1. FULL TITLE

Implementation of a Digital Cognitive Behavioural Therapy Intervention for Insomnia in First Episode Psychosis in the Context of Covid-19: A Mixed Methods Study

2. TRIAL INFORMATION

Trial Identifiers

REC ID	280858
REC reference	21/WS/0010
Clinicaltrials.gov registration	TBC – will be registered
Protocol Version Number	5.1
Date	12.03.2021

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Study Synopsis:

Study Title	Implementation of a Digital Cognitive Behavioural Therapy Intervention for Insomnia in First Episode Psychosis in the Context of Covid-19: A Mixed Methods Study
Protocol Short Title/ Acronym:	Implementation of a digital Cognitive Behavioural Therapy intervention for Insomnia in a first episode of psychosis
Study Phase If Not Mentioned in Title	Implementation study
Sponsor Name	NHS Greater Glasgow and Clyde
Chief Investigator	Prof Andrew Gumley
Clinicaltrials.gov registration	TBC – in progress
REC Number	21/WS/0010
Medical Condition or Disease	Psychosis (first episode)
Purpose of Research	The aim of this project is to develop a logic model for the implementation of a digital Cognitive Behavioural Therapy for Insomnia, ‘Sleepio’, in people recovering from a first episode of psychosis. This implementation is placed in the context of Covid-19 restrictions and their aftermath.
Primary Objective	Development of a logic model

Secondary Objective(s)	i) Assess the implementation of Sleepio ii) Gather measures of symptomatology at baseline and post-intervention iii) Ascertain staff and service user expectations and experience of Sleepio
Study Design	Mixed methods implementation study
Endpoints	Saturation
Sample Size	~8 service users, <10 keyworkers
Summary of Eligibility Criteria (service users)	Inclusion: 1. Service users under the care of Esteem First Episode Psychosis Service in NHS GGC 2. Aged >=16yrs and ≤35 years (the service serves individuals between these ages) 3. Potentially affected by Insomnia Disorder (defined by SCI-02 score ≤2) 4. Access to a device to use Sleepio Exclusion: 1. Moderate to severe learning disability 2. Acute Psychosis (recent crisis contact or hospitalisation) 3. Incapacity to provide informed consent 4. Insufficient English to access intervention 5. Organic impairment 6. No access to a device to use Sleepio
Summary of Eligibility Criteria (staff)	Inclusion: 1. Holds position of Keyworker in Esteem First Episode Psychosis Service in NHS GGC
Intervention (Description, frequency, details of delivery)	Sleepio is a digital Cognitive Behavioural Therapy (CBT) application which is responsive to input data (Espie et al., 2012). It is composed of six 20-minute sessions presented by an animated therapist, which are unlocked weekly. It can be accessed via browser or iOS smartphone. Participants complete an initial assessment on a browser and chose a treatment goal, which drives personalisation. Sleepio's components are those common to CBTi interventions: i) psychoeducation on sleep hygiene and processes; ii) cognitive components including restructuring, mindfulness, positive imagery, paradoxical intention training (trying to stay awake), and resolving thoughts about one's day; and iii)

	behavioural components including sleep restriction, stimulus control, and relaxation techniques. Participants are prompted to complete planned sessions and enter sleep data. Sleepio's algorithm tailors ongoing intervention based on this data and information about participants' physical and mental health. Sleepio also provides access to online psychoeducation and a moderated user forum. Keyworkers will have access to the Sleepio online 'Sleep Clinic', which allows them to monitor their service users' use of the application and their reported sleep. Other users of the Sleep Clinic cannot see these individuals' data.
Comparator Intervention	N/A.
Maximum Duration of Treatment	10 weeks
Version and Date of Final Protocol	V5; 12.03.2021

3. ABSTRACT

Background: Covid-19 lockdown regulations impact negatively on sleep and mental health. These impacts disproportionately affect individuals with pre-existing mental health difficulties. Sleep disorders, particularly insomnia, are common in first episode psychosis (FEP) and are associated with increased symptomatology. Mood and worry mediate the relationship between sleep and psychosis symptomatology. Cognitive Behavioural Therapy is effective in treating insomnia (CBTi). Pilot research suggests that insomnia is a tractable clinical target in psychosis. Digital CBTi (dCBTi) reduces both insomnia and paranoia, offering a non-contact intervention during Covid-19 lockdown and its aftermath.

Aims: To inform the development of a logic model to support dCBTi (Sleepio) implementation in FEP services.

Methods: People experiencing a FEP and Insomnia will be eligible to access Sleepio. Usage data will be collated. Symptomatology measures will examine changes in service user psychosis, insomnia, and mood symptomatology, and Covid-19-related worry at baseline and post-intervention. Service users and keyworkers will be invited to participate in semi-structured interviews to elicit their views of Sleepio implementation. We will summarise implementation data and describe changes in psychosis, insomnia, mood, Covid-19-related worry, and the relationships between these. A framework analysis will be used to analyse themes arising from interviews.

Impact: We aim to develop a logic model to support future implementation of Sleepio in FEP services.

4. BACKGROUND AND RATIONALE

4.1 The Context of Covid-19

Following the emergence of severe acute respiratory syndrome Coronavirus 19 (Covid-19), UK governments introduced regulations in order to protect public health. In Scotland, the Health Protection (Coronavirus) (Restrictions) (Scotland) Regulations 2020 implemented measures to prevent, control and mitigate the spread of infection (Scottish Government, 2020a). These included requirements for individuals to have contact only with those in their household, stay 2 metres apart from others, and only leave home for approved reasons. Potentially infected individuals were required to quarantine. These regulations are planned to change in a phase-based approach in concordance with the prevalence of Covid-19 in the Scottish population. The Coronavirus Scotland Act amended the responsibilities of health and social care organisations to the populations they serve (Scottish Government, 2020b). The presence of Covid-19, quarantine, restrictions to normal life and impacts on health and social care provision bring challenges to population mental health.

4.2 Mental Health during Pandemic

Quarantine and physical distancing measures in response to pandemics impact on the psychological health of the population (Brooks et al., 2020; Hossain, Sultana & Purohit, 2020). Systematic reviews suggest regulations raise the incidence of insomnia, low mood, post-traumatic stress (PTSD), avoidance of other people and of illness symptoms (e.g. coughs or sneezes; Brooks et al., 2020; Hossain et al., 2020). Research emerging from the Covid-19 pandemic in China and Italy (both of which imposed population-wide quarantine) has found increased anxiety and depression symptoms, poor sleep quality, and general psychological distress (Casagrande et al., 2020; Yan & Huang, 2020). In China, the prevalence of insomnia has increased significantly during lockdown, to almost 1/3rd of those studied (Lin et al 2020). In Italy, anxiety, poor sleep, and psychological distress were together predictive of Covid-19-related PTSD symptomatology (Casagrande et al., 2020). Morrin and Carrier (2020) have suggested that there is a high rate of acute insomnia associated with Covid-19 in the general population, with a risk of an ongoing increase in the prevalence of chronic insomnia. In Scotland, Covid-19 is anticipated to reduce psychological wellbeing and increase sleep disorder, particularly in those with pre-existing mental health difficulties (Public Health Scotland, 2020). There is an opportunity and need for appropriate interventions, which can be delivered within the current context.

4.3 Pre-Existing Mental Health Conditions

Particular subpopulations are likely to be disproportionately affected by the psychological impacts of Covid-19; such as those who live in deprived areas, the elderly, people with disabilities, and people with pre-existing mental health conditions. Previous mental illness diagnosis, higher fear of infection, being a healthcare worker, loss of routine, and lack of supplies access are associated with worse psychological outcomes during pandemics (Brooks et al., 2020). Pre-existing mental health conditions have been shown to be a risk factor for poorer psychological outcomes during Covid-19 lockdown regulations specifically (Li et al., 2020). People recovering from a first episode of psychosis (FEP) are one such group. This population typically present with mental, physical and social comorbidities (Gates et al., 2015), which may further increase their vulnerability to distress (Wright, Steptoe and Fancourt, 2020).

4.4 Sleep Disorder in Psychosis

As above, several reviews suggest that pandemics and Covid-19 specifically impact on sleep, particularly in raising the incidence of insomnia (Brooks et al., 2020; Hossain et al., 2020; Casagrande et al., 2020; Yan & Huang, 2020). Sleep disorders are common in persons affected by psychosis outwith the context of a pandemic (Reeve, Sheaves & Freeman, 2015; Laskemoen et al., 2019). Common presentations include Insomnia (~50% Freeman et al., 2019; Laskemoen et al., 2019 Freeman et al., 2009; Palmese et al., 2011), Nightmare Disorder (~50%, Sheaves, Onwumere, Keen, Stahl, & Kuipers, 2015), Sleep Apnea (Sharafkhaneh et al., 2005) and Hypersomnia (~30% Laskemoen et al., 2019; Hawley et al., 2010). Sleep disorders are prevalent at early and first episode stages of psychosis (~80% have at least one Sleep Disorder, Davies et al., 2017; Ma et al., 2018; Reeve, Sheaves & Freeman, 2018a; Reeve et al., 2019b).

Insomnia Disorder is a clinically significant difficulty in initiating or maintaining sleep. Insomnia is the best recognised and most studied sleep disorder in people affected by psychosis. The estimated prevalence of insomnia in those experiencing a first episode of psychosis is ~50% (Reeve et al., 2015; Davies et al., 2017; Reeve, Sheaves & Freeman, 2018a). In this population, sleep disorder is highly comorbid, with most individuals experiencing three or more sleep disorders (Reeve et al., 2019).

4.5. Insomnia and Psychosis Symptomatology

Sleep disorder has been explored as a contributing and causal factor in experiences of psychosis (Harvey et al., 2011). In the general population, sleep disorder is related to psychosis-like experiences, such as auditory hallucinations (Koyanagi & Stickley, 2015). In people affected by psychosis, severity of sleep disorder is related to flattened affect,

increased hallucinations, cognitive disorganisation, and paranoia, and poor clinical outcomes (Afonso et al., 2014; Taylor et al., 2015; Davies et al., 2017; Hou et al., 2017; Kilicaslan et al., 2017; Li et al., 2017; Chung et al., 2018; Reeve et al., 2018a; Villa et al., 2018; Reeve et al., 2018b). In a first episode inpatient group, Subramaniam et al (2018) found that insomnia was associated with reduced quality of life. In people at ultra-high-risk of psychosis, sleep disruption has been associated with positive and negative symptoms (Lunsford-Avery et al., 2015; Poe et al., 2017), disrupted cognitive functioning (Lunsford-Avery et al., 2017), severity of psychotic experiences such as hallucinations and delusions (Reeve et al., 2019a), and overall functioning (Poe et al., 2017). In individuals affected by psychosis there is an interaction between sleep disorder, psychotic symptoms and medication status (Reeve, Sheaves & Freeman, 2015). Those who are medication naive or not taking medication experience different sleep disorders than those who are taking antipsychotic medications (Chouinard, Poulin, Stip, and Godbout, 2004).

Whilst few studies have examined the relationship between sleep disorder and psychosis symptoms across time, sleep disorder does seem to predict psychotic experience (Reeve, Sheaves & Freeman, 2015). In the general population, sleep disorder predicts paranoia (Freeman et al., 2012; 2013). Insomnia in particular has been proposed to act as a mediator in psychosis (Dolsen, Asarnow & Harvey, 2014). Increased insomnia is related to increased paranoia (Freeman et al., 2011) and hallucinations (Sheaves et al., 2016). Insomnia is predictive of the persistence of psychosis symptomatology, specifically hallucinations (Reeve et al., 2018b). A high proportion of those who develop symptoms of psychosis report sleep disorder prior to this (~77%, Tang and Ang, 2001). Sleep-wake abnormalities predict symptomology in youth at high risk of developing psychosis (Lunsford-Avery, LeBourgeois, Gupta, & Mittal, 2015).

It is currently not clear whether psychosis symptoms can lead to disordered sleep, however it is possible that the relationship is bidirectional (Reeve, Sheaves & Freeman, 2015). Paranoia is known to increase insomnia, therefore suggesting that the relationship between insomnia and paranoia is bidirectional (Reeve et al., 2018b).

4.6 The Role of Mood Disorder

The interaction between insomnia and psychosis symptomatology is thought to be mediated by mood disorder. In the general population, the relationship between paranoia and sleep is partially mediated by depression and anxiety symptoms (Freeman et al., 2009; 2011; Taylor et al., 2015). In psychosis populations, sleep disorder and psychosis symptomatology are related to mood (Reeve et al., 2018a; Villa et al 2018). In first episode populations, Reeve et al (2019) found patients with sleep disorders had more severe depression, and anxiety.

Cognitive models of paranoia and persecutory delusions suggest that negative affect specifically may link sleep disorder and paranoia (Freeman et al., 2009). More recent

models suggest that anxiety, depression and worry contribute to the development of paranoia and sleep disorder, then paranoia is then heightened by insomnia (Freeman et al., 2009; Reeve, Sheaves & Freeman, 2015). More recently, Kasanova et al (2019) found that whilst poor sleep quality predicts paranoia in a psychosis population, this is fully mediated by negative affect.

Mood is also a mediator of insomnia in the context of Covid-19. Higher Covid-19-related worry, depression symptoms and anxiety have been found to be associated with higher insomnia in Greece (Voitsidis et al., 2020). In France, Covid-19 related worry was found to be a major predictive factor for insomnia, in addition to previous mental illness diagnosis (Kokou-Kpolou et al 2020). Adverse experiences and worry have been shown to be together related to the development of poor sleep during the UK lockdown, which then impacted on mental health (Wright, Steptoe and Fancourt, 2020). In the current context of Covid-19, related worry and governmental regulations based on Covid-19, sleep may deteriorate in people affected by a first episode of psychosis, impacting on mood, psychosis symptomatology and other mental health variables.

4.7 Intervention for Insomnia in Psychosis

The relationship between sleep disorder and psychotic symptomatology has led to exploration of sleep as a primary therapeutic intervention target (Freeman et al., 2015; Waite et al., 2020). Current DSM-V guidelines suggest that clinically significant sleep disorder should receive clinical input, regardless of the presence of psychosis (APA, 2013). Additionally, patients with psychosis highlight a preference for intervention around sleep disorder as part of overall treatment (Waite et al., 2015). Intervention around sleep also presents the opportunity for a low-stigma intervention in a population who experience high levels of stigma (Freeman et al 2017).

Insomnia is a tractable clinical target in this population, for which intervention shows promising results. Cognitive Behavioural Therapy has been shown to be effective in treating insomnia in non-psychosis populations (CBTi; Mitchell et al., 2012; Trauer et al., 2015). A case series study demonstrated large reductions in insomnia symptoms and persecutory delusions, and reductions in anxiety, depression and anomalous experience following CBTi (Freeman et al., 2015; Myers, Startup & Freeman, 2011). A large single-blind RCT of CBTi in outpatients experiencing psychosis found the intervention was effective in reducing insomnia in this population, with large effect sizes, but was inconclusive regarding impacts on psychosis symptomatology (Freeman et al., 2015). Chiu et al (2018) examined the use of CBTi in addition to treatment as usual in people affected by psychosis and found that the greatest improvement in sleep was observed in those persons who experienced ‘classic’ severe insomnia.

Whilst CBTi is effective, there are concerns about whether it can be scaled to meet the need in the general population affected by psychosis or in specific populations such as those experiencing an FEP, given the prevalence of insomnia (Espie, 2009; Reeve et al.,

2018). In the current context, there is an opportunity and need for digital psychological interventions, delivered remotely. Internet-delivered CBTi is effective in improving sleep in adults with insomnia (Seyffert et al 2016). Digital CBTi application, Sleepio, reduces insomnia in non-clinical populations, with a comparative efficacy to 1-1 input (Espie et al., 2012). Sleepio has been shown to reduce insomnia, hallucinations and paranoia in a large non-clinical population (Freeman et al., 2017). In this study, change in insomnia was responsible for ~60% of the variance in participants' paranoia. Additionally, digital application-based interventions have been increasingly used in FEP populations (Rus-Calafell & Schneider, 2020).

4.8. Why is this research needed?

Sleepio therefore provides a psychotherapeutic intervention which can be offered remotely in the current context of Covid-19. This intervention targets Insomnia - one of the most common comorbid difficulties in FEP, a common psychological impact of pandemic-related regulations - and may also demonstrate effects on wider psychological wellbeing in this population.

Sleep disorder in psychosis is a complex problem, affected by interacting psychological, social, and biological factors (such as sleep beliefs, quality of living situation, and physiological arousal). We therefore intend to study the implementation of the Sleepio intervention through the lens of the Medical Research Council Complex Interventions Framework (Moore et al., 2015). The proposed work aims to collect data to build a model of digital CBTi implementation in NHS Greater Glasgow and Clyde Esteem FEP services, based on this framework.

5. AIMS AND OBJECTIVES

Informed by the Medical Research Council MRC complex interventions process evaluation framework (Moore et al., 2015); we aim to develop a logic model of Sleepio implementation in people recovering from FEP, in the context of Covid-19 restrictions and their aftermath.

We will assess:

5.1. Implementation

1) What is the rate of ineligibility and why?
2) What is the rate of consent into the study?
3) Can we characterise participant sleep disorder?
4) Do participants complete Sleepio initial assessment?
5) Do participants enter daily and weekly data?
6) How many sessions do participants complete?
7) What is the rate of attrition from intervention?

5.2. Symptomatology Measures

At baseline and post-intervention:

1) What are the characteristics of participants' insomnia?
2) What are the characteristics of participants' psychotic symptomatology?
3) What are the characteristics of participants' mood?
4) What are the characteristics of participants/ Covid-19-related worry?

5) What is the relationship between insomnia, psychosis symptoms, mood and Covid-19 related worry?

5.3. Staff and Service User Expectations

1) What are staff expectations of Sleepio implementation?
2) What are service user expectations of Sleepio implementation?
3) How do staff and service user views compare and contrast?

5.4. Staff and Service User Experiences

1) What are staff experiences of Sleepio implementation?
2) What are service user experiences of Sleepio implementation?

3) How do staff and service user views compare and contrast?

5.5. Logic Model

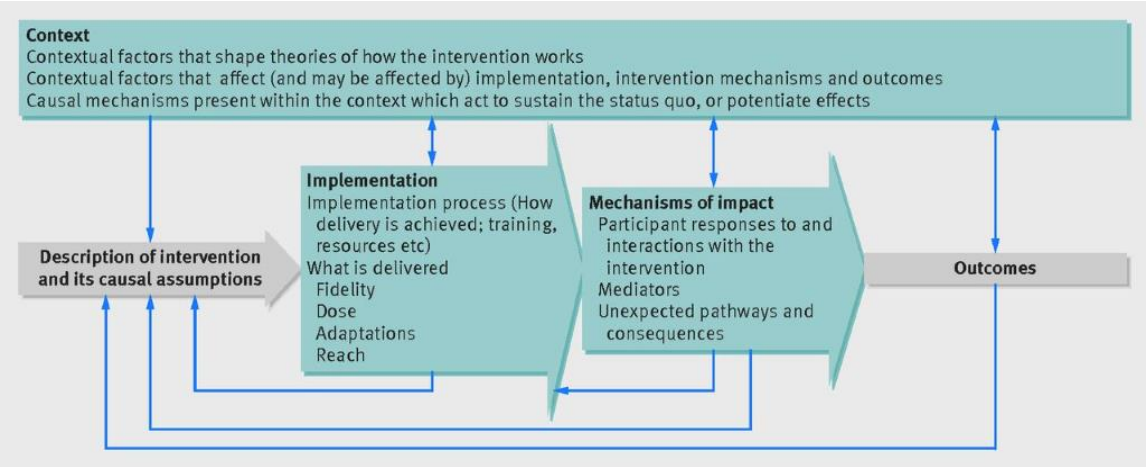

Figure 1. Key functions of process evaluation and relations among them from MRC Complex Interventions guidance.

From these data, we aim to develop a logic model for the implementation of Sleepio intervention in FEP services. This model will graphically represent the hypothesized context, the process of implementing Sleepio, the mechanisms of its impact, outcomes of Sleepio and other factors acting upon this (Moore et al., 2015).

6. METHOD

6.1 Study Design

The proposed study is a mixed methods implementation study of the dCBTi application 'Sleepio' in the context of the Esteem First Episode of Psychosis service in NHS Greater Glasgow and Clyde. We plan to record data about the profile of sleep disorders, uptake and usage of Sleepio, complete pre- and post-intervention symptomatology measures with participating service users, and undertake qualitative interviews with keyworkers and service users. The primary aim is to characterise the implementation of Sleepio by integrating these data into a logic model.

6.2 Setting

The study will take place within the NHS Greater Glasgow and Clyde (NHS GGC) First Episode Psychosis (FEP) Service, 'Esteem'. This service has two teams – one covering the North of the city and one covering the South and Inverclyde areas.

6.3 Participants

This study utilizes two groups of participants:

6.3.1 Service users of Esteem
6.3.2 Esteem keyworkers

6.4 Inclusion and Exclusion Criteria

6.4.1 Inclusion and exclusion criteria for service user participants:

64.1.1 Inclusion criteria

i. Service users under the care of Esteem First Episode Psychosis Service in NHS GGC
ii. Aged >=16yrs and <=35 years (the service sees individuals between these ages)
iii. Potentially affected by Insomnia Disorder (defined by SCI-02 score ≤2)
iv. Who have access to a device they can use Sleepio on (a computer device with Safari or Google Chrome browser, or an iPhone device).

6.4.2.1 Exclusion Criteria

i. Moderate to severe learning disability
ii. Acute Psychosis (recent crisis contact or hospitalisation)
iii. Incapacity to provide informed consent
iv. Insufficient English to access intervention
v. Organic impairment
vi. No access to a device which can be used for Sleepio intervention.

6.4.2 Inclusion and exclusion criteria for keyworker participants:

6.4.2.1 Inclusion criteria

i. Holds position of Keyworker in Esteem

6.5 Intervention

This study provides service users of Esteem with access to a digital CBTi application, 'Sleepio'. It aims to model factors of the implementation of this intervention in FEP services in NHS Scotland. Service user participants will be asked to continue to engage with their treatment as usual whilst accessing Sleepio. Esteem keyworkers will be involved in providing information and referral to the study for service users with sleep difficulties, then supporting service users' use of the intervention through the 'Sleep Clinic' online interface.

6.5.1 Treatment as Usual (TAU)

Esteem provides multidisciplinary input over a two-year timeline to those affected by a FEP. Treatment may consist of different therapies determined by clinical need. Treatment will include regular contact with a care coordinator ("keyworker"), medication management by a Psychiatrist and access to psychosocial interventions (e.g. psychological therapy or occupational therapy), as considered appropriate by the clinical team. Esteem clinicians conduct routine enquiry about sleep difficulties and may provide psychoeducation about sleep improvement as part of TAU. TAU will be free to vary for service user participants in the study.

6.5.2 Sleepio

Participating service users will receive access to a comprehensive sleep assessment carried out by researcher FR and to the Sleepio intervention. Sleepio is a dCBTi application which is personalised in response to input data (Espie et al., 2012). Sleepio's components are those common to CBTi interventions: i) Psychoeducation on sleep hygiene and processes; ii) cognitive components including restructuring, mindfulness, positive imagery, paradoxical intention training (trying to stay awake), and resolving thoughts about one's day; and iii) behavioural components including sleep restriction, stimulus control, and relaxation techniques. Sleepio is composed of six 20-minute

sessions presented by an animated therapist ("the Professor"), which are unlocked weekly. Participants complete an initial assessment (please see 'Sleepio Onboarding Questions') and chose a treatment goal, which drives initial personalisation of the application. Participants book digital 'appointments' with the Professor and receive prompts to complete these 6 sessions, to enter sleep data and to complete the Sleep Condition Indicator. The Sleepio algorithm tailors ongoing intervention based on this sleep data and other data about participants' physical and mental health. Sleepio also provides access to online psychoeducation and a clinician-moderated user forum. Sleepio can be accessed via web browser (Safari or Google Chrome) or iOS smartphone. It cannot currently be accessed using an Android smartphone.

Keyworkers will be asked to monitor service users' progress with using the Sleepio application. They will be provided with access to the 'Sleep Clinic' in order to support this role. The Sleepio Sleep Clinic is an online platform where health professionals can observe completion, data entered and Sleep Condition Indicator scores for service users they have clinical responsibility for. Service users will be made aware of keyworker access to this, prior to consenting to participate.

6.6 Recruitment and Consent

6.6.1. Sample Size

6.6.1.1 Service Users

The Esteem population includes ~250 service users, with ~150 new users per year. Around 80% would be expected to experience clinically significant sleep difficulties (~200/250) and around 50% to experience Insomnia Disorder (~125/250; Reeve et al., 2018a). It is difficult to estimate the rate of eligible persons who will be willing to participate and will be retained in the study. A sample of ~8 for use of the Sleepio intervention has been considered feasible in terms of study resource. Sample size throughout (e.g. recruitment, withdrawal, participation in follow-up) will act as implementation data. As the study is not designed to identify change in symptomatology measures, power calculations have not been carried out. We aim to recruit ~5 service users to participate in optional interviews.

6.6.1.2 Keyworkers

There are approximately 20 clinicians working as keyworkers in Esteem. We aim to recruit ~10 to interview.

6.6.2. Integration into the Esteem Service

Esteem are strongly in support of the project and are agreeable to their planned level of involvement in recruitment and monitoring. Evidence of management approval will be supplied. Two of the research applicants (AG and MS) work clinically in these services.

We plan to continue to present the study to the clinical staff teams and demonstrate the Sleepio application and Sleepio Clinic, in order to ensure keyworker familiarity and support for the project. Applicant MS provides supervision to keyworkers in Esteem for low intensity psychosocial interventions. Through this, she intends to support sleep enquiry and monitoring service user participants' use of Sleepio. Keyworkers will be provided with information about the study and their role as clinicians and as research subjects. We will offer an appointment with each keyworker to reflect upon their caseload and consider service users who may be appropriate to access the study and intervention.

6.6.3. Recruitment and Consent Procedures

6.6.3.1 Service Users

Keyworkers in Esteem FEP services will be approached to identify service users affected by sleep difficulties that may benefit from Sleepio. Service user participants will be recruited through their treatment as usual with their Esteem keyworker (sleep monitoring is part of this). Where service users report sleep difficulties, keyworkers will offer an information leaflet about the study and referral into the research study or contact details for researchers (study email address). Keyworkers will record that service users have agreed to keyworkers providing their details to researchers and to being contacted by the researchers in their casefile.

Those service users who wish to find out more about the study and meet eligibility criteria will be sent an easy-read Participant Information Sheet and Consent Form. They will be given the opportunity to ask questions and will be encouraged to speak to others about their potential participation (such as their keyworker). It will be made clear that in consenting to participate they are consenting to participate in sleep assessment, complete symptomatology measures pre- and post-intervention and use the Sleepio intervention. It will be made clear that participation does not affect their TAU. They will provide written consent if they wish to participate. Consenting service user study participants will receive access to Sleepio. They will register for the intervention with a researcher during the baseline symptomology measures assessment session.

They will be given the option of additionally participating in semi-structured interviews prior to and after using the intervention, to talk about their expectations and experiences of Sleepio.

6.6.3.2 Keyworkers

As above, keyworkers will be introduced to and supported in their role in referring service users to the study and monitoring use of Sleepio through presentations, psychosocial supervision, and reflection sessions. Keyworkers will be provided with an easy read information sheet which clarifies their role as clinicians (attending a session to reflect on their caseload and service user suitability for the study and providing suitable service users with information about the study) and potentially as research participants (in semi-structured interviews) via email and letter. They will be given the opportunity to ask

questions and will be encouraged to speak to others about their potential interview participation (such as their colleagues). They will provide written consent if they wish to participate in semi-structured interviews, to talk about their expectations and experiences of Sleepio use in Esteem.

6.6.4 Randomisation

Service user participants will not be randomized to treatment. All service user participants will be provided with access to Sleepio. Research will focus on developing a model for the implementation of this intervention.

6.7 Data Collection

6.7.1 Implementation Data

We will gather data on eligibility, consent rates and the rate of service user participants beginning intervention. We will gather data on clinical sleep disorder assessment outcomes. Sleepio intervention will span week 0 to week 10. Usage data will be collated throughout these 10 weeks via the application. This data will comprise the rate of completion of the six sessions contained in the intervention and of sleep diaries. These metrics will allow us to ascertain intervention adherence, attrition and completion. We will further record rates of attendance to complete symptomatology measures. In analysis, these data will be represented by rates and summary statistics.

6.7.2 Measures

Symptomatology measures will be completed with service user participants using NHS Attend Anywhere or at in-person appointments at baseline (week –1), and at week 11. Researchers completing these appointments are NHS GGC employees with pre-existing access to Attend Anywhere. We will complete symptomatology measures using Online Surveys (https://www.onlinesurveys.ac.uk/; formally **Bristol Online Surveys**). Online Surveys is UK based, Data Protection Act 2018-compliant and has ISO certification. If sessions are undertaken in person, these measures will be completed on paper. The study researchers are not aware of any issues in relation to the suitability, ease of use or acceptability of these measures in this service user group. The baseline appointment will also allow participants to set up the Sleepio application and complete its initial assessment.

Service user participants will be assessed with measures of:

6.7.2.1 Insomnia

Service users will be screened for insomnia after completing consenting procedures, using the Sleep Condition Indicator – 2 Item (SCI-02; Luik et al, 2019). This is a reliable and validated shortened screening measure for insomnia, which correlates well to full

insomnia measures. Service users who's scores are not indicative of insomnia will be ineligible for study participation.

Insomnia symptoms will be assessed using the Insomnia Severity Index (Bastien, Vallieres, and Morin 2001) at baseline and week 11. This is a brief self-report questionnaire, designed to assess the severity of nighttime and daytime components of insomnia. It is widely used, demonstrates good reliability and validity, and is responsive to change through clinical treatment.

Additionally, participants will be regularly prompted within the Sleepio intervention to complete the full Sleep Condition Indicator (SCI, Espie et al., 2012). SCI is an 8-item scale which measures sleep problems against DSM-5 criteria for Insomnia Disorder. It has good validity and reliability and is sensitive to change (Espie et al., 2014). These scores will be available for analysis by researchers.

6.7.2.2 Mental Health Symptomatology

Psychotic symptoms will be assessed using the Specific Psychotic Experiences Questionnaire; hallucinations subscale (SPEQ(H), Ronald et al., 2014) and Revised Green et al Paranoid Thought Scales (R-GPTS, Freeman et al., 2019). The SPEQ is a transdiagnostic self-report measure of psychosis symptomatology, which comprises subscales of paranoia, hallucinations, cognitive disorganization, grandiosity, anhedonia, and parent-rated negative symptoms. The R-GPTS is a two-factor measure of paranoid thoughts, with subscales distinguishing persecutory ideation and ideas of social reference.

Mood symptoms will be assessed using the Depression, Anxiety and Stress Scales 21 item (DASS-21, Lovibond and Lovibond, 1995; Anthony et al., 1998). The DASS-21 is a widely used measure assessing symptoms of depression (low positive affect, low self-esteem, hopelessness), anxiety (physiological symptoms, situational anxiety), and stress (negative affect, tension, agitation).

Covid19 worry will be assessed using the Fear of Covid19 Scale (Ahorsu et al., 2020). This scale is new but has relatively good metrics and has been validated in several populations.

6.7.3 Qualitative Interviews

6.7.3.1 Service Users

Service users will be provided with the *option* to participate in semi-structured interviews prior to beginning intervention and/or after completing the intervention. Each interview appointment will last ~45 - 60 minutes. Pre-intervention interviews will be undertaken prior to the baseline symptomatology measures appointment, at approximately week -2. They will focus on service users' expectations for the Sleepio intervention (see Interview Schedule).

Post-intervention interviews will be undertaken after completing follow-up symptomatology measures, at approximately week 12. They will focus on service users' experiences of the Sleepio intervention (see Interview Schedule). Post-intervention, participants will be purposively sampled to include a range of service users reflecting their engagement with the Sleepio App.

Interviews will be undertaken using a NHS Microsoft Teams meeting from an NHS GGC computer or in-person at an Esteem base. Attend Anywhere cannot be used as it is not possible to record on this platform. As with Attend Anywhere, researchers have pre-existing access to this as NHS GGC employees and it is considered secure for NHS use. Interviews will be digitally video recorded and auto-transcribed for purposes of analysis. These are inbuilt features of Microsoft Teams meetings. If interviews take place in person, data will be collected in the form of audio recordings on an encrypted recording device and transcribed by researcher FR.

Service users can participate in pre- or post-intervention interviews, or neither.

6.7.3.2 Keyworkers

Keyworkers in Esteem will be offered the opportunity to participate in semi-structured interviews prior to service users beginning intervention and/or after all service users have completed the intervention. Each interview appointment will last ~45 - 60 minutes. Pre-intervention interviews will focus on keyworkers' expectations for the Sleepio intervention (see Interview Schedule).

Post-intervention interviews will focus on keyworkers' experiences of the Sleepio intervention use in Esteem (see Interview Schedule).

Interviews will be undertaken using a NHS Microsoft Teams meeting from an NHS GGC computer or in-person at an Esteem base. As above, interviews will be digitally video or audio recorded and transcribed for purposes of analysis.

Keyworkers can participate in pre- or post-intervention interviews, or neither.

6.8 Participant Withdrawal

All participants will have the right to withdraw from the study at any time. It will be clearly stipulated at the time of consent that they have this right and that withdrawal will not affect their clinical treatment (service users) or role in Esteem (keyworker participants).

Withdrawal from the study can be at the request of the participant or at the discretion of the researchers. Withdrawn participants will be informed that they will no longer continue with the study protocol and that their withdrawal from the study will not influence their treatment/role within the service. Research data collected up to the time of withdrawal against anonymous participant IDs or Sleepio access IDs will be retained for use in the study. Video or audio recordings collected up to the time of withdrawal will be retained

for use in the study and transcription. Consent forms will be retained. Other non-anonymized or personal data will be destroyed should a participant withdraw from the study. All of this is made clear to interested persons prior to consenting to participate.

Service user participants may also choose to stop using the Sleepio intervention, without withdrawing from the study. These participants would still be asked to participate in the post-intervention assessment session and be given the option of participating in post-intervention interviews. This will be made clear to interested persons prior to consenting in the Participant Information Sheet.

The sponsor reserves the right to terminate the study at any stage for any reason, including funding considerations. Existing participants will be informed of the termination of the study and will be followed-up as part of their TAU clinical management.

6.9. Statistical Analysis

The main aim of the implementation study will be delivered via the development of a logic model describing the potential implementation of Sleepio within FEP services in NHS Scotland.

6.9.1. Quantitative

Descriptive quantitative information will be provided for implementation measures (percentages, rates, mean, median, variance, 95% confidence intervals). This will include reporting data on attrition rates and loss to follow-up.

Descriptive quantitative information will be provided for sleep assessment.

Analyses of symptomatology measurements will not be focused on statistical significance but will be quantitatively detailed (estimated 95% confidence intervals, variance) to assess the likely range of treatment effects. Our study is not designed nor powered to detect statistical differences in measures over time. Exploratory analysis of the relationship between symptomatology variables will be undertaken.

6.9.2. Qualitative

Information arising from qualitative interviews will analysed using a framework analysis based on the MRC Complex Interventions framework.

6.9.3. Modelling

A logic model of Sleepio implementation in FEP services will be developed from quantitative and qualitative data.

6.9.4. Other

A timeline of changes to Scottish government regulations regarding Covid-19 will be collated in order to contextualize study data.

7. ETHICS, PROJECT AND DATA MANAGEMENT

7.1 Ethics

7.1.1 Ethics

The proposed project will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with the UK policy framework for health and social care research.

7.1.2 Ethics Approval

Esteem service managers have confirmed Esteem service capacity and capability to undertake the project (see Service Manager Approval – V1). We will apply for NHS GGC Research and Development (R&D) approval. We will seek ethical approval from the NHS Research Ethics Committee (REC). This protocol and related documents will be submitted for review. The study will request approval from NHSGGC Information Governance.

FR will ensure that University of Glasgow Doctorate in Clinical Psychology Research Programme Lead 'Proceed to Ethics' letter, REC 'Favourable Opinion' and R&D approval are be in place before recruiting.

7.1.3 Consent Processes

Participation will not commence without informed consent, including ensuring participant awareness of confidentiality and limits to confidentiality. Consent will be taken by researcher FR. All study participants will be provided with a written information sheet and a written consent form for the study. All participants will have been judged to be capable of providing informed consent. It will be emphasised that potential participants may wish to contact others before making up their mind and that there is no hurry to decide. It will be made clear that study participation status will have no impact on TAU care or their role in Esteem.

At an Attend Anywhere appointment, the researcher will talk the participant through the consent form, verbal consent will be sought and participants will be asked to initial and sign two copies of the consent form and return one. For service users this will be via pre-addressed envelope, for keyworker participants this will be via scanning and email or pre-paid envelope. One copy will be retained by the participant and the other by the research team. The copy retained by the research team will be scanned and stored electronically on University of Glasgow servers. The paper original will be destroyed.

Aspects of the consent process will be optional, for example for service users to participate in interviews pre- and post-intervention.

Potential service user participants will be made aware that the study may pose a risk of distress prior to consenting. Keyworkers will be informed of participating service users.

Participants will be made aware of who to contact should they experience distress and the limits of confidentiality if there is risk to the participant or other persons.

7.2 Project Management

AG will be responsible for monitoring all research procedures and will supervise researcher FR during the study. MS will act as field coordinator and supervisor during the study. FR and MS will be responsible for recruitment of service users and keyworkers. FR will be responsible for collection of measures, rates of consent, interviewing, data monitoring and management, analysis and report writing. MS will be responsible for staff training and supervision associated with the study and regarding sleep difficulties in FEP more generally (although contribution will be made by AG, LB and FR). Big Health Ltd (CE, AH and CM) will be responsible for providing Sleepio usage data. The research group (AG, MS, LB and FR) will meet bimonthly throughout the trial to monitor progress and achievements.

NHS GGC Research and Development and the NHS Scotland Research Ethics Committee will establish the ethical standard of the study protocol. AG will have the responsibility to fulfil all the research governance arrangements and liaise with the NHS.

7.3 Data Management

7.3.1 Data Collection

Implementation, measures and interview data will be collected by the project researcher FR, under the supervision of AG and MS. Big Health Ltd will collate usage data for Sleepio.

7.3.2 Data Management and Storage

Please see the Data Protection Impact Assessment (V3 – 03.03.2021) for this study. Personally identifiable data will be held separately from research data, which will be paired with anonymous participant IDs. Interview recordings will be saved against participant IDs, although these do contain non-anonymised data as they are video recordings. Transcriptions will have personal or identifiable information removed and will be saved against participant IDs.

Personal identifiable data (e.g. names, email addresses and telephone numbers) will be kept separately from research data and will be stored within NHS GGC premises and electronic servers. Interview video or audio recordings will be stored on NHS GGC servers. There will be a key which links participant IDs to personal identifiable data and participant IDs to Sleepio access codes. These will be stored separately from all research data, in locked folders in NHS GGC. These will never be stored in the University of Glasgow and can be accessed only by the lead researcher (Dr Fiona Robb) and chief

investigator (Prof Andrew Gumley). Pseudonymized study data will not be identifiable without access to these anonymization keys.

The study will hold and analyse pseudonymised data outwith NHS GGC (at the University of Glasgow) in locked storage and password protected electronic files. This data will be held in accordance with NHS GGC and University of Glasgow policies, the Data Protection Act and the Data Protection Act 2018. Core research team members are all contracted staff of the University of Glasgow and NHS Greater Glasgow and Clyde. All researchers are trained in and will be familiar with current laws, rules and protocol (governed by the NHS, university ethics guidelines and the Data Protection Act 2018) regarding consent, anonymity and data storage.

No data will be sent from NHS GGC nor the University of Glasgow to Big Health. Pseudonymised usage data will be sent from Big Health to the University of Glasgow. The pseudonymized data will be labelled with the individual Sleepio access codes which researchers initially share with participants to enable them to access Sleepio for free. The list of paired access codes, participant IDs and participant names will be stored within NHS GG&C only, not the University of Glasgow. The pseudonymized data will not be identifiable without access to the anonymization keys. All data in the Sleepio system is encrypted both "in transit" and "at rest". This means that the data is protected en-route from users' computer to the Sleepio servers, and also protected once it reaches the final destination of the Sleepio servers. The research team will be provided with psuedonymized data assessed by Sleepio such as adherence to treatment, sleep diary, engagement and measures collected with the application. This will be shared using an encrypted file. This data may be compared to other pseudonymized data, stored by participant ID but will never be paired with identifiable personal information.

Personal identifiable data is captured directly by Sleepio and stored by Big Health Ltd as standard for users of its application (for example name, email address, age, sex). Big Health treat these data as confidential in line with appropriate UK, EU and US regulations for protecting data. This data is not collected for the purposes of this research. This data will **not** be transferred to the University of Glasgow and only pseudononymized data will be sent. Big Health Ltd retain this personal identifiable data for 5 years, after which it is deleted. App users can also request deletion of this data at an earlier time.

Prior to providing consent to participating in the study, participants will be made fully aware of how their study data will be handled and who will have access to it. Only those in the core research team (AG, MS, LB, and FR) will have access to study research data.

Following study completion, anonymized research data, consent forms and interview transcriptions will be held for 10 years, as per University of Glasgow policy. It will be stored in secure electronic folders and accessible only to the Chief Investigator.

8. HEALTH AND SAFETY

8.1. Researcher Safety Issues

Use of Attend Anywhere or Microsoft Teams in home environments may reveal researchers' personal information. Researchers will ensure this is used in private spaces, will use blur background functions and will adhere to Esteem operational policy around its use.

Recruitment, follow-up and data collection may require significant practical and emotional labour. Supervision and time-management skills will be used to manage this. Researcher availability and monitoring of inboxes will be made clear to participants to maintain boundaries.

8.2. Participant Safety Issues

Participant sample may be associated with impulsive, irrational or unpredictable behaviour, and/or poor emotional control. Service users will be considered for their suitability by their keyworker. Participating service users will be in active contact with services at the time of their participation. Prior to consenting, participants will be made aware that keyworkers will be informed of their participation and will be able to monitor their Sleepio usage and sleep diaries. Researchers have a duty of care to report significant risks to a participant or to others to the mental health team in the event of a disclosure. These limitations to confidentiality will be made clear during consent processes. Researchers will ensure that appointments are undertaken in private spaces.

Symptomatology measures and Sleepio intervention may be associated with emotional distress. Use of this application is novel to this participant group and may cause distress, particularly in those affected by paranoia regarding technological devices. Potential participants will be made aware of the risk of distress prior to consenting.

8.3 Adverse Events

Any adverse events (as defined by HRA) will be reported to study sponsors and REC.

We will record and consider serious adverse incidents, consistent with organizational policy. These are defined as deaths, life-threatening illness or injury, suicidal or non-suicidal self-injury, serious violent incidents, admissions to hospital or units, any event which results in persistent or significant disability or incapacity, any event for which medical or surgical intervention required to prevent the above and any event otherwise considered medically significant by the Chief Investigator. We will also record adverse events, including but not limited to increased paranoia associated with using the Sleepio application. Additional events will be categorized by study researchers using their clinical judgement.

In case of a serious adverse incident, the responsible clinical team and the ethics committee will be informed. Appropriate actions in response to events will be determined on a case by case basis.

9. FINANCIAL CONSIDERATIONS

There will be no cost associated with Sleepio access for the purpose of this study.

10. DISSEMINATION

The planned project will be written-up to meet the requirements of a Doctorate in Clinical Psychology at the University of Glasgow. Additionally, we plan to disseminate our findings via publication in a peer-reviewed journal. AG and FR will submit a final report at conclusion of the study to the Sponsor(s). Results of the project will also be disseminated within the host service, Esteem. A plain language summary of project results will be disseminated to study participants.

11. PRACTICAL APPLICATIONS

Digital CBT intervention presents a psychological intervention that can be offered under current conditions and is likely to be efficacious. Exploration and treatment of sleep disorders are intended to become part of TAU care in NHS GGC FEP services. A logic model of Sleepio implementation will help inform this.

12. PROJECT TIMETABLE

- August 2020
    - Submission to NHSGGC Research and Development
    - Redrafting as required
- January 2021
    - Ethics submission through IRAS to Research Ethics Committee (REC)
    - Book REC meeting
- February 2021
    - Redrafting as required
    - Approval granted
    - Resubmit to NHSGGC R&D for final approval
- March 2021
    - Begin data collection
- June 2021
    - End data collection
    - Analysis
- July 2021
    - Submission
- August 2021

    - Draft paper submission
- September 2021
    - Viva
- Oct 2021
    - Corrections, paper submission

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