc; and no studies have considered the broader economic perspective (eg, postintervention effects on rates of sick leave, etc). Furthermore, few studies have explored the putative moderators of or the mechanisms through which CBT-I (delivered face-to-face or online) may work.[26]

Aims

This paper describes the protocol for a two-arm RCT that assesses the benefits of online CBT-I compared with an alternative, active control intervention (online patient education about sleep (PE)). First, we will examine any differential change in the severity of insomnia, immediately after completing the interventions. Second, we will examine if there are differential changes in symptoms of physical and mental health (eg, psychological distress, fatigue and health-related quality of life) immediately postintervention, and whether any improvements in insomnia or other symptoms are reported at further follow-ups (6 months and 24 months post-treatment). Third, we will use national registry data collected routinely in Norway to compare rates of time off work due to sick leave days for up to 2 years before and after participating in the RCT, as well as monitoring medication and health resource utilisation according to condition in the same time interval. Fourth, we will try to extend the knowledge base about online interventions by undertaking exploratory analyses to assess whether change in specific clinical variables (eg, sleep variability, psychological measures of beliefs about sleep) mediate the effects of the CBT-I intervention. Lastly (subject to additional funding to collect saliva samples), we will examine a subset of psycho-biosocial factors to try to identify potential treatment moderators that might inform the stratification of individuals with insomnia into 'treatment-relevant' subgroups in the future.

METHODS AND ANALYSIS

The protocol for the RCT follows the Standard Protocol Items for Randomised Trials (SPIRIT) statement guidelines[27] and is registered with the Clinical Trials website (ClinicalTrials.gov identified: NCT02558647). A completed
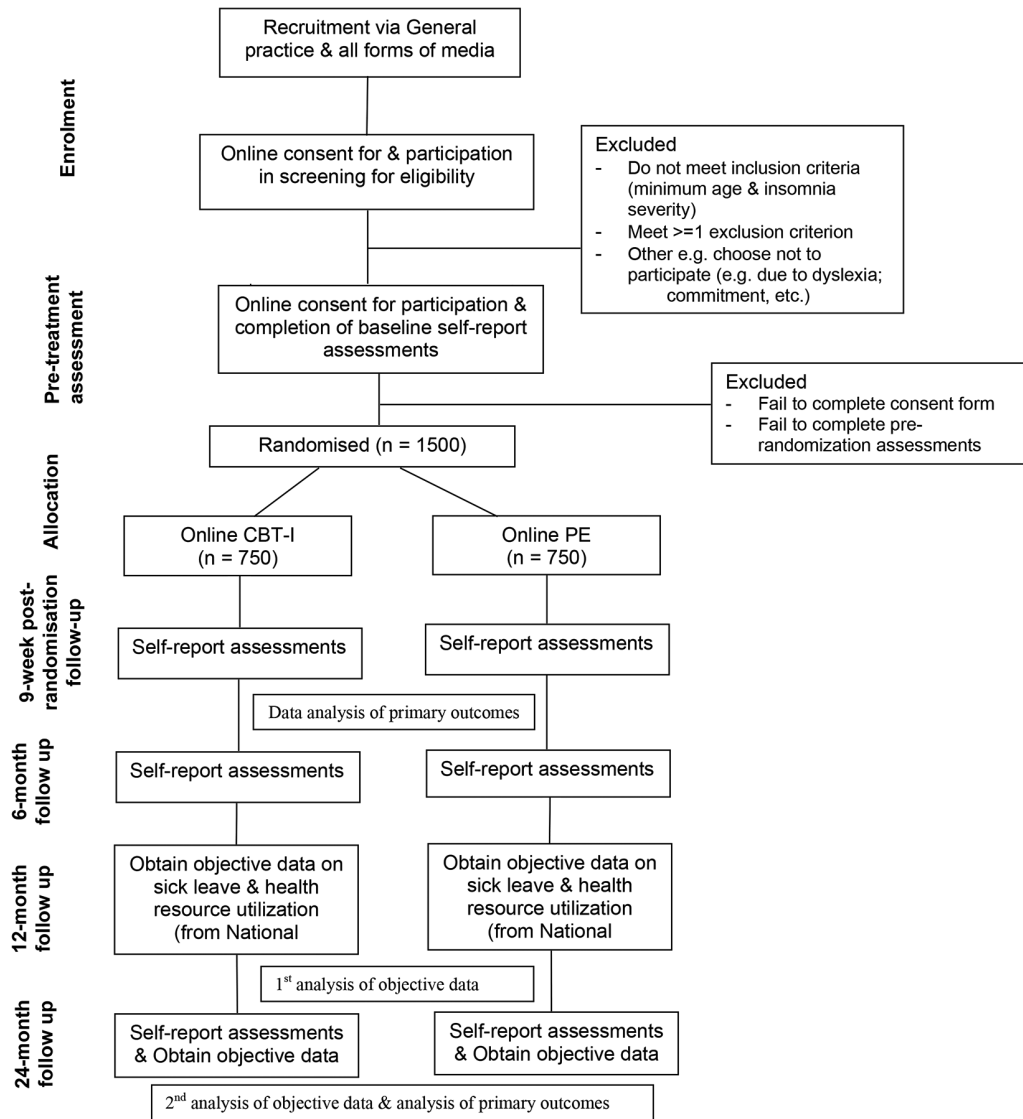
Figure 1 Flow chart of timeline for a randomised controlled trial of online interventions for insomnia (see text for predicted attrition rates). CBT-I, cognitive behaviour therapy for insomnia; PE, patient education about sleep.

SPIRIT statement can be found in online supplementary files 1 and 2, and a completed WHO Trial Registration Data Set can be found in online supplementary file 3.

The flow chart for the timeline for recruitment, follow-up assessments and for undertaking primary and secondary analyses of the RCT is shown in figure 1.

Research design

This is a parallel-group superiority RCT comparing internet-delivered CBT-I (a Norwegian language version of SHUTi) with online PE. Recruitment for the study commenced in February 2016 and it is anticipated it will be completed by August 2018.

The consent and screening processes, self-rating procedures and interventions will be undertaken entirely online. Potential participants will be first granted access to an online website where they will receive information about the RCT and be asked to provide online written informed consent to take part in the screening. If the screening process indicates the individual is eligible to participate, they are asked to complete a separate online consent process agreeing to take part in the randomisation process and the RCT.

Participants and procedure

Recruitment

Participants will be recruited from a variety of settings, for example, convenience sampling from health settings (undertaken by providing information about the RCT to general practice clinics, mental health and psychiatric outpatient settings), as well as self-referral via general advertisements and news stories in printed, online and social media.

As the investigators do not influence the online recruitment procedure, we cannot stop recruitment as soon as 1500 participants have given consent to be randomised and been allocated to an intervention. However, we can request information on the total sample size at intervals

of about 3 months. Thus, we will cease recruitment when a minimum sample of 1500 individuals have been randomised and given direct access to the interventions (ie, 750 per arm of the RCT).

Eligibility

Individuals who are interested in participating will enter an online screening portal (https://sovnmestring. no) where they will be asked to provide online written consent to complete a series of self-ratings to ensure that they meet study eligibility criteria. These are as follows:

Inclusion criteria: individuals aged ≥18 years who score ≥12 on the Insomnia Severity Index (ISI)[28] (a score indicative of insomnia symptoms that significantly impact on individuals).

Exclusion criteria: individuals scoring >10 on the Epworth Sleepiness Scale[29] (which is suggestive of excessive daytime sleepiness), and/or answering that they usually or every day snore and stop breathing and have difficulties staying awake during the day (ie, they positively endorse preselected indicators of sleep apnoea); self-report of the presence of any medical conditions where a fully automated CBT-I may be contraindicated (eg, epilepsy, bipolar disorder, schizophrenia or psychotic disorders and recent heart surgery) and/or participating in shift work.

All individuals deemed eligible for the RCT are provided with an onscreen notification stating that the online treatment is text-based and if they have a reading disability (eg, dyslexia), they may find elements of the programme difficult to follow at times. After the prompt, the individuals are then asked to respond to a further question to indicate that they still want to be included.

All individuals who are eligible for inclusion are provided with onscreen information that the intervention will require changes in their patterns of behaviour and are advised that this will imply that they need to set aside sufficient time to participate in the full course of therapy (usually, the six sessions can be completed within 6 to 9 weeks). The notification indicates that potential participants have the option to delay commencement of the programme if they wish. After the prompt, individuals are then asked to indicate whether they wish to continue and to be included in the randomisation process immediately.

Individuals who provide online written consent to participate are also asked to consent to the researchers accessing information about their health service use, medication prescriptions and selected national insurance data (related to time off work due to sick leave) from the relevant National databases (described below).

Randomisation

Eligible participants who have provided online written informed consent will be randomised to one of two online conditions in a 1:1 ratio. The randomization procedure is automated, and the research team do not have any access to the process and cannot influence it in any way. Participants are blinded to the group to which they are assigned.

Interventions

Online CBT-I

The online version is a fully automated, interactive and tailored web-based program that incorporates the primary tenets of face-to-face CBT-I, including sleep restriction, stimulus control, cognitive restructuring, sleep hygiene and relapse prevention.[20 22–24 30] Development of SHUTi is grounded in the model for internet interventions,[22] and follows best practice recommendations from the field of instructional design.[23] The intervention targets the distinct needs of users, sets measurable learning objectives and performance requirements and assesses users' achievement of the targeted outcomes.

The SHUTi program is presented in six 'cores', metered out over time, with a new 'core' available 7 days after completion of the previous one. Each core has been developed to reflect the topics in the traditional weekly face-to-face CBT-I sessions and follows a similar general structure, namely: 1) examination of core objectives, 2) review and feedback on homework and sleep diary data from the previous week, 3) teaching of new intervention material, 4) summary of the main points of the core and 5) assignment of homework. The content of the intervention is enhanced through a variety of interactive features, including personalised goal-setting, graphical feedback based on self-reported symptoms, animations and illustrations to enrich comprehension, quizzes to test and enhance user knowledge, vignettes to promote identification with material and video-based expert explanations. Also, automated emails are sent to users to increase their engagement and encourage program adherence.

Online PE

The online PE program employed in this trial has been used as a comparator for SHUTi in other published RCTs.[23 24] The PE website provides fixed information about insomnia symptoms; the impact, prevalence and causes of insomnia; when to seek input from a doctor and basic lifestyle, environmental and behavioural strategies that may help to improve sleep. The content of the sleep education programme is based on a review of recommendations provided on insomnia-focused websites.[24]

Both the PE and the CBT-I programmes incorporate some principles of CBT and both offer options for self-monitoring via sleep diaries and ratings of insomnia severity, but only the CBT-I programme employs online tools for self-monitoring. The PE programme offers printable pdf-documents. In contrast to CBT-I, the PE programme (1) does not personalise or individually tailor treatment recommendations based on user input; (2) presents significantly less detailed content, and in a simple, fixed format, without any interactive elements and (3) provides access to the entire programme content all at once, meaning the user can examine all the materials and content immediately (rather than the content being delivered in a step-by-step manner, or for access to each component to be available over time).

Concomitant care
There will be no restrictions on seeking other kinds of care during treatment.

Assessments
Descriptions for all measures used in this study are provided below and the timing of the assessments is summarised in table 1.

The primary outcome is change in severity of insomnia symptoms measured using the ISI[28] at baseline and 9 weeks postrandomisation. Other measures relate to secondary outcomes or are being used in exploratory or subsidiary analyses.

Demographics
Information will be collected at baseline on sex, age, marital status, years of education, employment status and if the participant has children living at home. Items recording marital status, children living at home and employment status will be repeated at 6 and 24 months assessments.

Sleep measures
Primary outcome measure
Insomnia severity index (ISI)[s28]: the ISI is a well-established, brief self-report instrument measuring the patient's perception of his or her insomnia that has good psychometric properties and is validated for online use.[31] It contains seven questions that assess the patients' symptoms and consequences of insomnia, and any associated distress on a 0–4 rating scale. The ISI is administered at baseline, postintervention and 6 and 24 months follow-ups.

Other sleep measures
Sleep diary[32]: individuals are asked to provide daily subjective estimates of their sleep the previous night (eg, bed-time, sleep onset latency, wake after sleep onset, etc). Individuals keep a record for at least 10 of 14 consecutive days and recordings are repeated at baseline, postintervention and 6 and 24 months follow-ups; the data will be used in the secondary outcome and the mediation analyses.

Bergen Insomnia Scale[33]: comprises six items that assesses symptoms of insomnia based on the insomnia criteria found in the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (American Psychiatric Association).[34] The self-rating is repeated at each assessment.

Brief Horne-Östberg Morningness-Eveningness Questionnaire[35] (MEQ): the MEQ is the most widely used measure of chronotype (so-called 'morningness' or 'eveningness'),[36] and gives an indication of the respondents preferred (as opposed to actual) rise-time and bed-time.[37] We rate the brief 5-item version of the scale at baseline, 6 and 24 months.

Brief Dysfunctional Beliefs and Attitudes Scale (DBAS-16)[38]: a self-report questionnaire designed to identify maladaptive sleep-related and insomnia-related cognitions. Patients are given a list of 16 statements reflecting different beliefs and attitudes about sleep, and they are asked to indicate on a 10-point scale how much they agree with the statements. The rating is completed at each assessment point and data will be used in the outcome and mediation analyses.

Resource use and work productivity
Self-report information on these parameters will be analysed in conjunction with objective data from Norwegian national registries.
a. Self-report ratings are based on those used in studies of SHUTi and will allow for selected comparisons between the findings of the current RCT and other published research. The present protocol extends the duration of the follow-up period for these assessments (see table 1 for the schedule for each measure). The ratings include the following: *use of healthcare services* (five items, eg, recording use of primary and secondary health services, etc); *medication use* (reason for use, dosage, timing, adherence); *help seeking behaviour* (a 10-item questionnaire that records what help or treatments were sought for a given time period); a*bsence from work due to health problems* (five items); *influence of health problems on productivity* (two items recording self-perceptions of any negative effects of health status on work or leisure activities).
b. National registry data: data from national registers can be linked to individuals via their social security number. We will make requests for access to national data on at least two occasions: at 12-month follow-up, we will request data covering the 12 months pretreatment and 12 months post-treatment; likewise, at 24-month follow-up, we will request data covering the 24 months pretreatment and 24 months post-treatment. This will allow a review of the entire time frame of the study, to link objective data to the 6-month self-report assessments, and to undertake mirror image analyses of rates of sick leave and of medication and health resource utilisation. The data that will be requested are as follows:

Norwegian Patient Registry (NPR): this contains information about all patients who are waiting for, or have received treatment, as outpatients in the specialist health service. The data retrieved from the NPR include diagnoses (according to the 10th revision of the International Statistical Classification of Diseases criteria), name of healthcare provider, service use (eg, outpatient appointments) and hospital admission and discharge dates.

National Insurance Administration: this records all periods of sick leave >13 days, as well as information on all disability pension awards (self-report information will allow us to estimate shorter periods of sick leave).

Norwegian Prescription Database (NorPD)[39]: this is a national health register comprising information on all prescriptions dispensed at Norwegian pharmacies (since January 2004). The NorPD provides detailed information that will allow us to identify the medication, its class and information on dispensed prescriptions (which can be

Table 1 Key measures and timing of assessment

	Screening* and/or baseline	Postintervention	6 months	12 months	24 months
Demographics					
Sex	X				
Age	X				
Marital status	X		X		X
Number of children living at home	X		X		X
Years of education	X				
Employment status	X	X	X		X
Sleep					
Insomnia Severity Index	X	X	X		X
Bergen Insomnia Scale	X	X	X		X
Brief Morningness-Eveningness Questionnaire	X		X		X
Sleep diary	X	X	X		X
Brief Dysfunctional Beliefs and Attitudes Scale 16	X	X	X		X
Physical and mental health					
Hospital Anxiety and Depression Scale	X	X	X		X
Chalder Fatigue Questionnaire	X	X	X		X
Short Form-12	X	X	X		X
Physical health	X	X	X		X
Mental health	X	X	X		X
Pain problems	X	X	X		X
Changes in health status		X	X		X
Resource use and work productivity					
Health service utilisation (self-report and Norwegian Patient Registry)	X		X	X	X
Prescribed medications (self-report and Norwegian Prescription Database)	X	X	X	X	X
Sick leave (self-report and National Insurance Administration)	X		X	X	X
Impact on work productivity	X		X		X
Help seeking behaviours		X	X		X
Health-related parameters					
Body mass index	X	X	X		X
Alcohol Use Disorders Identification Test- Consumption	X	X	X		X
Physical activity	X	X	X		X
Electronic media and internet use					
Internet use	X				
Electronic media use	X	X	X		X
Internet intervention evaluation		X			X
Long-term use of strategies					X
Negative effects of treatment					X

*See text for details of measures used only at screening.

used as a proxy for medication consumption), especially those used to improve sleep.

Other health measures

Given the known associations between insomnia and mental and physical disorders, alcohol use, body mass index (BMI), etc, we will also record other key items that will be relevant to statistical analyses that incorporate covariates. As shown in table 1, the following are completed at each assessment.

Physical and mental health

The following self-ratings will be repeated at each assessment and findings from the postintervention assessment will be reported in the first publication (alongside sleep outcomes).

Hospital Anxiety and Depression Scale (HADS)[40]: the HADS comprises 14 items pertaining to non-vegetative symptoms of anxiety and depression, which makes it a suitable measure of general psychological distress in populations likely to have physical comorbidities (eg, general practice and liaison psychiatry settings).[41]

Chalder Fatigue Questionnaire (CFQ)[42]: the CFQ comprises 11 items addressing physical and psychological fatigue, and two items addressing the duration and the intensity of fatigue complaints.

Short Form-12 (SF-12)[43 44]: this is an abbreviated version of the MOS 36-item short-form health survey (SF-36), and measures the individuals' perceived physical and mental health status. The SF-12 is scored using the recommended MOS software program that creates two summary scores, mental health (MCS12) and physical health (PCS12). The scores are represented as T-scores that are linear transformations with a mean of 50 and a SD of 10 in the general US population.

Other health assessment: additional instruments assessing various health domains are adapted from the HUNT study (the Nord-Trøndelag Health Study)[45] and assess: *pain* (eg, location, duration, stiffness, etc)*; physical health* (a 20-item checklist of common medical conditions and any impact on work or personal life); *mental health* (an 8-item checklist of common psychiatric conditions based on a template used for physical health).

Other health-related parameters

BMI: height will be recorded at baseline and weight will be recorded at baseline, postintervention, 6 and 24 months to allow estimation of BMI at these time points.

Alcohol use disorders identification test-consumption (AUDIT-C)[46]: the AUDIT-C scale comprises three items and will be used to assess the frequency and quantity of alcohol consumption at all assessment points.

Physical activity: will be measured using six items (from the HUNT study) that assess frequency, intensity and duration of the activity.

Additional measures related to exploratory analyses or subsidiary projects

Engagement with and acceptability of interventions

The acceptability of online interventions after completion of the programmes. The latter will be assessed using the *internet intervention evaluation,*[30] which comprises two questionnaires used in SHUTi research: the *Internet Intervention Utility Questionnaire* and the *Internet Intervention Impact Questionnaire.*

Self-report ratings will record participants' familiarity with use of the internet at baseline and their *electronic media use*[47] (five items) over time. These ratings will be used in subsidiary analyses as for example, baseline skills in using the internet may affect engagement with internet interventions and whether electronic media use changes post-treatment.

Views of internet treatment

To assess views regarding the interventions, we will ask participants to complete the Negative Effects Questionnaire (NEQ).[48] The NEQ is a self-report measure that contains 32 items that are scored on a five-point Likert-scale (0–4) and differentiates between negative effects that are attributed to psychological therapies and those possibly caused by other circumstances, as well as one open-ended question.

Use of sleep strategies questionnaire

A self-report questionnaire was developed in order to assess patients continued use of sleep strategies after the intervention. The questionnaire comprises six items assessing how much patients have used six different therapeutic techniques (kept a stable rise time, refrained from sleeping during daytime, used the bed and the bedroom only for sleeping, practised sleep restriction, got out of the bed when unable to fall asleep within 15–20 min and kept a sleep diary) and how useful each technique was. This will be administered at 24 months follow-up.

Potential moderators and mediators

We aim to undertake exploratory analyses of potential moderators (a moderator variable is one that influences the strength of a relationship between two other variables) and mediators (a mediator variable is one that explains the relationship between the two other variables) of the effects of CBT-I.[49] For example, some of the data collected on demographics, physical health and mental health can be used to examine psycho-bio-social factors that may moderate the impact of CBT-I. However, if feasible, we will also extend the exploratory analysis of moderators to include 'therapy-genetics'.

While pharmacogenetic studies are increasingly being undertaken in psychiatry, exploration of 'therapy-genetics' is a relatively novel area of research,[50] which aims to investigate the impact of specific genetic variants on differences in therapy outcome.[51] Heritability estimates for insomnia range from 30% to 45%[52 53] suggesting that genetic factors may partly explain individual differences

in the vulnerability to develop insomnia. We are seeking additional funding and ethical approval to undertake a subsidiary study to obtain (by post) a single salivary sample at 24 months from participants who provide specific written informed consent. If this subsidiary project will be implemented, we would aim to examine whether selected genotypes (which we demonstrated to be associated with insomnia in the HUNT study) are associated with larger improvements in insomnia symptoms following CBT-I (boosting effect) compared with other genotypes (including several single nucleotide polymorphisms).

As noted in the descriptions of measures, exploratory analyses of mediators of CBT-I will focus on data from the sleep diaries[32] and the DBAS-16.[38]

Sample size

The primary outcome is the difference in the change in ISI score from preintervention to postintervention according to group using an intent-to-treat (ITT) analysis. Findings from previous publications[22 24] indicate large effect size (ES) differences even for comparisons between CBT-I and active control interventions such as PE (Cohen's d>0.8). As such, we estimated that a sample size of approximately 486 participants would be sufficient to detect a moderate-to-large ES for the difference in the ISI score, at p<0.05 and with 80% statistical power. Importantly, this estimate takes into account a predicted attrition rate of 50%[22 24] and allows for missing data (which is often higher in studies undertaken online and/or reliant on self-report assessments). Also, this sample size allows us to detect significant ES differences for all secondary analyses undertaken at each follow-up point, including smaller effects (d~0.3 to 0.5) for selected variables (eg, HADS score), etc.

The larger sample size (n=1500) was selected because our goal is to have sufficient statistical power (80%) to detect significant differences (p<0.05) in rates of sick leave and health resource use. Guidance is limited regarding sample size estimates for these additional analyses but, for example, we noted in a previous study by our research team that about 12% of patients diagnosed with insomnia at a sleep clinic in Norway are on sick leave.[54] If we assume a similar prevalence of sick leave in the current study and predict an overall reduction in the prevalence of sick leave of 50% in the CBT-I group (from n=90 to 45) and of 30% in the PE group (from n=90 to 63) by 24 months follow-up, then a sample size of 1500 will allow detection of a significant between-group difference (OR 1.7; 95% CI 1.01. to 2.79). Furthermore, even though the data recorded in national registries are unlikely to be subject to loss over time, we have allowed for 10% missing data (which would reduce the estimate OR 1.5), for example, due to failure to provide or accurately record social security number or difficulty in tracking personal information.

Given the exploratory nature of the moderator and mediator analyses and the lack of similar relevant studies in the literature, we did not undertake a sample size or statistical power calculation for these analyses. However, we note that the current sample exceeds the size of other completed or proposed mediator and moderator analyses of therapies.

Data analysis plan

Outcome data will be released for analysis on three occasions: after the total sample has completed the postintervention assessments, and again after the total sample has completed the 12-month and 24-month follow-ups, respectively.

We plan to use a linear mixed model analysis to examine the primary outcome of change in ISI score between baseline and postintervention assessment, and to analyse secondary outcomes of the preintervention to postintervention change in other sleep and health measures. A mixed-model analysis (without constraints on the covariance structure) uses maximum likelihood estimation and is robust in the face of the predicted loss of data. The first publication will focus on the ITT analyses, but may be accompanied by selected per-protocol analyses (if these provide a more direct comparison of our findings with others reported in the literature) and with preliminary findings regarding the acceptability of internet interventions. The results from the mixed-model analyses (estimated means and their SEs) will be used to calculate within-group and between-group preintervention to postintervention ES (Cohen's d with 95% CIs) according to published recommendations.[55 56] The same approach will be used for the planned analyses of self-report data obtained at 6-month and 24-month follow-ups.

The main analysis of data regarding sick leave will examine time off work as a categorical variable (prevalence of sick leave per group) with findings reported using X^2 and Fischer's exact tests and ORs. However, number of days off sick will be assessed as a continuous variable and comparisons will include a mirror image study using t-tests to compare total days off per annum in the 12 (and then 24) months time period before and after randomisation according to group. Similar univariate and multivariate approaches will be used to analyse objective data regarding other health resource utilisation such as number of outpatient contacts, or of different classes of medication prescribed per group. Lastly, if the available data on sick leave meets requirements for complex survival analyses (eg, Weibull proportional hazards model), we will consider modelling time to return to work (from sick leave) and/or time before taking sick leave according to group allocation.

Mediator and moderator analyses are exploratory, but both will follow the basic principle outlined by Kraemer et al.[57] For example, we will explore whether change in level of DBAS-16 or variability in sleep patterns are potential mediators of outcome for CBT-I. Likewise, we will examine whether demographics (eg, age, sex), or co-occurring health conditions, are moderators of the effect of CBT-I. Other subsidiary analyses will be reported separately at a later date.

Ethics and dissemination

All participants are required to provide informed consent before allocation to the online intervention programmes. The recruitment and consent process explain that participation is voluntary; individuals can withdraw from the study at any time point without any consequences (eg, regarding their care or treatment) and access to the intervention programmes is independent of completion of follow-up self-ratings. Self-report data are recorded in electronic files that are encrypted and password protected. No identifying information is stored alongside the self-report data. Furthermore, only researchers directly involved in data analysis will be granted supervised access to de-identified participant data.

The RCT findings will be disseminated in peer-reviewed publications and conference presentations. We expect to publish the findings regarding between-group differences in insomnia severity and daytime functioning at postintervention, followed by an analysis of outcomes from later follow-ups. Findings from the analyses of data on sick leave and resource use will be published separately. Preliminary findings on putative mediators and moderators of online CBT-I will be submitted only after the main outcome papers are published. User-friendly summaries of the findings and implications will be produced and disseminated to relevant patient-advocacy and other organisations.

The genotyping will be undertaken following ethical approval and adequate funding for postal collection of saliva samples.

PATIENT AND PUBLIC INVOLVEMENT

The 'Regionalt brukerutvalg, Helse Midt-Norge' (patient user group for Central Norway Health Trust) were consulted regarding the original study outline (as submitted for funding) and provided feedback on the aims of the trial, the study design (eg, the assessment package and online screening procedure) and provided their endorsement for the protocol described in this manuscript. The findings of the study will be disseminated via academics, and by patient advocacy and other relevant public and community groups.

DISCUSSION

A major advantage of the RCT is that it provides eligible participants with direct access to online interventions that they can undertake without requiring clinical input or support. Ease of access and online recruitment enable us to draw on a national population and to recruit a larger sample size than most previous studies. However, it is possible that the sample recruitment may be biased in ways that are difficult to measure, for example, the RCT participants may be biased towards those who are reluctant to seek help from healthcare professionals, those with intractable problems or those with multiple physical and mental comorbidities. Alternatively, if the sample comprises those with lower levels of impairment, the study may be underpowered to assess changes in resource utilisation, such as sick leave.

If CBT-I is shown to be statistically significantly more effective in the short- term and medium-term compared with PE, this may encourage its wider dissemination and utilisation within healthcare settings. As a minimum, it might be offered to individuals on waiting lists for face-to-face therapy or online CBT-I could be recommended alongside other interventions provided by healthcare professionals. These initiatives would all help to increase the total number of individuals who could receive effective care.

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