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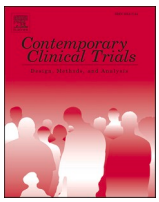

Protocol of a randomized controlled trial into guided internet-delivered cognitive behavioral therapy for insomnia in autistic adults (i-Sleep Autism)

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ABSTRACT

Background: Sleep problems, especially insomnia, are prevalent among autistic adults, affecting about 60 %, and significantly impact their quality of life. Internet-based cognitive behavioral therapy for insomnia (iCBT-I) could provide accessible and scalable treatment. Given the unique sensory- and information processing, and social challenges at play in autism, a tailored treatment approach may be essential to tackle sleep problems. Yet, interventions developed and tested specifically for autistic adults were scarce. Addressing this gap is crucial to meet the urgent need for effective insomnia treatments in this population.

Methods: With this two-arm, parallel, superiority randomized controlled trial, we will assess the effectiveness of a guided iCBT-I intervention for adults ($N = 160$) with autism and insomnia (i-Sleep Autism). In co-creation, i-Sleep Autism has been adjusted from an existing intervention (i-Sleep). Inclusion criteria are: age ≥ 18, an ASD diagnosis, and at least sub-threshold insomnia (Insomnia Severity Index ≥ 10). Participants are randomly assigned to either i-Sleep Autism or an information only waitlist control condition (online psychoeducation and sleep hygiene). After 6 weeks, the control group receives the intervention. Insomnia severity is the primary outcome. Secondary outcomes include pre-sleep arousal, general mental health, depression, anxiety, daily functioning, and quality of life. Assessments will occur at baseline, mid-intervention (3 weeks), post-intervention (6 weeks), and at 6-month follow-up (the intervention group). Linear mixed-effect regression models are employed to evaluate the effectiveness of i-Sleep Autism, alongside exploration of potential moderators and mediators.

Conclusion: This trial can reveal whether autistic adults with insomnia benefit from a guided e-health intervention.

Trial registration: NL-OMON56692.

1. Introduction

Autism Spectrum Disorder (ASD), hereafter 'autism', presents a profound and lifelong challenge, affecting approximately 1 % of the global population [1]. Sleeping problems, including insomnia symptoms and poor sleep quality, are among the most common complaints of adults with autism, with prevalence rates reported as high as 89 % [2–4]. These sleep problems may manifest in childhood, and often persist into adolescence and adulthood [5]. Compared to non-autistic adults, adults with autism face significantly more impairments in the majority of subjective and objective sleep parameters, including lower sleep efficiency (SE), longer sleep onset latency (SOL), and wake after

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sleep onset (WASO) [6]. Insomnia symptoms are among the most frequently reported sleep problems of adults with autism, with an estimated prevalence of about 60 % [7–9]. Insomnia can be defined as patient-reported complaints of difficulties falling asleep or maintaining sleep, in the form of frequent awakenings, difficulty returning to sleep after awakenings, or awakening too early with inability to return to sleep [10]. Sleeping problems are significantly associated with more clinical symptomatology of autism, worse daytime functioning [11], and lower quality of life of autistic adults [12,13]. Despite the magnitude of this issue, there is a lack of treatments adequately addressing and treating sleeping problems in the autistic population.

Poorer physical health (e.g., gastrointestinal problems), self-reported anxiety symptoms, unemployment, and female sex at birth, are found to be important predictors of all aspects of sleep problems in autistic adults [14–16]. Furthermore, studies are hinting at an association between sensory processing issues and sleep problems at play in autism [17]. For example, sensory hyper-reactivity could lead to bright light avoidance, affecting photoperiodic input to the circadian rhythm [18]. Given the unique social- and communication factors and preferences of autistic individuals, an adjusted treatment approach in collaboration with autistic individuals themselves is needed. In this randomized controlled trial, we will investigate the effectiveness of i-Sleep Autism, a guided, internet-delivered, cognitive behavioral intervention for insomnia that has been adapted from an existing intervention (i-Sleep) in co-creation.

Across all adult populations, including those with autism, Cognitive Behavioral Therapy for Insomnia (CBT-I) is the first choice recommendation for treatment of chronic insomnia, in which symptoms persist more than 3 months [19–21]. CBT-I is designed to break patterns of maladaptive thinking and behavior that are common in insomnia. CBT-I commonly consists of a combination of psychoeducation on sleep, advice on sleep hygiene, relaxation training, stimulus control, sleep restriction and cognitive therapy [19–21]. A large body of evidence in the general population has shown that CBT-I interventions can reduce insomnia severity with moderate to large effects (Hedges g' for Insomnia Severity Index, $g = 0.82$) [22,23]. In addition, CBT-I can improve mental health outcomes (including anxiety and depression) [24], and sleep-related quality of life [25], up to a year after therapy [26]. Yet, CBT-I (based) interventions for autistic adults are scarcely investigated [27], with only one pilot study ($n = 10$) investigating a CBT-based group treatment for sleep-wake rhythm disturbances in adults with autism and/or ADHD [28]. Sleep disturbances improved significantly from pre- to post-intervention, depression and anxiety symptoms remained unchanged. Another pilot study with eight autistic adults found that an acceptance and commitment therapy group insomnia intervention, a third-wave therapy, was efficacious in improving insomnia and anxiety symptoms [29].

Similar to the general population, few autistic individuals seek help for their sleeping problems [30–32]. Moreover, those who seek care are often prescribed psychopharmacological therapies, whilst evidence for such therapies is limited [33]. Most autistic adults prefer non-medication options such as education, advice and talking therapies for the treatment of their insomnia [30]. These findings underscore the importance of developing interventions that have a greater reach than those currently available and take into account the preferences of autistic adults themselves [30].

One promising way to enhance the reach and accessibility of treatment in autistic adults, is to employ e-health. E-health interventions have become increasingly popular in the autistic population during the last years [34], particularly in the age of the COVID-19 pandemic [35]. General advantages of e-health programs are their easy accessibility, and their ability to be completed at the participant's own pace [35]. Internet delivered CBT-I (iCBT-I) has also been shown to be more cost-effective when compared to face-to-face CBT-I [36]. For autistic individuals specifically, e-health interventions facilitate autonomy [37], are predictable and structured in nature [38], and they bring along less sensory sensitivity difficulties than regular face to face care [39,40]. However, it's important to note that not all autistic adults find telehealth suitable or satisfactory, especially those with high psychological distress or intellectual disability [41]. Despite its increase in popularity, most digital supports available to the autistic community have little or no evidence to support their effectiveness [42].

In other adult populations, internet-delivered CBT-I interventions, particularly guided ones, have been shown to be effective in the treatment of insomnia ($g = 0.68–1.09$), with effects comparable to face-to-face CBT-I, generally maintained at follow-ups ranging from 4 to 48 weeks [22,26,36,43]. Yet, research on online psychological sleep interventions, including CBT-I, in autistic individuals is very limited, and has primarily focused on youth populations [27,44,45]. In a recent pilot study in autistic adolescents, iCBT-I was perceived positively across all participants, and a large preliminary effectiveness on sleep diary parameters was observed [45]. Another recent pilot study in children with autism showed that telehealth CBT-I could improve child and parent sleep, child behavior and arousal, and parent fatigue [44]. No studies on (guided) iCBT-I interventions in autistic adults are known to us.

In summary, there is a significant gap in the research on sleep interventions for autistic adults, with minimal studies on CBT-I, E-Health interventions, or any psychological sleep treatments for this population. Given the high prevalence of sleep problems in autistic individuals and the limited evidence on effective interventions, addressing this need is crucial.

2. Objectives

We employed co-creation to tailor i-Sleep, an evidence-based iCBT-I intervention for insomnia [46], to meet the needs of autistic adults. This has resulted in i-Sleep Autism, an online guided self-help insomnia intervention for autistic adults. The primary objective of this randomized controlled trial is to evaluate the effectiveness of i-Sleep Autism in reducing insomnia severity among adults with autism. Additionally, we seek to assess its impact on pre-sleep arousal, mental health (including depression, anxiety, and broader aspects of wellbeing such as self-image), daily functioning, and overall quality of life. We will investigate the sustainability of treatment effects at a 6-month follow-up. Finally, we aim to explore potential moderators (e.g., baseline symptom severity, duration of insomnia) of the intervention effect and predictors of treatment outcomes.

3. Methods

3.1. Study design

This study will be a two-arm, parallel group, superiority randomized controlled trial with repeated measurements, comparing a guided e-health CBT-I intervention for insomnia with a minimally active waitlist control condition with psychoeducation (PE) on sleep and sleep hygiene. Participants will be randomized to either condition in 1:1 ratio. After the intervention period has ended (6 weeks), the control group will also receive access to i-Sleep Autism if desired. This study was approved by the Medical Ethical Committee of the Amsterdam University Medical Centre (METC Amsterdam UMC) and registered at Overview of Medical Research in the Netherlands (OMON) (NL-OMON56692). See Fig. 1 for the study flow.

3.2. Participants

Autistic adults are eligible for the study when they are at least 18 years of age, experience clinically relevant insomnia symptoms (ISI $\geq$10 [47]), are able to read and write in Dutch language, and have a formal clinical diagnosis of Autism Spectrum Disorder (ASD) as established by an authorized professional. Participants must possess a desktop, laptop, tablet or mobile phone with internet connectivity. Exclusion criteria are: working in night shifts (work between 2 AM and 6 AM), and current or

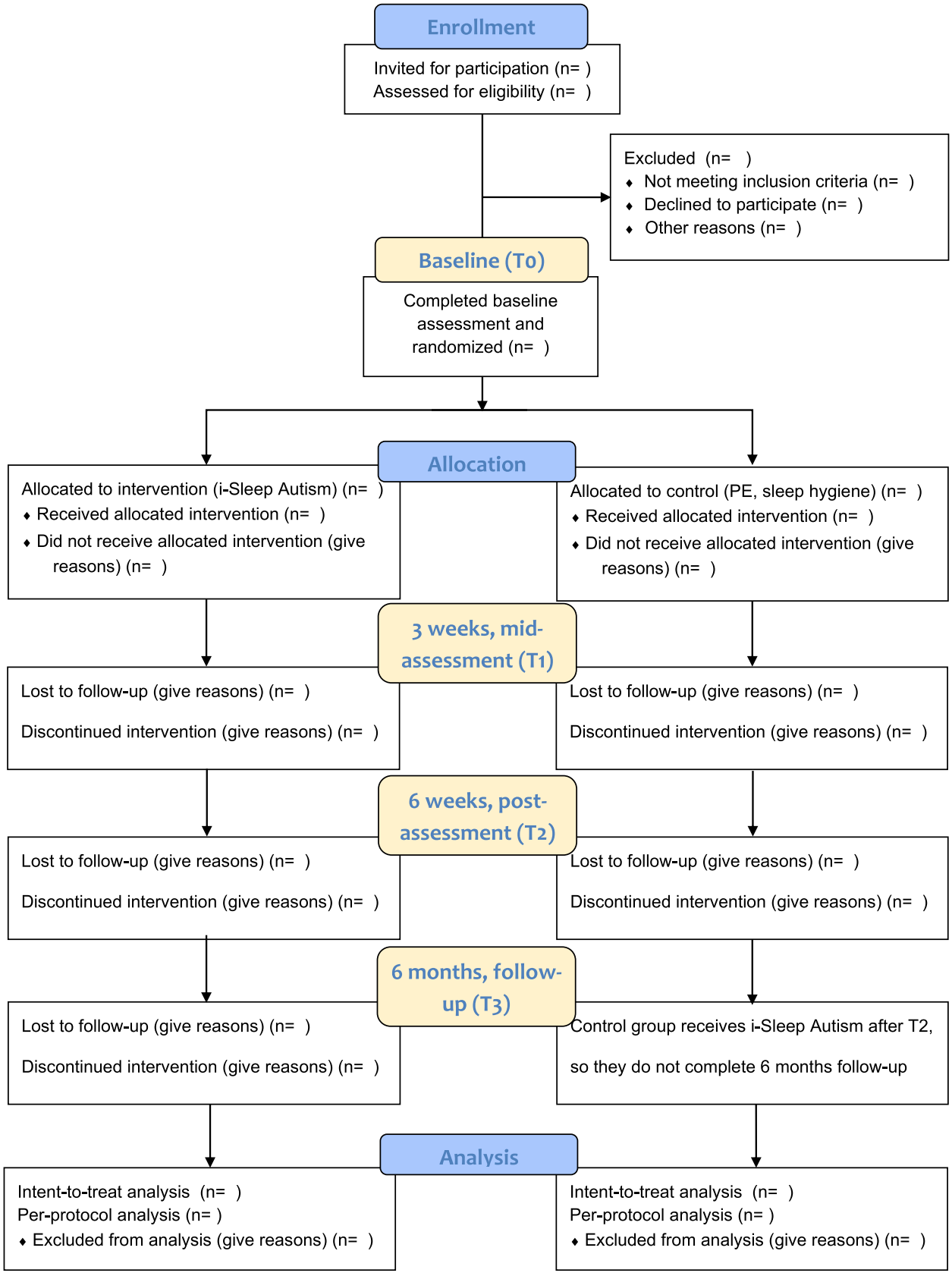

Fig. 1. CONSORT Flowchart diagram.

planned pregnancy or breast feeding. Other co-occurring psychological disorders and somatic diseases among eligible participants are not excluded, given the high prevalence rates of co-occurring conditions (81 %) in autistic individuals [48] and the potential of CBT-I to alleviate co-occurring mental health problems [24,49]. Similarly, co-occurring sleep disorders or symptoms are no exclusion criteria since previous studies have shown that CBT-I can be effective in treating insomnia when other disorders are present [50–52]. The use of (sleep) medication is also allowed and monitored, as is the use of cannabis.

3.3. Recruitment

Participants are recruited from the Netherlands Autism Register (NAR), which encompasses over 3500 individuals diagnosed with autism in the Netherlands (www.nar.vu.nl). The NAR includes three study populations: self-reporting autistic adults, parents reporting on their autistic children, and parents or legal representatives of autistic adults. Recruitment methods for the NAR include outreach through the Dutch Association for Autism (NVA), autism conferences, social media, and referrals from psychologists.

For this trial, we will recruit from the self-reporting adult population (80 % of total population) in batches of 50–150 invites randomly drawn from the cohort until reaching our target enrollment of 160 participants. Potential participants receive detailed study information, including an information letter and explanatory video included, via the invitation email, which also contains a link to a digital informed consent form in Qualtrics. We recommend a minimum reflection period of one week before signing consent.

When interested, participants complete the digital consent form and proceed to an online questionnaire including screening questions. For those ineligible, the questionnaire ends after the screening questions. They receive notification of their ineligibility along with information on alternative resources for their sleep issues. Eligible participants continue to the full baseline assessment before randomization.

3.4. Randomization, blinding and treatment allocation

After completing the T0 baseline assessments, participants are randomized to either the intervention or control condition. A built-in randomizer of Qualtrics randomly assigns participants to either condition, whilst ensuring equal group sizes with use of blocks. Participants will then be automatically allocated to the assigned condition. Blinding of study participants is not possible due to the nature of the intervention. The researcher responsible for the analysis will be blinded for the study condition of participants.

3.5. Procedures

Participants who are randomized to the intervention group will receive an e-mail invite to activate their personal account at Minddistrict, an e-health platform for health care organizations to provide digitally enabled therapy to their patients in the Netherlands (https://www.minddistrict.com/). The intervention group follows the guided i-Sleep Autism intervention, and the control group receives online PE and sleep hygiene. After 3 weeks, participants in both groups fill out a brief questionnaire (T1). After 6 weeks, both groups receive the T2 questionnaire, with additional questions for the intervention group. After T2, the control group can start with i-Sleep Autism if desired. Only

Table 1
Overview of enrolment, interventions, assessments and timepoints for study participants.

	STUDY PERIOD			
	Enrolment, Allocation	Post-allocation		Follow-up**
TIMEPOINT	**T0 Week 0**	**T1 Week 3**	**T2 Week 6**	**T3 Month 6**
ENROLMENT				
Informed consent	X			
Eligibility screen	X			
INTERVENTIONS				
i-Sleep Autism	←	→		
Control: PE & sleep hygiene	←	→		
ASSESSMENTS				
Demographics	X*			
ISI	X	X	X	X**
Insomnia duration	X			
PSAS	X		X	X**
HADS	X		X	X**
WSAS	X		X	X**
MHQoL	X		X	X**
Stressful life events	X	X	X	X**
Adverse events	X	X	X	X**
CSQ-8			X**	
WAI-SR			X**	
WAI-TECH-SF			X**	
Care and medication use	X		X	X**
AUDIT-10	X			
DAST	X			
Total nr. of items assessed	80	10	57–86***	57
Estimation of minutes	15–20	2–3	10–20	10–15

Note. ISI = Insomnia Severity Index [23], PSAS = Pre-Sleep Arousal Scale [53], HADS = Hospital Anxiety and Depression Scale [54], WSAS = Work and Social Adjustment Scale [55], MHQoL = Mental Health Quality of Life Questionnaire [56], CSQ-8 = Client Satisfaction Questionnaire [57], WAI-SR = Working Alliance Inventory – Short Revised [58], WAI-TECH-SF = Working Alliance and Technical Alliance Short Form [59], AUDIT-10 = Alcohol Use Disorder Identification Test [60], DAST = Drug Abuse Screening Test [61].

* These variables will be derived from the annual NAR measurement that has taken place in February and March of 2024.

** Only assessed in the intervention group.

*** Control group receives 57 questions, intervention group 86.

the intervention group is assessed after 6 months (T3). See Table 1 for an overview of the assessments, the number of included items, and the estimated duration of each assessment.

3.6. Intervention

3.6.1. Intervention condition

3.6.1.1. Intervention set up. The intervention group undergoes a 5-week i-Sleep Autism program, a guided digital self-help intervention based on CBTi principles and adapted from 'i-Sleep' [46] for autistic adults. i-Sleep Autism includes five online sessions integrating evidence-based elements of face-to-face CBTi. Each session features self-help materials such as texts, question boxes, exercises, and audiovisual components (e.g., case examples, summary videos, relaxation audios). The sessions cover: 1) psychoeducation on normal sleep, sleep disorders, sleep hygiene, and light exposure, 2) sleep restriction (limiting time in bed to enhance sleep pressure) and stimulus control (strengthening the bed's association with sleep), 3) techniques for managing rumination and promoting relaxation, 4) cognitive restructuring (altering common misconceptions about sleep), and 5) strategies for preventing relapse.

Participants are recommended to allocate 30 to 60 min per week to complete each module, ideally one module per week. In addition to this weekly commitment, participants will be encouraged to integrate exercises and cognitive-behavioral strategies into their daily routines, requiring daily effort. Participants will complete a daily online sleep diary during the intervention period (about 2 min), for self-monitoring and monitoring by coaches (see 3.6.1.3) with regards to progress and sleep habits. Daily reminders for the sleep diary are optional. The entire i-Sleep Autism intervention spans approximately 5 weeks.

3.6.1.2. Adaptation process. The adaptation process involved collaboration with autistic adults experiencing insomnia and healthcare professionals specializing in sleep disorders among autistic individuals. We conducted in-depth interviews with three healthcare professionals and established a panel of seven autistic individuals with insomnia (6 females, 1 male, aged 24 to 57, varying educational backgrounds). This panel provided feedback through evaluation forms, emails, and focus groups to refine the intervention.

Using this collective input, we adapted the text to match the situation of autistic individuals (e.g., psychoeducation on insomnia in autism specifically), put extra emphasis on certain elements that were deemed important (e.g., light exposure, day time relaxation, bed time rituals), we adapted the style of language and formulation of the text and exercises (e.g., clearer, informative rather than directive instructions, more concrete examples), and we replaced the current case examples with examples fitting to the life of people with autism, including unemployment, enhanced sensory sensitivities, and social difficulties. These case examples are integrated into each session, facilitating recognition, enabling the sense of simultaneous progress, and providing practical tips.

3.6.1.3. Guidance by coaches. Each participant is supported by a coach who provides asynchronous written feedback after each session to enhance motivation and adherence. Coaches, who are clinical psychology students, undergo approximately 15 h of training supervised by a licensed psychologist. Training includes studying a coaching protocol, an e-learning module on CBT-I, a live session covering autism, CBT-I, and online coaching, and ongoing supervision during the intervention. Training emphasizes effective communication and support tailored to autistic participants.

Coaches deliver feedback via the secured Minddistrict platform within three working days or on a fixed weekday per participant preference. Personal reminders are sent to participants inactive for over two weeks. Coaching concludes eight weeks after registration, with ongoing access to the intervention website for six months. In cases of adverse events or crises (e.g., suicidal ideation), coaches promptly report to the team. A licensed psychologist assesses and refers participants to appropriate healthcare professionals as needed.

3.6.2. Control condition

Participants in the waitlist control condition receive online psychoeducation and sleep hygiene. This is based on the psychoeducation and sleep hygiene that is provided in the first session of i-Sleep Autism, and thus it is also autism-adapted, but less extensive and does not contain exercises or interactive components. For six weeks, they will not have access to the i-Sleep Autism intervention, nor will they be coupled with a coach. After the post-test assessments, control participants will receive access to the guided i-Sleep Autism intervention, if desired.

3.7. Outcome measures

3.7.1. Primary outcome measure

3.7.1.1. Insomnia severity index – 7 items (ISI). The ISI will be used to assess our primary outcome insomnia severity [23]. Comprising 7 items rated on a 5-point Likert scale (0 = not at all, 4 = extremely), the ISI yields scores ranging from 0 to 28, where higher scores denote more pronounced insomnia symptoms. A score of 0–7 indicates no clinically significant insomnia, 8–14 means subthreshold insomnia, 15–21 is clinical insomnia with moderate severity, and 22–28 indicates severe clinical insomnia. The ISI exhibits robust psychometric properties ($\alpha = 0.90$) [47]. Importantly, the ISI has undergone validation for online applications [62]. A 6-point reduction is considered a clinically meaningful improvement [63].

3.7.2. Secondary outcome measures

3.7.2.1. Mental health and (daily) functioning

3.7.2.1.1. Pre-sleep arousal scale (PSAS). The 16-item PSAS measures symptoms of cognitive and somatic arousal experienced at bedtime [53]. The items are scored on a 5-point Likert scale, with higher scores reflecting more arousal. The sum of scores of the first 8 items measures somatic pre-sleep arousal (PSAS-somatic), and the last 8 item scores-cognitive pre-sleep arousal (PSAS-cognitive). The clinically relevant cut-off scores reported for PSAS-somatic and PSAS-cognitive are $\geq$14 and $\geq$ 20, respectively. The PSAS is a commonly used scale with appropriate psychometric properties [53]. The scale has also shown good internal reliability in an autistic sample for the cognitive and somatic subscales survey, respectively (Cronbach's $\alpha = 0.89$ and Cronbach's $\alpha = 0.81$) [64].

3.7.2.1.2. Hospital anxiety and depression scale (HADS). The HADS will be used to assess anxiety and depression [54]. The scale comprises 14 items, with seven items dedicated to each subscale. Each item is scored on a 4-point Likert scale (0–3), resulting in separate scores for anxiety and depression, with higher scores indicating greater symptom severity. Scores for each subscale can range from 0 to 21, with the following cut-off points: 0–7 (Normal), 8–10 (Mild), 11–15 (Moderate), and 16–21 (Severe). Reliability analyses have demonstrated the robustness of the HADS as an instrument for assessing psychological distress in autistic individuals (Anxiety: Cronbach's α = 0.82–0.84; Depression: Cronbach's α = 0.60–0.72) [65].

3.7.2.1.3. Work and social adjustment scale (WSAS). The WSAS will be used to evaluate functional impairment in various life domains due to mental health issues [55]. It consists of five items that assess the impact of mental health symptoms on work, social leisure activities, private leisure activities, home management, and the ability to form and maintain close relationships. Each item is rated on a 9-point Likert scale, with higher scores indicating greater impairment. The psychometric properties of the WSAS have been well-established, demonstrating good

reliability and validity. The scale has good internal consistency in measuring functional impairment (Cronbach's coefficient of $\alpha = 0.82$) [55].

3.7.2.1.4. Mental health quality of life questionnaire (MHQoL). The MHQoL assesses mental health and quality of life, and is designed to be specifically sensitive to identify the effects of mental health interventions [56]. The MHQoL comprises seven items encompassing self-image, independence, mood, relationships, daily activities, physical health, and future. Next to these seven items, the MHQoL also includes a general visual analogue scale (VAS) for overall quality of life. The MHQoL yield scores ranging from 0 to 21, where higher scores denote better quality of life. The VAS ranges from 0 to 10, where higher scores denote higher psychological wellbeing. The MHQoL has demonstrated strong internal consistency (Cronbach's $\alpha = 0.85$) [56].

3.7.3. Adherence, satisfaction, working- and technical alliance

3.7.3.1. Client satisfaction questionnaire (CSQ-8). The CSQ-8 measures client's satisfaction with the intervention [57]. It comprises eight 4-point Likert-scale items, offering response choices ranging from 1 to 4 [57]. Items 2, 4, 5, and 8 are reverse scored. Total scores range from 8 to 32, with higher scores corresponding to increased client satisfaction [57]. The CSQ-I demonstrates good internal consistency, factorial structure, and construct validity as an instrument (McDonald omega of 0.93–0.95) [66].

3.7.3.2. Working alliance inventory – short revised (WAI-SR). The WAI-SR will be used to assess the therapeutic alliance (TA) between participants and their coaches [58]. It comprises 12 items scored on a 5-point Likert scale, focusing on three key aspects of therapeutic alliance: agreement on tasks, agreement on goals, and the development of an affective bond between client and therapist. Each domain can have scores ranging from 5 to 20, with higher scores indicating higher therapeutic alliance. Its psychometric properties demonstrate good reliability (alpha >0.8) and convergent validity ($r > 0.64$), making it a valuable instrument for assessing the quality of the therapeutic relationship in short-term therapy contexts [67].

3.7.3.3. Working alliance and technical alliance short form (WAI-TECH-SF). The 12-item WAI-TECH-SF is a modified version of the WAI-SF, that assesses TA between clients and the online program [59]. Respondents use a seven-point Likert scale, ranging from 1 (never) to 7 (always), to rate their responses. The total score ranges from 12 to 84 [59]. The questionnaire maintains the same structural dimensions as the original scale, encompassing therapeutic goals (items 1, 2, 8, 10), tasks (items 4, 6, 10, 11), and bonds (items 3, 5, 7, 9). The scale has excellent reliability (Cronbach's $\alpha = 0.97$) [59].

3.7.4. Participant characteristics

Demographic variables, such as age, gender, years of education, marital status, living arrangements, and co-occurring conditions/diagnoses will be derived from the Netherlands Autism Register database and most recent annual survey (conducted in spring 2024), to decrease the length of the study assessments. All participants of the NAR have signed informed consent for utilization of their data for research.

Since these variables are important for sleep outcomes, we will gather (descriptive) data on alcohol and drug usage at baseline (T0) with use of the Alcohol Use Disorders Identification Test (AUDIT-10) and the Drug Abuse Screening Test (DAST) [60,61]. Data on insomnia duration is collected in years and months. Lastly, the type and frequency of healthcare and sleep medication use during the study are assessed in both study arms.

3.7.5. Stressful life- and adverse events

We will assess stressful life events (e.g., divorce or breakup, moving, physical/sexual violence), and life-threatening or serious accidents or illness at T0, T1, T2, and T3. Furthermore, adverse events possibly related to the application of sleep restriction will be assessed at T1, T2, and T3, encompassing queries about 1) falling accidents, 2) traffic accidents, or 3) any other incidents linked to fatigue or sleepiness and their consequences.

3.8. Power and sample size calculation

We opt for an effect size of Cohen's $d = 0.50$ on the primary outcome insomnia severity at the post-intervention measurement, which is more conservative than average effect sizes of previous meta-analyses [22,43]. To ensure 80 % statistical power with a 2-sided α-value of 0.05, we estimate that a total number of 128 participants (64 per group) is needed to detect a medium effect size of $d = 0.50$. We anticipate a 20 % risk of dropout, based on previous studies [22]. Therefore, we aim to recruit a total number of 160 participants (80 per study arm).

3.9. Statistical analyses

All statistical analyses will be carried out using SPSS version 27 and the R statistical programming package. A two-tailed significance level of $\alpha = 0.05$ will be applied. Both primary and secondary endpoints are continuous. Analyses will adhere to the intention-to-treat approach, analysing all participants as originally randomized, irrespective of actual treatment or study completion. Furthermore, a per-protocol analysis will be conducted for participants who completed the post-intervention and follow-up assessments, and this analysis will be segregated for those who completed session 1 to 4.

Linear mixed models will be utilized to assess the primary outcome, change in ISI score from baseline to post-test assessment, considering time effects and time-group interactions. These models acknowledge the hierarchical nesting of observations within participants. Group allocation is featured as the independent variable, and insomnia severity (ISI) as the dependent variable. At post-treatment, we will determine the Cohen's d effect size by dividing the difference between the mean insomnia severity scores of the intervention and control group at post-treatment by the pooled standard deviation.

Linear mixed models are employed to analyze our secondary outcomes as well. Exploratively, we will examine baseline insomnia severity, duration of insomnia (in years), and other co-occurring conditions as potential moderators of effect of the intervention on insomnia severity, following the principles by HC Kraemer, GT Wilson, CG Fairburn and WS Agras [68].

4. Conclusion

This parallel, superiority randomized controlled trial will assess the effectiveness of i-Sleep Autism, a guided iCBT-I treatment for adults with autism and insomnia. To our knowledge, this is the first internet-delivered CBT-I intervention to be empirically tested in this population. The strengths of our study lie in its robust design, large sample size, and our focus on co-creation in the tailoring of the i-Sleep Autism intervention. Beyond its impact on sleep outcomes, our trial includes outcome measures that reflect a broader representation of wellbeing.

Our trial aims to contribute to the scarce array of internet-delivered interventions that currently exist for autistic adults. Empirically testing and evaluating i-Sleep Autism will allow us to refine and improve treatment of sleeping problems of autistic individuals. If proven effective and replicated by further studies, i-Sleep Autism could potentially be implemented as standalone intervention, as augmentation of regular treatment, or serve as waiting time support for autistic individuals waiting to receive (specialized) mental health care.

This trial can be of value for clinicians working with autistic adults who suffer from sleep problems, and for those designing e-health or in-person (CBT-I) interventions for this population. Ultimately, the

outcomes of this study hold promise for enhancing the broader-scale quality of life and well-being of adults with autism by addressing this critical, yet often overlooked, aspect of their (mental) healthcare needs.

Trial status

Recruitment has started at the end of May 2024, and stopped at the end of August 2024 due to reaching the target number of participants. Currently conducting assessments & providing the intervention.

Ethics approval and consent to participate

This study will be performed according to the principles of the Declaration of Helsinki (October 2013) and is in accordance with the Medical Research Involving Human Subjects Act (WMO).

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CRediT authorship contribution statement

Kirsten L. Spaargaren: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Conceptualization. **Sander M. Begeer:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. **Kirstin Greaves-Lord:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. **Heleen Riper:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Annemieke van Straten:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

All the authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data collected in this study will be available from the corresponding author upon reasonable request and after publication of findings.

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SB, AS, KGL, HR secured funding for the project. All authors were responsible for the design of the study. KS and AS co-developed the i-Sleep Autism intervention together with eight autistic adults. KS coordinated the trial, recruited participants together with SB, and communicated with participants. All authors critically read, contributed to, and approved the manuscript.

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