Insomnia in Psychosis: Prevalence and Implementation of an Intervention

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Statement on the Impact of Covid19

The coronavirus 2019 pandemic had significant impacts across NHS Scotland. The NHS board and service in which our research was situated adapted its structure, policies, and ways of working in response to the pandemic and associated regulations. Covid19 and its impacts led to reconsideration of this major research project's design and practicalities.

Our study initially aimed to recruit a larger sample of service user participants and compare pre- and post-intervention measures; however, this was not feasible within adapted timelines. We have collected usable data towards the intended work, but the nature and amount of the data differs from what was planned in initial proposals. This work has therefore been submitted under Acceptable Portfolio Variation 1 – containing a reduced amount of data from what was intended.

In Chapter 2, we therefore present preliminary data for a project that is ongoing; specifically reporting initial summary quantitative data and a qualitative analysis of keyworker clinicians' expectations for digital CBT intervention for insomnia. A preliminary logic model is described, developed from the available data. Limitations of the analysis and resulting interpretations are clearly explored.

Chapter 1. The Prevalence of Insomnia in Nonaffective Psychosis and its Relationship to Symptomatology: A Systematic Review and Meta-Analysis

Prepared in accordance with submission guidelines for Sleep Medicine (Appendix 1.1.)

1.1. Abstract

Dysfunction in the amount, timing, quality, or characteristics of sleep are common in people experiencing nonaffective psychosis. Sleep dysfunction occurs during prodromal phases of psychosis, in people experiencing a first episode, and in established psychosis. Insomnia, which describes a difficulty initiating or maintaining sleep, is particularly common. The prevalence of insomnia in nonaffective psychosis is not established. We present a systematic review and meta-analysis of i) the prevalence of insomnia disorder and symptoms in nonaffective psychosis and ii) its relationship to psychosis symptomatology. We searched electronic databases to identify articles published prior to March 31st 2021. Eighteen studies were included. Fifteen reported an estimated prevalence of insomnia and ten described the relationship between insomnia and psychosis symptoms. Random-effects meta-analyses indicated a pooled prevalence of insomnia symptoms of 36.5% (95%CI=27.2–46.4%; n=10) for those studies primarily aiming to establish prevalence and 34.8% (95%CI=27.4–42.6%; n=15) for all studies reporting a prevalence statistic. For studies using the Insomnia Severity Index, pooled prevalence was 45.6% (95%CI=32–59.6%, n=7). More severe insomnia was related to increased positive symptoms of psychosis and mood difficulties. Included papers were highly variable in methods and resulting prevalence estimates. Further research investigating the prevalence of insomnia, symptom correlates, and the relationship to treatment protocols across the spectrum of nonaffective psychosis would be beneficial to inform clinical practice. Future research should use robust standardised methods of establishing insomnia.

1.2. Introduction

Psychosis describes a group of symptoms which include disorganised thoughts and speech, voice-hearing, visual hallucinations, unusual strongly held beliefs (together referred to as 'positive symptoms'); alogia, avolition, asociality, anhedonia and reduced affect expression (together referred to as 'negative symptoms'; Wigman et al., 2011). Nonaffective psychosis describes a group of diagnoses including schizophrenia spectrum disorders, schizophreniform disorder, schizoaffective disorder, delusional disorder, and psychosis not otherwise specified (American Psychiatric Association, 2013). They are differentiated from affective psychoses (e.g. bipolar 1 or postpartum psychosis) by the extent to which mood disorder is the core feature. Some theoretical approaches consider all psychosis diagnoses or symptoms as part of an underlying continuum (Craddock and Owen, 2010). Previous work exploring nonaffective psychosis included people at ultra-high risk of developing psychosis or experiencing emerging initial symptoms (referred to as prodromal psychosis; Olsen and Rosenbaum, 2006), people experiencing a first episode or early psychosis (Birchwood et al., 1998), or people with an established nonaffective psychosis spectrum diagnosis.

Insomnia describes a set of symptoms including difficulties with initiating sleep, maintaining sleep and early morning wakening, which have a negative impact on subjective sleep quality, functioning, and/or emotions. Diagnosis of insomnia disorder requires these features to be relatively severe, occurring at least three times per week over three months, and not better explained by inadequate sleep opportunity nor another sleep disorder (American Psychiatric Association, 2013). Sleep dysfunction has become a focus of research in psychosis, as a potential causal mechanism and treatment target (Waite et al., 2020). Several reviews and experimental studies have examined sleep disorder in nonaffective psychosis (Chouinard et al., 2004, Reeve et al., 2015, Waite et al., 2020), including in prodromal subpopulations (Goines et al., 2019, Poe et al., 2017) and in first episode psychosis (Davies et al., 2017). Sleep disorder is common, related to more severe psychosis symptomatology and poorer quality of life, and often remains untreated (Kaskie et al., 2017). Of the sleep disorders, insomnia is seemingly particularly prevalent (Reeve et al., 2015, Waite et al., 2020). Insomnia has been proposed to act as a mediator in many psychiatric conditions, including psychosis (Dolsen et

al., 2014). Systematic review of the prevalence of insomnia in prodromal psychosis, first episode, or established nonaffective psychosis has not been undertaken.

Establishing the prevalence of insomnia and its relationship to symptoms associated with psychosis may raise awareness of this unmet need, enabling health services to prioritise comprehensive assessment and treatment of insomnia in relevant services, and providing a stronger basis to estimate requirements of future studies to determine insomnia prevalence in non-affective psychosis. Therefore, this systematic review and meta-analysis primarily aims to establish the prevalence of insomnia or insomnia symptoms in people with nonaffective psychosis. The secondary aims are to explore its relationship to symptomology. We intend to review published works assessing people experiencing prodromal psychosis, first episode psychosis, or established as having nonaffective psychosis.

1.3. Method

A systematic review was conducted according to guidance provided in the PRISMA statement (Page et al., 2021). The protocol for this review was established but not published prior to beginning data extraction (Appendix 1.2.).

1.3.1. Search Strategy

Searches (Appendix 1.3.) were carried out across four electronic databases (Medline R, Embase, APA PsychInfo and CINAHL) for English language publications, where the title or abstract contained the following terms: (insomn* OR sleep OR sleep initiat* OR sleep maintain* OR sleeplessness) AND ((schizo* OR psychos?s OR psychotic OR Delus* OR Hallucinat*) OR (first?episode OR early psychosis) OR (Prodrom* OR ultra?high?risk OR at?risk?mental?state OR clinical?high?risk)), published from database beginning until 31 March 2021.

Duplicate records were removed from search results using Endnote X9.3.3. (2019; Clarivate Analytics, London, UK) de-duplification and hand screening. Titles and abstracts were screened, and irrelevant records were removed. This process was repeated twice to reduce the risk of records being removed erroneously. Records passing title and abstract screening were reviewed as full-text, to ascertain whether they fulfilled inclusion and exclusion criteria. The reference lists of relevant papers were hand-scanned for further citations, which were screened as full-text. Where studies were excluded at full-text screening, the reason for exclusion was noted.

1.3.2. Eligibility

1.3.2.1. Inclusion Criteria

Included papers reported quantitative studies published in English in peer-reviewed journals that included i) people experiencing prodromal psychosis, defined by the comprehensive assessment for at risk mental states (Yung et al., 2005) or structured interview for prodromal symptoms (Miller et al., 1999) or another recognised diagnostic system to identify those at risk of developing psychosis, or ii) people described as recently experiencing a first episode of

psychosis (based on standardised clinical assessment or a recognised diagnostic system to identify a nonaffective psychosis diagnosis for retrospective studies), or iii) people with nonaffective psychosis (based on standardised clinical assessment or diagnosis). Studies were also required to assess i) the prevalence of insomnia disorder or ii) symptoms of insomnia, or iii) assess the relationship between insomnia and psychosis symptomatology, in their sample. Insomnia should be defined using self-report questionnaires, clinical assessment, semi-structured interview, or any other standard clinical diagnostic technique. Insomnia should not be defined by items within a measure of another construct (e.g. using items within depression measures). Where included studies assessed the relationship between insomnia and psychosis symptomatology, validated measures of psychosis symptomatology must be used. Psychosis symptoms must not be defined solely by items within a measure of another condition.

1.3.2.2. Exclusion Criteria

Book chapters, case studies, reviews, systematic reviews, commentary, opinion papers, theses and conference proceedings were excluded. Studies with samples predominantly (>50%) composed of participants where the primary cause of psychosis symptomatology was organic (e.g. brain injury, illness, dementia) or with affective psychosis diagnoses (e.g. bipolar disorder, postpartum psychosis) were excluded. Studies examining psychotic-like experiences in non-clinical participants were excluded.

1.3.3. Data Extraction

A study-specific proforma was created and piloted (Appendix 1.4.). Study authors, year, title, journal, volume (issue), country in which the study was undertaken, study design, and sample size was extracted. Demographic data (age, gender or sex, ethnicity or race, diagnosis (diagnostic method), and participant setting (inpatient, outpatient, first episode) were collated where available. The primary outcome was the assessed prevalence of insomnia (disorder or symptoms). This was defined as the percentage of sample participants with insomnia at the time point the research was conducted. We collated data on methods of assessing insomnia and psychosis symptomatology. If available, we collected information on assessed relationships between insomnia and psychosis symptomatology.

1.3.4. Quality Appraisal

The quality of papers selected for review was appraised using i) the Joanna Briggs Institute (JBI) Checklist for Prevalence Studies (Munn et al., 2015; Appendix 1.5.) if their primary aim was to estimate prevalence (n=10) and/or ii) JBI Checklist for Analytical Cross-Sectional Studies (Aromataris, 2020; Appendix 1.6.) if they were cross sectional in design (n=16). Authors FR and HL co-rated a sub-selection of five papers, to calibrate quality appraisal. FR and HL then separately rated five papers to establish inter-rater reliability, with an initial agreement of κ=0.78 for prevalence papers and complete agreement for cross-sectional studies. Following discussion, complete agreement was reached. FR rated the remaining eight papers alone. Studies were not removed based on their quality rating, however quality was considered in narrative synthesis and statistically weighted in quality-effects meta-analysis. JBI Checklist outcomes were transformed into a score from 0-1 for use in quality-effects meta-analyses. This was calculated as 1 point for each 'yes' answer and 0 for each 'no' or 'unknown' answer, divided by the number of items in the checklist (see Appendices 1.7. and 1.8.). Where possible, Checklist for Prevalence Studies ratings were used in meta-analysis.

1.3.5. Analysis

Our primary aim was to present a meta-analysis of the prevalence of insomnia in nonaffective psychosis. We summarise the estimated prevalence of insomnia in nonaffective psychosis overall, in relation to how insomnia was assessed, and by subgroups. Meta-analysis was carried out using MetaXL version 5.3. (Barendregt et al., 2013; EpiGear International, Sunrise Beach, Queensland, Australia; 2016) an open-access software implemented in Microsoft Office Excel. We used fixed, random and quality-effects meta-analyses with double arcsine transformation to estimate the pooled prevalence of insomnia disorder or symptoms across i) those ten studies where the primary aim was to establish the prevalence of insomnia, ii) all fifteen studies reporting an estimated prevalence of insomnia, and iii) in those studies using the Insomnia Severity Index (Morin et al., 2011) to estimate the prevalence of insomnia. The use of a quality effects model allows the weighting of studies to be adjusted by their methodological quality, assigning lower weight to studies of lower quality, thus reducing a primary source of heterogeneity (variance in method between studies; Doi and Thalib, 2008). Double arcsine transformation acts to stabilise the variance between estimated prevalence statistics (Barendregt et al., 2013). Cochran Q test and I^2 were used to assess heterogeneity

among studies. Pooled prevalence estimates are reported using 95% confidence intervals (CIs). These are back-transformed to percentages for ease of interpretation.

Our secondary aim was to describe the reported relationships between insomnia symptoms and psychosis symptomatology.

1.4. Results

Database searches yielded 17,123 results (Figure 1). 6,902 duplicates were removed, leaving 10,221 records. 54 records passing title and abstract screening were full-text reviewed. 30 were added to full-text review through hand searching of references, resulting in full-text review of 84 papers. These were compared against eligibility criteria and reasons for exclusion were recorded. Eighteen papers investigating insomnia in the context of nonaffective psychosis were identified for inclusion (Table 1).

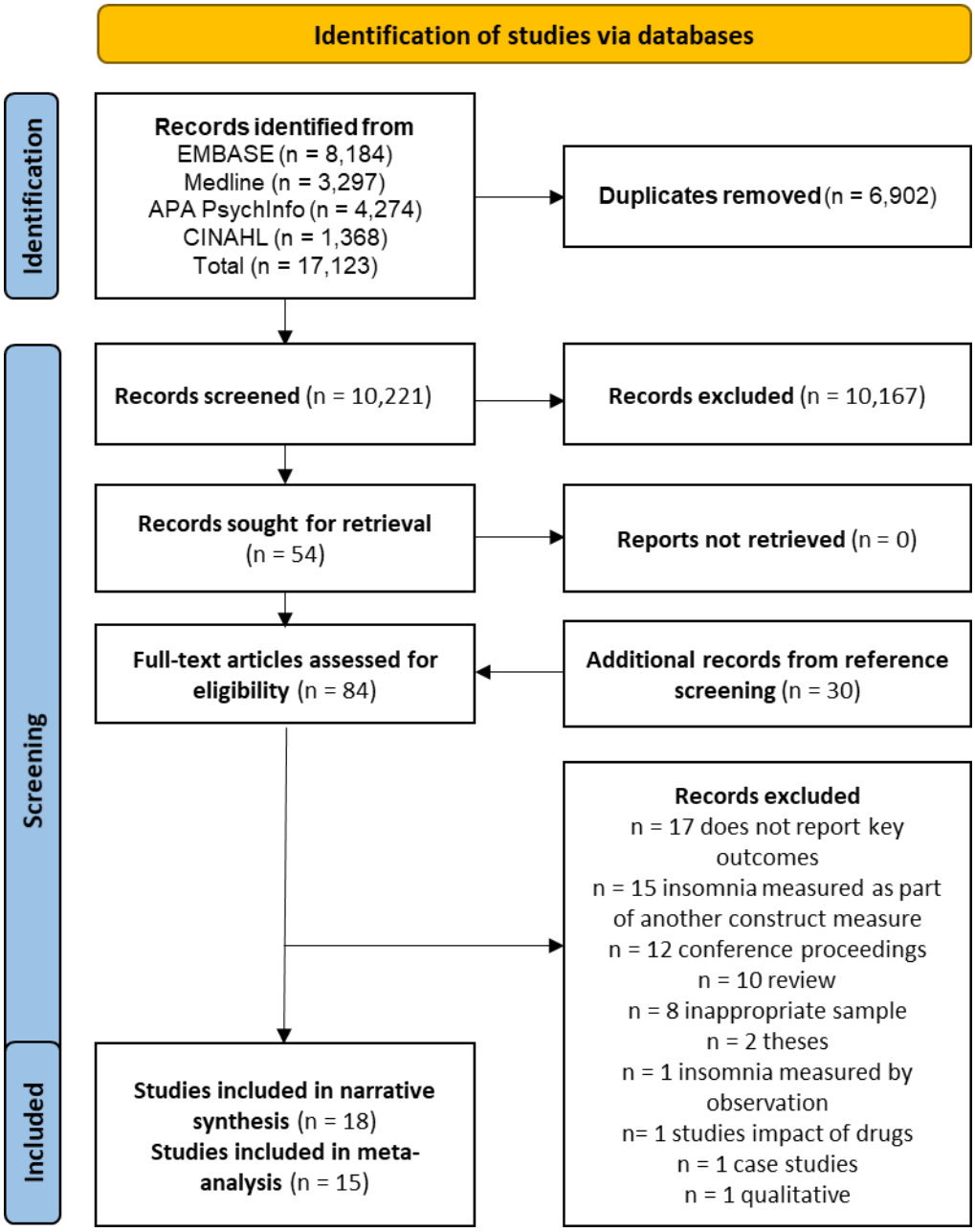

Figure 1. PRISMA Flow Chart

1.4.1. Study Characteristics

Included studies reported data for 7,524 participants, of which 6,160 were individuals with psychosis (n=29–1802; % of sample 9.1%-100%). Studies represented independent cohorts (n=18). Studies were undertaken in: China (n=3), China and Hong Kong (n=1), Hong Kong (n=1), England (n=4), the USA (n=3), Singapore (n=2), Germany (online), India, Nigeria and Spain. Most were descriptive or analytical cross-sectional in design (Table 1). Included descriptive studies describe the prevalence of insomnia in studied populations, whilst included analytical studies examine cause and effect relationships between insomnia and other symptomatology and may also describe the sample prevalence of insomnia. Study design is therefore relevant in considering the primary aim of included studies.

Table 1. Characteristics of studies included in systematic review.

Study	**Country**	**Sample n** (% of overall)	**Design**
Batalla-Martin et al. (2020)	Spain	267	Analytical cross-sectional
Freeman et al. (2009)	England (UK)	30 (9.1%)	Analytical cross-sectional
Freeman et al. (2019)	England (UK)	1802	Descriptive cross-sectional
Grezellschak et al. (2017)	Germany (online)	46 (13.7%)	Analytical cross-sectional
Hou et al. (2017)	China	623	Analytical cross-sectional
Li et al. (2016)	Hong Kong	388	Analytical cross-sectional
Li et al. (2017)	China	612	Analytical cross-sectional
Miller et al. (2019)	USA	108	Analytical cross-sectional
Miller et al. (2020)	China	328	Analytical cross-sectional
Miller et al. (2021)	USA	598	Analytical cross-sectional
Mondal et al. (2018)	India	124 (24.8%)	Descriptive cross-sectional
Ogbolu et al. (2012)	Nigeria	66 (35.9%)	Descriptive cross-sectional
Palmese et al. (2011)	USA	175	Analytical cross-sectional
Reeve et al. (2018)	England (UK)	29	Longitudinal observational
Reeve et al. (2019)	England (UK)	60	Analytical cross-sectional
Seow et al. (2018)	Singapore	120 (30%)	Descriptive cross-sectional
Subramaniam et al. (2018)	Singapore	279	Analytical cross-sectional
Xiang et al. (2009)	China & Hong Kong	505	Analytical cross-sectional

Sample n reflects the number of people with nonaffective psychosis in the sample. Where studies include participants without nonaffective psychosis, the n(%) of the sample with nonaffective psychosis is provided.

1.4.2. Sample Characteristics

Thirteen studies sampled only people with a nonaffective psychotic disorder, whilst five studies included other populations. Of those five studies which included other populations, three estimated the prevalence of insomnia across psychiatric diagnoses (Mondal et al., 2018,

Ogbolu et al., 2012, Seow et al., 2018) and two included non-clinical populations (Freeman et al., 2009, Grezellschak et al., 2017).

We were able to extract age and gender or sex demographics for most included studies (Table 2). Mean age ranged from 23.6 to 50.4yrs. Studies recruiting primarily or exclusively from early intervention services had a lower mean participant age (Reeve et al., 2018, Reeve et al., 2019b, Subramaniam et al., 2018). The percentage of male participants ranged from 34.8 to 75.2%. Eight studies provided data regarding ethnicity or race for nonaffective psychosis participants. Of these, demographics varied depending on where the study was undertaken. Specific diagnosis was provided in fifteen studies and schizophrenia was the most common diagnosis. Most samples were composed of adult outpatients receiving care in the community. One study recruited exclusively from inpatient services (Miller et al., 2020). Two other studies recruited from inpatient services and other settings (Freeman et al., 2019, Miller et al., 2019).

Table 2. Characteristics of study participants.

Study	**Mean Age** (SD)	**Gender or Sex** (% m/f)	**Ethnicity or Race** (%)	**Diagnosis** (%)	**Diagnostic Framework**	**Patient Setting** (%)
Batalla-Martin et al., 2020	50.4 (N/R)	59.9/40.1%	N/R	Schizophrenia 100%	DSM-IV / ICD-10 clinical diagnosis	Outpatient 100%
Freeman et al., 2009	44.2 (11.7)	60/40%	White 53.3% Black 36.7% Asian 3.3% Other 6.7%	Schizophrenia 80% Schizoaffective Disorder 13.3% Delusional Disorder 6.7%	Clinical diagnosis	Outpatient 100%
Freeman et al., 2019	41.3 (12.9)	69.6/30.4%	White 72.3% Black 14.7% Asian 8.3% Mixed 3.8% Other 1.2%	Schizophrenia 64.4% Schizoaffective Disorder 15.9% Schizotypal 0.2% Brief Psychotic Disorder 1.9% Psychosis NOS 8.2% First Episode 7.1% Delusional Disorder 1.9% Organic Psychotic Disorder 0.1%	Clinical diagnosis	Inpatient 32.4% Outpatient 59.4% EI/FEP 8.6%

				Drug Induced Psychosis 0.6%		
Grezellschak et al., 2017	36.2 (11.6)	34.8/65.2%	N/R	Schizophrenia 63% Schizoaffective Disorder 19.6% Brief Psychotic Disorder 6.5% Psychosis NOS 10.9%	Self-reported diagnosis	Unclear 100%
Hou et al., 2017	47.7 (10.3)	54.7/45.3%	N/R	Schizophrenia 100%	ICD-10 clinical interview	Outpatient 100%
Li et al., 2016	41 (11.4)	45.1/54.9%	N/R	Schizophrenia 79.4% Schizoaffective Disorder 6.7% Brief Psychotic Disorder 3.6% Psychosis NOS 5.9% Delusional Disorder 4.4%	ICD 10 clinical diagnosis	Outpatient 100%
Li et al., 2017	47.7 (10.3)	55.1/44.9%	N/R	Schizophrenia 70.5% First Episode 29.5%	ICD10 diagnostic interview	Outpatient 100%
Miller et al., 2019	45.1 (11.8)	59.8/40.2%	N/R	Schizophrenia 100%	ICD10 clinical diagnosis	Inpatient 57.4% Outpatient 38.9%
Miller et al., 2020	41.6 (12.9)	66.7/33.3%	White 30.6% Black 65.7% Hispanic 1.9% Asian 0.9% Other 0.9%	Schizophrenia 48.1% Schizoaffective Disorder 47.2% Schizophreniform 1% Psychosis NOS 3.7%	DSM V SCID	Inpatient 100%
Miller et al., 2021	38.6 (N/R)	75.2/24.8%	White 26.4% Black 66.4% Hispanic 1.2%	Schizophrenia 100%	DSM IV clinical diagnosis	N/R

			Asian 3.7% Other 1.3%			
Mondal et al., 2018	N/R	N/R	N/R	N/R	Mini International Neuropsychiatric Interview	Outpatient 100%
Ogbolu et al., 2012	N/R	N/R	N/R	Schizophrenia 100%	SCID	Outpatient 100%
Palmese et al., 2011	N/R	57.1/42.9%	White 33.7% Black 56.6% Hispanic 8.6% Other 1.1%	N/R	Clinical diagnosis	Outpatient 100%
Reeve et al., 2018	23.6 (3.8)	44.8/55.2%	White 51.7% Black 10.3% Asian 17.2% Mixed 20.7%	N/R	Clinical diagnosis	EI/FEP 100%
Reeve et al., 2019	23.7 (3.2)	65/35%	White 50% Black 18.3% Asian 16.7% Mixed 11.7% Other 3.3%	Schizophrenia 28.3% Schizoaffective Disorder 6.7% Schizophreniform 1.7% First Episode 20% Psychosis NOS 41.7%	Clinical diagnosis	Outpatient 25% EI/FEP 75%
Seow et al., 2018	N/R	N/R	N/R	Schizophrenia 100%	Clinical diagnosis	Outpatient 100%
Subramaniam et al., 2018	25.8 (6.2)	50.9/49.1%	Asian 95% Other 5%	Schizophrenia 90.2% Mood disorder with psychosis 9.8%	SCID	EI/FEP 100%
Xiang et al., 2009	43 (8.4)	48.1/51.9%	N/R	Schizophrenia 100%	DSM IV clinical diagnosis	Outpatient 100%

N/R = not reported. EI/FEP = Early Intervention/First Episode Psychosis service.

1.4.3. Measuring Insomnia

Ten studies reported that their primary aim was to estimate the prevalence of insomnia. However, fifteen papers reported a prevalence statistic for insomnia in nonaffective psychosis populations (Table 3).

There was significant variation in the measures used to estimate the prevalence of insomnia disorder or symptoms of insomnia. Five studies reported that insomnia was established using bespoke interview or question sets (Hou et al., 2017, Li et al., 2016b, Li et al., 2017, Miller et al., 2021, Xiang et al., 2009), with two studies (Li et al., 2017, Xiang et al., 2009) specifying that these were based on DSM-IV criteria for insomnia disorder (American Psychiatric Association, 1980).

Table 3. The prevalence of insomnia in nonaffective psychosis populations.

			Feature			Severity		
Study	**Insomnia Measure**	**Prev.**	**DIS**	**DMS**	**EMA**	**Mild**	**Mod**	**Severe**
Batalla-Martin et al. (2020)	ISI (>10) OSQ (ICD-10) OSQ (DSM-IV) Any symptom	41.2% 23.2% 7.9% 63.7%				27.7%$^{+}$	10.5%$^{+}$	3%$^{+}$
Freeman et al. (2009)	ISI (>10) Sleep-50	84%* 60.0%				30%$^{+}$	27%$^{+}$	27%$^{+}$
Freeman et al. (2019)	ISI (>10)	50.1%						
Hou et al. (2017)	Bespoke questionnaire	28.9%						
Li et al. (2016)	Bespoke questionnaire	19.0%						
Li et al. (2017)	Bespoke questionnaire	28.9%						
Miller et al. (2020)	ISI (>7)	17.7%						
Miller et al. (2021)	Bespoke questionnaire	45.0%	45%		27%			
Mondal et al. (2018)	Harding (2004) ISI (>10)	75.0% 66.7%*				38.7%$^{+}$	23.7%$^{+}$	4.3%$^{+}$
Ogbolu et al. (2012)	Sleep-50	10.6%						
Palmese et al. (2011)	ISI (>15)	48%				35%$^{+}$	35%$^{+}$	13%$^{+}$
Reeve et al. (2019)	DISP Sleep diaries & actigraphy ISI	50%				 3.3%$^{+}$	 18.3%$^{+}$	 28.3%$^{+}$

	Sleep-50 (n=29/60)							
Seow et al. (2018)	BIQ	25.0%	28.3%	18.3%	6.7%			
Subramaniam et al. (2018)	ISI (>15)	22.6%				39.1%[+]	22.6%[+]	
Xiang et al. (2009)	Bespoke questionnaire	36.0%	21.2%	23.6%	11.9%			

*Those in grey aimed to establish insomnia prevalence. Prev. = Prevalence. *Indicates prevalence statistics created by summarising ISI severity, + indicates ISI score categories. Features comprise delayed initiation of sleep (DIS), disrupted sleep maintenance (DMS) and early morning awakening (EMA).*

Seven studies used the Insomnia Severity Index (ISI; Bastien et al., 2001). The ISI is based on DSM-IV insomnia disorder (American Psychiatric Association, 1980) and aims to assess the symptoms of insomnia disorder during the prior two weeks (delayed sleep initiation (DIS), disrupted sleep maintenance (DMS), early morning wakening (EMA)), functional impairment, and related distress. ISI score brackets indicate no clinically significant insomnia (<7), subthreshold (8-14), moderate (15-21), or severe (22-28) clinical insomnia. Although the ISI was designed to measure change in insomnia symptoms, an ISI cut off of 10 has been suggested to be optimal for identifying insomnia in community samples (Morin et al., 2011). Included studies used a variety of cut-off scores to identify any insomnia (score >7; Miller et al., 2020) to moderate or severe insomnia (score >15; Palmese et al., 2011, Subramaniam et al., 2018).

Three studies reported a prevalence based or partially based on the Sleep-50 (Spoormaker et al., 2005). The Sleep-50 was developed based on the DSM-IV. The insomnia subscale assesses some symptoms of insomnia (DIS, DMS), sleep length, and worries affecting sleep over the previous month. One study used the Brief Insomnia Questionnaire (BIQ; Kessler et al., 2010). This is based on DSM-IV, ICD-10 (World Health Organization, 1994), Research Diagnostic criteria (Edinger et al., 2004), and International Classification of Sleep Disorders-2 criteria (American Academy of Sleep Medicine, 2005); specifically assessing DIS, DMS, EMA, sleep quality, daytime functional impairment and associated distress over the previous month. One study used the Oveido Sleep Questionnaire (OSQ; Bobes et al., 1998), which measures DSM-IV and ICD-10 insomnia disorder; specifically assessing DIS, DMS, EMA, sleep quality, daytime functional impairment and associated distress over the previous month.

Four studies reported prevalence statistics based on more than one criterion. Batalla-Martin et al. (2020) reported prevalence statistics based upon i) reporting of any insomnia symptom, ii) the ISI (>10), iii) the OSQ using ICD-10 criteria and iv) the OSQ using DSM-IV criteria for insomnia disorder. Freeman et al. (2009) reported prevalence statistics based on the i) ISI (score >10) and ii) Sleep-50. Mondal et al. (2018) reported prevalence statistics based on i) the ISI (>10) and ii) using screening questions based on Harding (2004; cited in Mondal et al., 2018). Reeve et al. (2019b) specified a single prevalence of insomnia in early psychosis using a testing process composed of the Diagnostic Interview for Sleep Disorders (Merikangas et al., 2014), consensus sleep diaries, and actigraphy. They additionally used the Sleep-50 in a subset of participants (29/60 participants; 48.3%).

1.4.4. Measuring Psychosis Symptomatology

Ten studies examined the relationship between psychosis symptomatology and insomnia. Psychosis symptomatology was assessed using a variety of measures (Table 4). Four studies used the Positive and Negative Symptom Scale (PANSS; Kay et al., 1987). Two studies used the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1988). One study used the Green et al. Paranoid Thoughts Scale – B (R-GPTS-B; Freeman et al., 2021) and the Cardiff Anomalous Perceptions Scale (CAPS; Bell et al., 2006). One study used the Paranoia Checklist (PC; Schlier et al., 2016). One study used the Clinical Global Impression Scale - Schizophrenia Version (CGI-S; Haro et al., 2003). Lastly, one study used the Specific Psychotic Experiences Questionnaire (SPEQ; Ronald et al., 2014).

1.4.5. Study Quality

The quality of included studies primarily assessing prevalence (n=10) was variable (see Appendix 1.7.). Included studies of prevalence typically used an appropriate sample frame to address their aim, provided a thorough description of the study setting and of included participants, and had sufficient coverage of data. Several studies failed to characterise the method of assessing insomnia in adequate detail to appraise their approach or standardisation. Studies typically did not sample from the underlying population in a representative manner or did not report how sampling was undertaken. They often did not

report the number of approached persons who chose not to participate (response rate). Only one study presented a statistical confidence interval around their estimated prevalence of insomnia.

The quality of included cross-sectional studies (n=16) was good (see Appendix 1.8.). Most studies reported inclusion and exclusion criteria, described their setting and participant characteristics well, and used appropriate definitions of diagnosis and of their outcome measure. Several studies did not address confounds in their dataset and did not incorporate strategies to manage confounds in analysis.

1.4.6. Outcomes of Interest

1.4.6.1. Prevalence of Insomnia

Fifteen papers reported one or more prevalence statistic for insomnia (Table 3). The measured prevalence of insomnia/insomnia symptoms ranged from 7.9% to 75% (Batalla-Martin et al., 2020, Mondal et al., 2018). The prevalence of insomnia varied with the subpopulation measured. Those studies which assessed first episode or early psychosis populations report a prevalence of insomnia symptoms of 39.1 to 50% (Reeve et al., 2019b, Subramaniam et al., 2018). Those which examined community outpatients report a prevalence of 7.9% to 75%. Miller et al. (2020) reported a prevalence of 17.7% for an inpatient group.

A group of studies used a bespoke set of questions, based on DSM-IV criteria for insomnia disorder. These provided prevalence statistics between 19 and 45%. For those prevalence statistics measured using a validated questionnaire (e.g. ISI. BIQ, Sleep-50), the estimated prevalence was 10.6 – 83%. Estimated prevalence based on scoring on or above ISI 'subthreshold' insomnia (ISI score >7) was 17.7% in one study. Several studies based their prevalence estimate on scoring on or above ISI 'mild' insomnia (ISI score >10), giving estimations of 41.2 to 50%. Others based their overall estimate on scoring on or above 'moderate clinical insomnia' (ISI score >15), giving an estimated prevalence of 22.6 to 48%. Several studies included prevalence rates for each ISI severity category. These studies reported subthreshold or mild insomnia (ISI score >7) for 3.3 to 39.1%, moderate clinical insomnia (>15) for 10.5 to 35%, and severe clinical insomnia (>21) for 3 to 28.3%. Three studies using the Sleep-50 produced prevalence statistics of 10.6 to 60%. The BIQ gave an

estimated prevalence of 25% in an early intervention population. The OSQ based on DSM-IV criteria gave a prevalence of 7.9% and on ICD-10 criteria, 23.2% in the same sample.

Four studies reported prevalence based on more than one criterion. Batalla-Martin et al. (2020) report a prevalence of between 7.9% based on the OSQ using DSM-IV criteria for insomnia disorder, to 63% for any insomnia symptom. Freeman et al. (2009) report a prevalence of 60% on the Sleep-50 and 84% on the ISI (score >10). Mondal et al. (2018) report a prevalence of 66.7% on the ISI (>10) and 75% based on Harding (2004). One study (Reeve et al., 2019b) used a mixed-methods protocol to assess sleep disorders in people experiencing psychosis, estimating an insomnia disorder prevalence of 50%.

Three studies reported the prevalence of elements of insomnia – DIS, DMS, and EMA (Miller et al., 2021, Seow et al., 2018, Xiang et al., 2009). These studies had used bespoke clinical questionnaires and assessment, or the BIQ to assess insomnia. The reported prevalence of DIS was between 20.5% and 28.3%. The reported prevalence of DMS was between 18.3% and 23.6%. One study provided a pooled prevalence for DIS and DMS of 45% (Miller et al., 2021). The reported prevalence of EMA was between 6.7% and 27%.

1.4.6.2. Meta-Analyses

Pooled estimates of prevalence were calculated for i) those ten studies for which a *primary aim* was to determine the prevalence of insomnia ii) all fifteen studies which *reported* a prevalence of insomnia and iii) those seven studies which *used the ISI* to establish insomnia prevalence. For additional tables and figures, see Appendix 1.9.

Across those studies *aiming to establish prevalence*, the random-effects pooled prevalence of insomnia disorder or symptoms in nonaffective psychosis was 36.5% (95% CI=27.2–46.4%; Figure 2). The quality-effects pooled prevalence was 32.3% (95% CI=20.9–45%). The fixed-effects pooled prevalence was 32.9% (95% CI=31–34.9%). There was significant heterogeneity and variability across studies (I^2 = 95.1%, 95% CI=92.7-96.7%). Publication bias was assessed using a funnel plot (Appendix 1.9.1.). Measured prevalence statistics were highly variable and more extreme prevalence estimates were extracted from studies with small or moderate sample sizes.

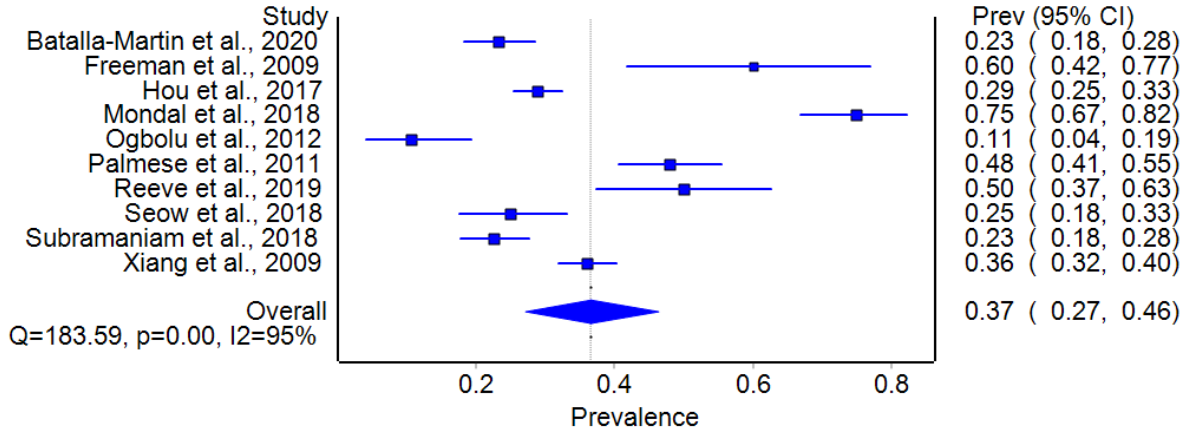

Figure 2. Random-effects forest plot for studies aiming to establish prevalence

Across *all studies reporting prevalence*, the random-effects pooled prevalence was 34.8% (95% CI=27.4–42.6%; Figure 3). The quality-effects pooled prevalence was 35.5% (95% CI=26–45.6%). The fixed-effects pooled prevalence was 36.9% (95% CI=35.6–38.1%). There was significant heterogeneity and variability (I^2 = 97.1%, 95% CI=96.2–97.8%). As this analysis included more studies, confidence intervals were narrower than those produced by only studies *aiming to establish prevalence*. Publication bias was assessed using a funnel plot (Appendix 1.9.2.). Measured prevalence statistics were highly variable and more extreme prevalence estimates were extracted from studies with small or moderate sample sizes.

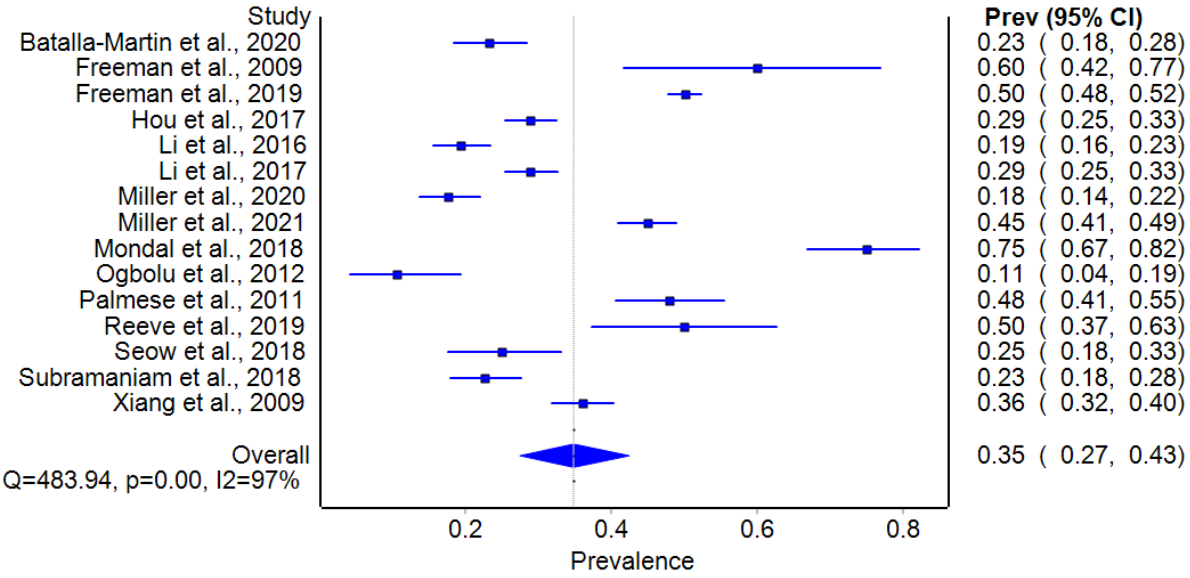

Figure 3. Random-effects forest plot for all studies reporting prevalence

Those *studies which used the ISI* to assess insomnia produced a random-effects pooled prevalence of insomnia disorder or symptoms of 45.6% (95% CI=32–59.6%; Figure 4). The

quality-effects pooled prevalence was 42.5% (95% CI=23.6–62.5%). The fixed-effects pooled prevalence was 43% (95% CI=42–45.5%). There was significant heterogeneity and variability (I^2 = 97.6%, 95%CI=96.4–98.3%). These pooled prevalence estimates are higher than those reported for *studies aiming to establish prevalence* or *reporting prevalence* statistics. The confidence intervals arising from this analysis were wider, suggesting that these results may be less reliable. This is partially due to fewer studies contributing to the estimate. Publication bias was assessed using a funnel plot (Appendix 1.9.3). This suggested that prevalence statistics were highly variable and that more extreme estimates were extracted from studies with smaller sample sizes.

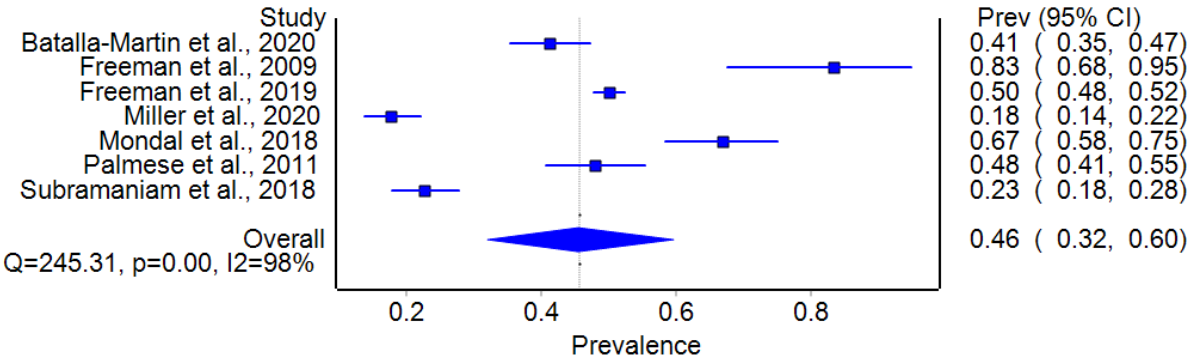

Figure 4. Random-effects forest plot for studies using the ISI

1.4.7. Insomnia and Symptomatology

1.4.7.1. Insomnia and Psychosis Symptomatology

Ten papers investigated the relationship between insomnia and psychosis symptomatology (Table 4). Most studies used ISI scores as a continuous variable in analysis (Freeman et al., 2019, Grezellschak et al., 2017, Miller et al., 2020, Miller et al., 2019, Palmese et al., 2011, Reeve et al., 2018, Subramaniam et al., 2018). The remaining three studies split their sample into those with or without insomnia, conducting between-group analyses (Hou et al., 2017, Miller et al., 2021, Xiang et al., 2009).

Two studies identified a significant positive relationship between insomnia severity on the ISI and PANSS total, positive symptom, and general scores (ρ=0.33, p=0.001; ρ=0.37, p<0.001; ρ=0.42, p<0.001, Miller et al. (2019); ρ=0.18, p<0.002; ρ=0.19, p<0.002; ρ=0.17, p<0.002, Miller et al. (2020)). Miller et al. (2021) demonstrated a correlation between early morning

awakening (as a yes/no categorical variable) and PANSS total, positive, and general scores (bivariate Spearman's rho ρ=0.11, p<0.001; ρ=0.1, p<0.001; ρ=0.13, p<0.001) but did not find a relationship between disrupted sleep initiation or maintenance and PANSS scores. In linear regression, controlling for confounding factors, early morning awakening was still associated with PANSS total, positive and general scores (β=0.12, p<0.001; β=0.11, p<0.001; β=0.14, p<0.001). In contrast, Subramaniam et al. (2018) found no relationship between ISI and PANSS scores in first episode of psychosis. Palmese et al. (2011) did not find a relationship between insomnia severity and CGI-S positive, negative or cognitive scores.

Table 4. Relationships between insomnia and psychosis symptomatology

Study	Insomnia Measure	Symptom Measure	Findings
Freeman et al., 2019	ISI	GPTS-B CAPS	Insomnia severity positively correlated with paranoia, hallucinations.
Grezellschak et al., 2017	ISI	PC	Insomnia severity positively correlated with paranoia; in a direct, total and indirect manner.
Hou et al., 2017	Bespoke questionnaire	BPRS	Insomnia presence related to more severe positive, negative, and anxiety symptoms.
Miller et al., 2019	ISI	PANSS	Insomnia severity significantly related to total positive, and general symptoms.
Miller et al., 2020	ISI	PANSS	Insomnia severity significantly related to total positive, and general symptoms.
Miller et al., 2021	Bespoke questionnaire	PANSS	EMA was associated with higher total, positive general symptoms.
Palmese et al., 2011	ISI	CGIS-S	Insomnia severity significantly associated with depressive and global symptoms.
Reeve et al., 2018	ISI	SPEQ	Insomnia predicts paranoia and hallucinations within and across time. This is mediated by depression and anxiety.
Subramaniam et al., 2018	ISI	PANSS	Insomnia severity not associated with positive, negative, or global symptom scores.
Xiang et al., 2009	Bespoke questionnaire	BPRS	Insomnia associated with severity of positive and anxiety symptoms.

Two studies using the BPRS found participants with insomnia had more severe positive and anxiety symptoms (Hou et al., 2017, Xiang et al., 2009). Hou et al. (2017) found that positive, negative and anxiety symptoms were more severe in the insomnia group (T/Z=5.4, p<0.001; T/Z=-4.7, p<0.001; T/Z=-6.1, p<0.001). Xiang et al. (2009) demonstrated that positive and anxiety symptoms were more severe in the insomnia group (T/Z=-5.3, p<0.001; T/Z=5.8, p<0.001), but negative symptoms were not.

Three studies examined a relationship between insomnia and paranoia or persecutory thoughts in people with nonaffective psychosis. Grezellschak et al. (2017) demonstrated that ISI scores are correlated with paranoia (ρ=0.47, p<0.01), insomnia has a direct effect on paranoia and that this is mediated by emotion regulation (t=2.18, 95% CI 0.55-1.99, effect=0.76, p=0.04). Freeman et al. (2019) found that ISI scores were significantly correlated with paranoia and with hallucinations (r=0.41, p<0.001; r=0.39, p<0.001). One other study found that insomnia was a significant predictor of paranoia and hallucinations within and across time (Reeve et al., 2018). These statistical relationships were mediated by depression and anxiety symptoms.

1.4.7.2. Insomnia, Psychotic Symptomatology and Mood

Whilst mood was not a focus of the review, several included studies assessed the relationship between insomnia and mood. Miller et al. (2021) found that EMA was significantly correlated with Calgary Depression Rating Scale for Schizophrenia total scores (CDSS; Addington et al., 1990; ρ=0.46, p<0.001). Hou et al. (2017) found that Montgomery–Åsberg depression rating scale scores were poorer in those with insomnia (Müller et al., 2003; T/Z=-8.4, p<0.001). Xiang et al. (2009) found that Hamilton Depression Scale scores were greater in those with insomnia (Hamilton, 1960; T/Z=-13, p<0.001). Palmese et al. (2011) found that insomnia severity was related to CGI-S depression scores and CDSS scores (F(3,109)=3.99, p=0.01; F(3,170)=9.03, p<0.001). As above, Reeve et al. (2018) found that anxiety and depression were significant mediators in the relationship between insomnia and paranoia or hallucinations, within and across time.

1.4.7.3. Insomnia, Psychotic Symptomatology and Suicidality

Four included studies examined the relationship between insomnia, psychosis symptomatology and suicidality (Li et al., 2016b, Miller et al., 2020, Miller et al., 2021, Miller et al., 2019). Miller et al. (2019) found that ISI scores were positively correlated with Beck Scale for Suicidal Ideation scores (BSSI; Beck et al., 1979; ρ=0.29, p=0.002). These remained significantly related to suicidal ideation in linear regression analysis controlling for confounds (including PANSS total; OR=1.14, 95% CI 1.01-1.28, p=0.029). BSSI scores also significantly varied across ISI categories. In logistic regression analysis controlling for confounding factors

(including PANSS total); ISI scores were significantly associated with a lifetime history of suicide attempt (OR=1.1, 95% CI 1.03-1.19, p=0.008). Insomnia was further associated with 15-fold increase in lifetime suicide attempt (OR=14.8, 95% CI 1.4-157, p=0.025).

Miller et al. (2020) found that participants reporting suicidal ideation (on the CDSS) had higher ISI total scores (p=0.03). The prevalence of insomnia was greater in those experiencing suicidal ideation (χ^2=9.39, p=0.02). Logistic regression, controlling for confounding factors, found that ISI score remained related to the presence of suicidal ideation (OR=0.10, 95% CI 1.02-1.19, p=0.017). However, they suggest that this relationship was caused by depressive symptomatology (related to both insomnia and suicidal ideation). In logistic regression analysis, insomnia was also associated with increased odds of lifetime suicide attempt (OR=1.07, 95%CI 1-1.13, p=0.046) and with a 2.5-fold increase in current suicidal ideation (OR=2.56, 95% CI 1.1-5.92, p=0.029).

Miller et al. (2021) studied suicidality and insomnia components. They identified that the prevalence of suicidal ideation was related to EMA (categorical variable; χ^2=5, p=0.03). Logistic regression, controlling for confounding factors, found that DIS and DMS were not significantly related to suicidal ideation. However, participants with DIS and DMS were more likely to have attempted to end their life by suicide in the last 6 months (χ^2=9.4, p=0.004). There was no relationship between EMA and recent attempt to end one's life. In logistic regression, controlling for confounds, DIS and DMS increased the risk of attempt to end one's own life by 5.5 fold (OR=5.5, 95% CI 1.4-21.2, p=0.013) but EMA did not.

Lastly, Li et al. (2016b) found a higher prevalence of suicide attempt in participants with insomnia at baseline (statistics not provided). Insomnia was also related to a higher likelihood of attempt to end one's life over the follow-up period (Hazard Ratio=4.63, 95% CI 1.4-15.36, p<0.05), after controlling for confounds.

1.4.7.4. Insomnia, Psychotic Symptomatology and Quality of Life

Several included studies examined quality of life. Batalla-Martin et al. (2020) assessed the relationship between the presence of insomnia and quality of life on the EuroQol (The EuroQol Group, 1990). Logistic regression demonstrated that the presence of insomnia was significantly related to poorer mobility (OR=3.54, 95% CI 1.88-6.65, p<0.001), self-care

(OR=2.69, 95% CI 1.36-5.32, p 0.004), activity (OR=3.56, 95% CI 1.97-6.44, p<0.001), pain/discomfort (OR=4.29, 95% CI 2.37-7.74, p<0.001), and anxiety/depression (OR=3.01, 95% CI 1.61-6.65, p=0.001) scores.

Subramaniam et al. (2018) demonstrated a relationship between ISI and WHOQOL (WHOQOL Group, 1994) scores in participants experiencing a first episode of psychosis. In multiple linear regression, controlling for confounding variables, higher ISI score was significantly related to poorer WHOQOL physical (β=-3.20, 95% CI -3.95-2.44, p<0.001), psychological (β=-2.46, 95% CI -3.45-1.48, p<0.001), social relationships (β=-3.06, 95% CI -4.01-2.12, p<0.001), and environment (β=-1.64, 95% CI -2.5-0.78, p<0.001) scores.

Hou et al. (2017) used the Short Form Health Survey (SF12; Ware Jr et al., 1996), demonstrating that SF12 mental scores were poorer in those with insomnia (T/Z=3.9, p<0.001). Using multiple linear regression, Li et al. (2017) found SF12 physical and mental scores were poorer in participants with insomnia (β=-1.96, p=0.01; β=-3.17, p<0.001). Xiang et al. (2009) demonstrated that WHOQOL physical (T/Z=-10.1, p<0.001), psychological (T/Z=-7.7, p<0.001), social relationships (T/Z= -5.9, p<0.001), and environment (T/Z=-4.9, p<0.001) scores were poorer for those with insomnia. When ANCOVA was used to control for confounding factors, those with insomnia still achieved poorer scores in the physical WHOQOL domain (F=6.6, p=0.01).

Palmese et al. (2011) found that insomnia severity (categorical) was related to Quality of Life Enjoyment and Satisfaction Questionnaire total scores (Ritsner et al., 2005; F(3,169)=8.52, p<0.001). Lower QOL was related to depression scores on the CDSS as well as insomnia severity (F(3,169)=44.9, p<0.001).

1.5. Discussion

We aimed to establish the prevalence of insomnia disorder or symptoms in people with nonaffective psychosis. As a secondary outcome, we characterise the relationship between insomnia and psychosis symptomology.

1.5.1. The Prevalence of Insomnia in Nonaffective Psychosis

Our results suggest that insomnia is prevalent in nonaffective psychosis, with an estimated pooled prevalence of 32.3% quality-effects and 36.5% random-effects across *studies primarily aiming to establish prevalence*, 35.5% quality-effects and 34.8% random-effects across *all studies reporting prevalence*, and 42.5% quality-effects and 45.6% random-effects in *studies using the ISI* to assess prevalence.

Across meta-analytic models, resulting pooled prevalence and estimated 95% confidence intervals varied. Fixed-effects models produced the narrowest confidence intervals, as they estimate only variance within studies and assume they are measuring a single underlying statistic (Tufanaru et al., 2015). They also lend the highest weighting to those studies with the largest samples. Where between-study heterogeneity is present, fixed-effects analyses greatly underestimate the variability in the resulting pooled prevalence (Brockwell and Gordon, 2001). Given the significant variability evidenced by I^2 and Q statistics in our analyses, fixed-effects models are not appropriate. Random-effects models produce wider confidence intervals as they estimate variance both within and between studies, and assume they are measuring an underlying statistic which differs between studies (Tufanaru et al., 2015).

Quality-effects models statistically estimate between-study variability weighted by study quality; therefore, the resulting confidence intervals depend partially on the appraised quality of included studies. They introduce another source of variance – the quality of the research undertaken. Whilst quality varied, assessed quality of reviewed studies was slightly lower in those reporting the highest prevalence of insomnia. Therefore, the resulting quality effects models typically provide a lower pooled prevalence than random-effects model results. However, most assessed quality ratings were moderate to high. Random-effects models can exacerbate bias in the resulting pooled prevalence when large study results differ from smaller study results, and when this difference is due to variability in the quality of studies

(Doi and Thalib, 2008). When a higher number of studies are included, confidence intervals narrow. As expected, the confidence intervals were narrowest when all studies reporting prevalence statistics are included and widest when only studies using the ISI are included.

It is not possible to directly compare the results of presented meta-analyses. The studies contributing to the pooled prevalence overlap between analyses (e.g. the n=7 studies using the ISI are included in the n=15 studies reporting a prevalence estimate). Studies using the ISI descriptively produce a higher pooled prevalence estimate for insomnia than both other prevalence estimates. This may suggest that use of the ISI overestimates insomnia prevalence. Importantly, these studies use different cut-off scores on the ISI to identify insomnia (from >7 to >15), and some of these studies use a lower cut-off to indicate insomnia than recommended (Morin et al., 2011). Future assessment of insomnia should use recommended cut-off values to identify clinically significant insomnia. Single prevalence statistics from included studies were extremely variable - between 7.9% and 75% across studies and methodologies. This resulted in relatively wide confidence intervals around pooled prevalence estimates.

The pooled insomnia prevalence statistics were above those estimates found in the general population (10-30%; Ohayon, 2002, Roth, 2007). Ohayon (2002) note that general population prevalence is highest for insomnia symptoms (approx. 30%) and lowest for insomnia disorder (approx. 6%). Morin et al. (2006) found that 29.9% of the general population present with one or more insomnia symptom and 9.5% meet criteria for DSM-V insomnia. Some studies included in our review estimate a much higher prevalence. Similarly, we found that those studies using strict DSM-IV or ICD-10 criteria produced the lowest prevalence estimates (7.9%), although most other included studies used validated measures based on DSM criteria. In research and clinical practice, valid and standardised definitions and assessment of insomnia symptoms or Insomnia Disorder should be used.

In the general population, western countries report higher prevalence of insomnia than Asian countries (Cao et al., 2017). The pooled prevalence of insomnia in China has been estimated as 15% (Cao et al., 2017), whilst the prevalence of insomnia in the USA and Europe is estimated as ~30% (Roth, 2007). The selected studies reviewed in this work originate in both Asian and western countries. Studies undertaken in China or Hong Kong (Hou et al., 2017, Li

et al., 2016b, Li et al., 2017, Miller et al., 2021) and Nigeria (Ogbolu et al., 2012) produced lower prevalence estimates than those undertaken in the western world. There is some evidence that insomnia may vary by ethnicity and socioeconomic status (Whinnery et al., 2014) and that severity is related to minority ethnicity and experiences of racial discrimination (Cheng et al., 2020). Most included studies described the race or ethnicity of their participants. However, prevalence data were not presented by ethnicity therefore these effects could not be studied. Clinicians working with people affected by psychosis should be aware that insomnia is likely prevalent in their population, particularly given the higher proportion of people of minority ethnicity.

Insomnia symptoms increase with age in the general population (Ohayon, 2002, Roth, 2007). Delayed sleep initiation is also more prevalent in adolescents and young adults (Kocevska et al., 2021). Participants sampled in our review were relatively homogenous in age and prevalence estimates found in first episode populations did not descriptively differ from those examining older participants. Insomnia prevalence is higher in women in the general population (Zeng et al., 2020, Zhang and Wing, 2006). Most studies included in our systematic review recruited more men (34.8 to 75.2% male), as is typical for populations of people with nonaffective psychosis (Aleman et al., 2003).

Only one included study provided a breakdown of prevalence estimate by diagnosis within nonaffective psychosis diagnoses (Li et al., 2016b). However, there were not sufficient participants in each category to draw any conclusions.

No included study examined insomnia prevalence in prodromal groups. Only three studies examined insomnia prevalence in first episode psychosis groups, limiting the conclusions that can be drawn about the prevalence of insomnia in different nonaffective psychosis subpopulations. Work to establish the prevalence of sleep disorders and insomnia specifically in these subgroups would be of use. Compared to nonaffective psychosis, the estimated prevalence of insomnia in bipolar disorder is ~40% (Laskemoen et al., 2019, Steinan et al., 2016) and in depression ~80% (Ohayon, 2002, Ohayon et al., 2000). It is difficult to directly compare estimated prevalence statistics between diagnostic groups due to large heterogeneity in study designs, sample size, recruitment methods and methods of measuring insomnia.

A small subset of studies deconstructed insomnia into associated features (difficulty initiating sleep, maintaining sleep, early morning wakening). As with overall prevalence estimates, these results were very variable but higher than those in the general population (Morin et al., 2006). Cohrs (2008) suggest that up to 80% of people with schizophrenia experience at least one symptom of insomnia. Polysomnographic work in nonaffective psychosis has identified that longer sleep onset latency, increased wake time after sleep onset and earlier wakening are common (Chan et al., 2017, Chouinard et al., 2004), all of which are features of insomnia. Actigraphy work has also identified features of insomnia including longer sleep onset latency and more fragmented sleep in schizophrenia (Wee et al., 2019). Additionally, overall time asleep, sleep efficiency, REM sleep and slow wave sleep are atypical in nonaffective psychosis (Chouinard et al., 2004, Reeve et al., 2015) and there is evidence that overarching circadian rhythms are affected (Monti et al., 2013). In addition to insomnia, the prevalence of sleep apnoea (Sharafkhaneh et al., 2005), hypersomnia (Hawley, 2006, Hawley et al., 2010) and nightmare disorder (Reeve et al., 2019b, Sheaves et al., 2015) are increased in nonaffective psychosis.

No included study examined insomnia symptoms across time. Previous research has suggested that sleep disturbance predicts the transfer from prodromal to first episode psychosis (Ruhrmann et al., 2010). Sleep disorder is prevalent in prodromal psychosis (Tan et al., 2001) and is tightly linked to experienced symptomatology across time in this group (Lunsford-Avery et al., 2015). Reeve et al. (2019a) found that shorter sleep duration is associated with increased symptomatology over time in people experiencing prodromal psychosis. The relationship between insomnia and psychosis symptoms are thought to be bidirectional in schizophrenia (Cosgrave et al., 2018). Longitudinal work examining the relationship between sleep disorder, emergent symptomatology, symptom severity and the recovery arc would be of great value.

1.5.2. Measuring Insomnia and Psychosis

Included studies used robust methods of insomnia assessment (including multiple measurements), specific questionnaire measurements of insomnia, and/or researcher or clinician-designed discrete questions about insomnia. Most included studies used self-report measures. This is a common diagnostic approach for insomnia disorder in addition to clinical

interview, however some authors suggest that self-report may be less reliable in determining sleep features than objective (actigraphy or polysomnography; Vadas et al., 2015). Our systematic review did not include identification of insomnia using tools intended to measure another construct, such as the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) or Epsworth Sleepiness Scale (Johns, 1991). These measures primarily aim to measure other constructs of sleep (quality and daytime somnolence) and do not accurately characterise insomnia (Faulkner and Sidey-Gibbons, 2019). Symptoms of psychosis were measured using validated questionnaires including the PANSS, BPRS, GPTS, CAPS, SPEQ, PC and CGIS-S. Measurement variability for both insomnia and psychosis symptoms will contribute to heterogeneity in pooled prevalence estimates and uncertainty in the relationship between insomnia and symptoms.

1.5.3. Insomnia and Psychosis Symptomatology

The quality of cross-sectional analytical studies included was high. Several studies provided evidence for a relationship between insomnia severity and overall or positive symptoms, including hallucinations and paranoia. The relationship between insomnia and negative symptoms was less clear – one study found that those with insomnia had higher negative symptoms, whilst others did not. Sleep disorder is related to psychosis-like experience in the general population (Barton et al., 2018). In people with psychosis, sleep disorder is associated with increased symptomatology; including severity of flattened affect, hallucinations, and delusion (Davies et al., 2017, Reeve et al., 2015).

Several included studies found a relationship between insomnia and anxiety and depression subscales within psychosis measures. Others found increased anxiety and low mood in participants with higher insomnia symptoms. In the general population, insomnia is associated with increased risk of low mood or anxiety (Ford and Kamerow, 1989, Li et al., 2016a) and the relationship between insomnia and mood disorder is bidirectional (Jansson-Fröjmark and Lindblom, 2008). Two included studies demonstrated that the relationship between insomnia and psychosis symptomatology is mediated by affect or affect regulation (Grezellschak et al., 2017, Reeve et al., 2018).

Insomnia is associated with increased risk of suicidal ideation and attempt in the general population (Russell et al., 2019, Lin et al., 2018). People affected by psychosis are at a higher risk of suicide than the general population (Depp et al., 2016). Included studies assessing suicide in nonaffective psychosis found that greater insomnia was related to higher suicidal ideation and a greater risk of attempting to end one's own life prior to assessment and by follow-up, thus suggesting insomnia increases the vulnerability in an already vulnerable population (Li et al., 2016, Miller et al., 2020, Miller et al., 2021, Miller et al., 2019). The relationship between insomnia and suicidality in psychosis may be mediated by depressive symptomatology (Miller et al., 2020).

Insomnia is associated with poorer quality of life in non-clinical populations (Kyle et al., 2010). Some included studies assessed quality of life, demonstrating that insomnia is related to poorer quality of life across domains (mobility, self-care, activity, pain, and anxiety or low mood). Research generally indicated that mental-health related quality of life was more impacted than physical quality of life. Published works have linked poorer sleep to positive symptom severity and poorer quality of life (Afonso et al., 2014).

1.5.4. Treatment for Insomnia

Cognitive behavioural therapy is effective in treating insomnia (CBTi; Okajima et al., 2011, Trauer et al., 2015) and is considered gold-standard treatment (Wilson et al., 2019). It has been shown to be more effective than medication (Trauer et al., 2015) and effective in diverse mental health populations (Mitchell et al., 2012). Whilst the evidence base for use with people experiencing psychosis is in its infancy, initial results suggest that CBTi is effective in reducing insomnia and has mixed impacts on psychosis symptomatology (Freeman et al., 2015, Myers et al., 2011). Different insomnia symptom profiles are associated with different response to CBTi in nonaffective psychosis (Chiu et al., 2018, Waters et al., 2020). Furthermore, people with nonaffective psychosis identify sleep disorder as a desirable target for intervention (Chiu et al., 2016, Waite et al., 2016) and express preference for CBTi over medication (Waters et al., 2015).

1.5.5. Limitations

There are several limitations to the present systematic review and meta-analysis. We included only studies published in English. Studies were not excluded by quality, due to the small number of studies meeting eligibility criteria. However studies were generally of moderate or good quality. The definition and assessment of insomnia disorder or insomnia symptoms was diverse, increasing the variance observed in results and limiting conclusions drawn. Between-study variations in sample size, design, and quality limit how findings can be interpreted, however as described we attempted to correct for this in meta-analysis. It is likely that publication bias impacted on the presented results. We did not consider the impact of psychoactive medication. Atypical antipsychotic medications have been shown to be related to improved sleep in psychosis (Haffmans et al., 2004), and may explain why lower insomnia prevalence was found in inpatient populations. No included papers assessed prodromal psychosis and few studies examined first episode populations. This meant that no conclusions could be drawn about the development of insomnia prevalence with the development of psychosis.

1.6. Conclusions

Insomnia is prevalent in nonaffective psychosis and is related to more severe positive and overall symptomatology, mood difficulties, suicidal ideation or attempt, and reduced quality of life. Clinicians working with people experiencing psychosis should be aware of the prevalence of insomnia and offer targeted assessment and evidence-based intervention for sleep disorder. Furthermore, they should be aware that insomnia is not simply an outcome of psychosis symptomatology but a primary disorder which may drive increased psychosis and mood symptomatology. Research investigating insomnia prevalence and symptom correlates should use standardised definitions of insomnia disorder and insomnia symptoms and standardised and validated methods of assessment of insomnia and psychosis symptomatology. Further research which explores i) the prevalence of insomnia in prodromal and first episode psychosis populations, ii) the relationship between psychosis symptom profiles and insomnia disorder or symptoms, and iii) how the presence of insomnia impacts response to treatment in nonaffective psychosis would be of benefit.

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Chapter 2: Implementation of a Digital Cognitive Behavioural Therapy Intervention for Insomnia in First Episode Psychosis in the Context of Covid19- A Pilot Mixed Methods Study

Prepared in accordance with submission guidelines for Digital Health (Appendix 2.1.)

2.1. Plain Language Summary

Background: Covid-19 and regulations negatively affect population mental health and sleep. They likely have a bigger impact on people who already have mental health conditions, including psychosis. Psychosis means experiencing or believing things that are not real and having confused thoughts. Difficulty falling or staying asleep ('insomnia') is common in people with psychosis, including people experiencing psychosis for the first time (a 'first episode'). People with worse insomnia have worse psychosis symptoms. We know worry makes insomnia worse. Due to Covid19, insomnia and worry could worsen and increase psychosis symptoms. Cognitive Behavioural Therapy is a psychotherapy that is effective in reducing insomnia (CBTi) in people with or without psychosis. CBT for insomnia can be delivered digitally (dCBTi) and could be accessed remotely during lockdown.

Method: We wanted to know if dCBTi could work for people experiencing a first episode of psychosis (FEP) and insomnia, during Covid19. We investigated how people use a dCBTi application. We studied whether symptoms of insomnia, psychosis, mood and worry changed when using dCBTi and how they related to each other. We also wanted to know what people with FEP and keyworkers in FEP services thought about the application. We used this information to build a model to describe how dCBTi can be used in services.

Keyworkers working with people experiencing a FEP provided information about the study. If they wanted to take part, we contacted them to seek consent and check if they had insomnia. We met participants by videocall to measure psychosis, insomnia, mood, and Covid-19-related worry before we began and after intervention. The intervention had 6 sessions, completed on an application. We recorded how people use the application. People with FEP and keyworkers had the option of taking part in interviews before and after they used it, to tell us about their expectations for and experiences of the application. This paper presents initial information from the study.

Results: 10 people talked to us about participating. 3 did not want to participate and 1 did not do the assessments. 5 people participated. Interviews with keyworkers helped us learn about their expectations for the application. They talked about people having lots of sleep difficulties, interventions they already have, beliefs about the application, and things about

service users and the service that might help or hinder the application being used. We used these results to build a model for how Sleepio might work or might not work in the service.

Ethical Issues: Joining or not joining the study will not have effect anyone's usual treatment. We will tell people that we will tell someone if we are worried about their safety or someone else's. We will warn them that it might be distressing to use the application or to talk about their symptoms. We have permission from NHS ethics to start the study. All data will be kept secure and only researchers will see it. Participants' data will not be linked to their name.

Practical Applications: We want to share our results in different ways with other researchers, clinicians, and people with psychosis. This research could help services use dCBTi to help people with psychosis.

2.2. Abstract

Background: Covid19 has impacted on population sleep and mental health; disproportionately affecting individuals with pre-existing mental health difficulties, including first episode psychosis (FEP). Given that insomnia is prevalent in FEP, associated with more severe psychosis, and can be ameliorated using digital Cognitive Behavioural Therapy (dCBTi); it may provide a viable treatment target during Covid19.

Aims: We present preliminary data from a mixed-methods process evaluation of the implementation of dCBTi (Sleepio) in FEP services in NHS Scotland, informed by the MRC complex interventions framework. We aimed to collect data on the implementation of Sleepio, characterise service user symptomatology, and elicit service user and clinician expectations for Sleepio. We provide a working logic model of implementation.

Method: People experiencing FEP and insomnia were eligible to access Sleepio. Implementation data was recorded and summarised (service integration, referrals, eligibility, consenting). Consenting service users' sleep, psychosis, mood and Covid19-worry were assessed and summarised. Service users and keyworkers were invited to participate in semi-structured interviews regarding expectations for Sleepio implementation. Interviews were recorded and transcribed. Framework analysis was used to analyse interviews.

Results: 10 service users were referred. 3 declined to participate and 1 did not engage. 5 were eligible to participate and completed assessment. Interviews revealed facilitators and barriers to Sleepio implementation related to: sleep difficulties, existing interventions, beliefs about Sleepio, service user factors and service-based factors.

We provide initial description of the implementation of Sleepio dCBTi application in FEP services in NHS Scotland, including a preliminary working logic model.

2.3. Introduction

Coronavirus-19 (Covid19), quarantine, restrictions to lifestyle and impacts on health and social care provision have challenged population mental health (Dean et al., 2021). The impacts of Covid19 and other pandemics increase insomnia and sleep disorder, low mood, anxiety and overall psychological distress (Brooks et al., 2020, Casagrande et al., 2020, Hossain et al., 2020, Lin et al., 2021, Yan and Huang, 2020). Morin and Carrier (2021) found a high rate of acute insomnia in the general population during Covid19, with a risk of this rate increasing (Casagrande et al., 2020). Covid19-related worry, depression symptoms and anxiety are each associated with increased insomnia (Kokou-Kpolou et al., 2020, Voitsidis et al., 2020, Wright et al., 2020). In Scotland, Covid19 reduced psychological wellbeing and increased sleep problems, particularly in those with pre-existing mental health difficulties (Public Health Scotland, 2020). There is therefore a need for scalable insomnia interventions, which can be delivered within the current context.

People with pre-existing mental health conditions are disproportionately affected by mental health impacts of pandemics (Brooks et al., 2020) and experience poorer psychological outcomes during Covid19 (Kokou-Kpolou et al., 2020, Li et al., 2020, O'Connor et al., 2021). People recovering from a first episode of psychosis (FEP) are one such group. Psychosis describes a group of symptoms including disorganised thoughts and speech, voice-hearing, visual hallucinations, unusual strongly held beliefs (together referred to as 'positive symptoms'); alogia, avolition, asociality, anhedonia and reduced affect expression (together referred to as 'negative symptoms'; Wigman et al., 2011). This population present with mental, physical and social comorbidities (Gates et al., 2015), which may further increase their vulnerability to distress (Wright et al., 2020). Covid19 may increase the risk of developing psychosis (Brown et al., 2020, Valdés-Florido et al., 2021) and may increase psychosis symptomatology (Kozloff et al., 2020, Strauss et al., 2021).

Outwith Covid19, sleep disorders are common in people with psychosis (Laskemoen et al., 2019, Reeve et al., 2015). Common sleep disorder presentations include nightmares (~50%, Sheaves, Onwumere, Keen, Stahl, & Kuipers, 2015), sleep apnea (Sharafkhaneh et al., 2005) and hypersomnia (~30% Laskemoen et al., 2019; Hawley et al., 2010). However, insomnia is

considered the most prevalent, with estimates ranging from 7.9% to 75% (Batalla-Martín et al., 2020, Freeman et al., 2009, Mondal et al., 2018, Palmese et al., 2011). Sleep disorders are prevalent in FEP – around 80% present with a sleep disorder and comorbidity is typical (Davies et al., 2017, Ma et al., 2018, Reeve et al., 2019b). The estimated prevalence of insomnia in those experiencing a first episode of psychosis is ~50% (Reeve et al., 2019b).

Sleep disorder and insomnia have been explored as contributing and causal factors in experiencing psychosis (Dolsen et al., 2014, Harvey et al., 2011, Koyanagi and Stickley, 2015). Sleep disorder predicts psychotic-like experience in the general population (Freeman et al., 2011, Freeman et al., 2012, Sheaves et al., 2016), symptoms in prodromal populations (Lunsford-Avery et al., 2017, Lunsford-Avery et al., 2015, Poe et al., 2017) and in early psychosis (Lunsford-Avery et al., 2015, Reeve et al., 2019a, Tan et al., 2001). In people with early or established psychosis, severity of sleep disorder is related to increased positive psychosis symptoms, increased cognitive disorganisation, and reduced affect (Chung et al., 2018, Davies et al., 2017, Kilicaslan et al., 2017, Reeve et al., 2018, Reeve et al., 2019b). The relationship between psychosis and insomnia occurrence is bidirectional (Reeve et al., 2018, Reeve et al., 2015).

In the general population, the relationship between paranoia and sleep is mediated by mood disorder (Freeman et al., 2011, Freeman et al., 2009, Taylor et al., 2015). In psychosis, sleep disorder and psychosis symptomatology remain related to mood (Dolsen et al., 2014, Reeve et al., 2018). Models of paranoia and persecutory delusions suggest that anxiety, depression and worry link the development of sleep disorder and paranoia (Freeman et al., 2009, Reeve et al., 2015). In the current context of Covid19-related worry and Covid19 regulations, sleep may deteriorate in people affected by FEP, impacting on mood and psychosis symptomatology.

The relationship between sleep disorder and psychosis symptomatology has led to exploration of sleep as an intervention target (Freeman et al., 2015, Waite et al., 2020). People with psychosis appreciate sleep disorder intervention (Waters et al., 2015). Insomnia is a tractable clinical target in this population and Cognitive Behavioural Therapy (CBTi) shows promising results in reducing insomnia and potentially paranoia (Chiu et al., 2018, Freeman et al., 2015, Myers et al., 2011). Whilst CBTi may be effective, it cannot be scaled to meet the

need in this population (Espie, 2009, Reeve et al., 2019b). In the current context, there is an opportunity for digital psychological interventions, delivered remotely. Digital CBTi (dCBTi) is effective in improving insomnia (Seyffert et al., 2016). dCBTi application Sleepio (Big Health Ltd) has a comparative efficacy to in-person CBTi (Espie et al., 2012). Freeman et al. (2017) found Sleepio reduced insomnia, hallucinations and paranoia in a non-clinical population. Additionally, digital interventions are increasingly used in FEP populations (Rus-Calafell and Schneider, 2020) and service users are positive about their use (Bucci et al., 2018).

Sleepio provides a psychotherapeutic intervention which can be offered remotely in the context of Covid19. This intervention targets insomnia, a common comorbid difficulty in FEP and common impact of the pandemic. Whilst highly scalable, dCBTi is a complex intervention for a multifaceted problem. The intervention comprises multiple interacting components which are implemented in a complex National Health system composed of a complicated population, staff factors, service user factors, and service factors (Craig et al., 2008). We therefore intend to conduct a process evaluation of the implementation of the Sleepio intervention through the lens of the Medical Research Council Complex Interventions Process Evaluation Framework (Moore et al., 2015).

2.4. Method

2.4.1. Aims and Objectives

We aimed to collect preliminary data to build a working logic model of digital CBTi implementation in NHS Scotland FEP services. The data comprises: a description of the initial process of implementation, characterisation of participating service users' symptomatology, and framework analysis of service user and keyworker expectations for Sleepio intervention.

2.4.2. Design

Informed by the Medical Research Council (MRC) process evaluation for complex interventions framework (Moore et al., 2015; Figure 5); the overarching project is a prospective, non-randomised process evaluation of Sleepio implementation in a FEP service in NHS Scotland, in the context of Covid19. Process evaluations aim to explore components of complex interventions, their implementation, and how stakeholders interact with them (Maar et al., 2017, Moore et al., 2015). They allow theories of implementation to be developed and elucidate factors that will likely impact upon future efficacy evaluations (Maar et al., 2017). A logic model is being developed to graphically describe the process of Sleepio implementation as adjunct to usual care of people recovering from FEP.

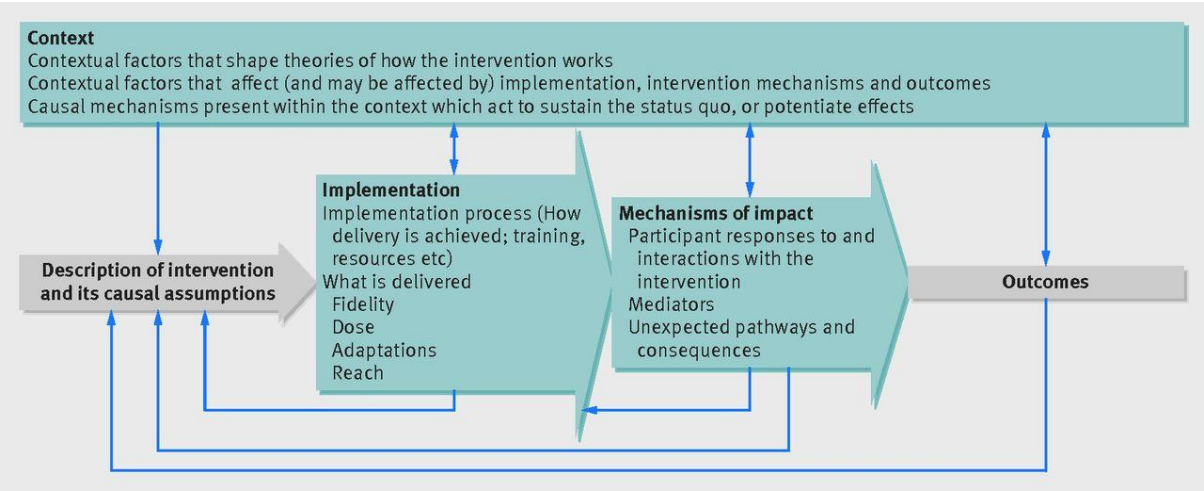

Figure 5. Process evaluation of complex interventions framework demonstrating key functions and components (blue boxes) of process evaluation and relations among them (Moore et al; 2015).

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This Major Research Project (MRP) provided initial data for a larger implementation study (for MRP proposal, see Appendix 2.2, for protocol see https://osf.io/2ja3s/). The wider project will continue to collect implementation data to understand the mechanisms of Sleepio's impact, outcomes and other factors acting upon the model.

2.4.3. Approvals and Ethics

The study has approval from the West of Scotland Research Ethics Service (ID 21-WS-0010; Appendix 2.3.), NHS Greater Glasgow and Clyde (ID GN21MH015; Appendix 2.4.), and service management (Appendix 2.5.). A controller-to-controller agreement was created between NHS Greater Glasgow and Clyde and the University of Glasgow. A contract was instigated between Big Health and the University of Glasgow. The timeline of these required approvals and contracts was eight months (September 2020-April 2021). The implementation trial was registered on ClinicalTrials.gov (NCT05050201).

2.4.4. Participants

Participants were service users of an FEP service in NHS Scotland and keyworker clinicians. Eligible service users were 16-35yrs old and had access to a device to use the application. They were required to pass screening for insomnia. Service users were ineligible to participate if their psychosis was thought to be organic, they were acutely unwell (contact with crisis team or hospitalization within the last month), had a moderate or severe learning disability, insufficient English to understand the application, or could not give informed consent. Eligible staff participants held the role of keyworker and were currently employed by the service. Keyworkers were community psychiatric nurses or occupational therapists.

2.4.5. Procedures

To establish study referrals and implementation, the study protocol was presented at the service journal club and each area multidisciplinary team meeting by researcher FR. Weekly emails were sent to service clinicians to maintain awareness about the study. Researcher FR met informally with 12 keyworkers to discuss service users who may be suitable for referral and to clarify eligibility criteria. Ongoing recruitment was prompted via weekly email to all

clinicians and discussion at psychosocial intervention supervision by author MS. Recruitment to the study took place over 11 weeks, between 20/04/2021 and 09/07/2021.

2.4.5.1. Keyworker Participants

Keyworkers were given an information leaflet describing the study, detailing i) eligibility criteria, ii) the pathway for recruiting service users and iii) the role of keyworkers as participants.

Keyworkers were given the opportunity to participate in semi-structured interviews with FR via Microsoft Teams videocall; about their expectations of Sleepio, and anticipated barriers and facilitators to its implementation. Interested keyworkers were provided with a Participant Information Sheet and Consent Form by email. Information Leaflets, Participant Information Sheets and Consent Forms are available at https://osf.io/2ja3s/. Participating keyworkers completed consenting procedures on Microsoft Teams and returned signed Consent Forms by email. Interviews were conducted by researcher FR, who is a clinician in the FEP service. Participants took part in interviews from private spaces; including their work, home, and car. Interviews lasted 24 to 35 minutes. Reflective notes were recorded after each interview. All interviews took place prior to service users beginning the intervention. Interviews were audiovisually recorded and transcribed and recordings were checked against transcriptions to ensure these were verbatim. Identifiable information was manually removed (e.g. service users' names). Recruitment was continued until no further keyworkers expressed interest in participation.

2.4.5.2. Service User Participants

Keyworkers in the service were offered the opportunity to meet informally with FR to learn about the study and consider service users who may be eligible.

Service users experiencing sleep difficulties were provided with an information leaflet by their keyworker. Interested persons were sent a Participant Information Sheet and Consent Form by post. Information Leaflets, Participant Information Sheets, and Consent Forms are available on https://osf.io/2ja3s/. Researcher FR called potential participants to give them the opportunity to ask any questions. They were encouraged to speak to others about potential participation. Participants completed consenting processes on an Attend Anywhere videocall and returned signed Consent Forms by post.

Participants were given the option to participate in semi-structured interviews prior to assessment, exploring their expectations of Sleepio, and anticipated barriers and facilitators to its implementation. Following consenting procedures, eligibility screening was undertaken, including the Sleep Condition Indicator-2 item insomnia screening tool (SCI-02; Espie et al., 2014, Luik et al., 2019). This is a reliable and validated screening measure, which correlates with insomnia measures. Where individuals' score indicated that they may be affected by insomnia, they were eligible to participate.

FR met with participants to complete initial assessment using Attend Anywhere. This comprised clinical assessment of participant sleep and completion of baseline symptomatology measures on Online Surveys (https://www.onlinesurveys.ac.uk/). Sleepio was launched and participants completed its initial assessment. The intervention period then began and adherence to and attrition from the intervention was collated.

2.4.6. Sleepio Intervention

Sleepio (Big Health Ltd) is a digital CBT intervention application, used on a computer or iOS smartphone. Sleepio is composed of six 20-minute sessions presented by an animated therapist, unlocked weekly. Participants complete initial assessment in the application and chose a treatment goal. Sleepio's sessions are based on a 6-session CBTi protocol (Harvey, 2002) and include: i) psychoeducation on sleep hygiene and processes; ii) cognitive components including restructuring, mindfulness, positive imagery, paradoxical intention training, and resolving thoughts about the day; and iii) behavioural components including sleep restriction, stimulus control, and relaxation techniques. Participants book digital 'appointments' with the therapist and receive prompts to complete them, enter sleep data, and complete the Sleep Condition Indicator on a weekly basis. The Sleepio algorithm tailors ongoing intervention based on input data about participants' sleep, physical and mental health. Sleepio also provides access to online psychoeducation and a clinician-moderated user forum.

Keyworkers were provided with access to the 'Sleep Clinic', Sleepio's clinician interface. Here, allocated professionals can observe session completion rates, data entered and Sleep Condition Indicator scores for participating service users. Service users explicitly consented to their keyworker having access to these data via the Sleep Clinic.

2.4.7. Data Collection

2.4.7.1. Process of Implementation

Implementation data aimed to capture the 'pathways' of the study and service users in the study. We summarised i) the pathway of approval for Sleepio in the context of a FEP service (required approvals, contracts, timelines), ii) the establishment of the referral pathway within the service (awareness raising events, meeting with clinicians) and iii) recruitment into the study (rates of referral, rates of consenting, reasons for not consenting, eligibility, reasons for ineligibility, completion of initial assessment).

2.4.7.2. Characterisation of Symptomatology

We aimed to characterise service users' insomnia, psychosis symptoms, mood, and Covid19-related worry prior to starting Sleepio intervention.

Insomnia symptoms were assessed using the Insomnia Severity Index (ISI; Bastien et al., 2001). This brief self-report questionnaire assesses the severity of night-time and day-time components of insomnia. It is widely used, reliable and valid, and is responsive to change.

Participants will be regularly prompted within Sleepio to complete the full Sleep Condition Indicator (SCI; Espie et al., 2014). The SCI is an 8-item scale measuring sleep problems against DSM-5 criteria for Insomnia Disorder. It has good validity and reliability and is sensitive to change. These scores will be available for analysis for the overarching project.

Psychotic symptoms were assessed using the Specific Psychotic Experiences Questionnaire; hallucinations subscale (SPEQ-H; Ronald et al., 2014) and Revised Green et al Paranoid Thought Scales (R-GTPS; Freeman et al., 2021) The SPEQ is a transdiagnostic self-report measure of psychosis symptomatology, with subscales for 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 were assessed using the Depression, Anxiety and Stress Scales 21 item (DASS-21; Antony et al., 1998). The DASS-21 is a widely used measure of depression, anxiety, and stress.

Covid19-related worry was assessed using the Fear of Covid19 Scale (Ahorsu et al., 2020). This scale is new but has relatively good psychometric properties and is validated (Bitan et al., 2020, Perz et al., 2020, Soraci et al., 2020).

2.4.7.3. Qualitative Interview Data

Semi-structured interviews were employed to ascertain service user and staff expectations of Sleepio implementation. Interview schedules were developed to explore service users and keyworkers expectations for digital intervention for sleep difficulties in EIP services; including their perceptions of any barriers and facilitators and anticipated mechanisms of change. Interview schedules are available on https://osf.io/2ja3s/. The schedules were developed from the MRC Complex Interventions Process evaluation framework (Moore et al., 2015), including questions exploring the i) context of the intervention, ii) factors of its implementation and iii) the anticipated mechanisms of its impact. The research team developed questions collaboratively in discussion. We aimed to develop dialogue based on the key topics of the guide, whilst allowing exploration of emerging themes.

2.4.8. Data Management

Raw data were stored within NHS Greater Glasgow and Clyde on a password-protected server. Anonymised data were stored in a password-protected server in the University of Glasgow. Anonymised Sleepio usage data were collated by Big Health Ltd and transferred to the University of Glasgow.

2.4.9. Analysis

2.4.9.1. Process of Implementation

Summary descriptive and quantitative information is provided for implementation measurements. These comprise: approvals and time taken to procure necessary approvals (data protection, ethical, contracts), number of presentations to the FEP service, number of information sessions delivered, number of meetings with service keyworkers, rate of referral, rate of consent to participate, reasons for not consenting, rate of eligibility, and the proportion completing Sleepio initial assessment.

2.4.9.2. Characterisation of Symptomatology

Symptomatology measurements are quantitatively described using measures of central tendency and dispersion. Our study was not designed nor powered to detect statistical differences in measures over time.

2.4.9.3. Qualitative Framework Analysis

We aimed to explore service user and keyworker expectations as an individual and collective phenomenon, within the context and social reality of participants (Holloway, 2005). Whilst framework analysis is not bound by an epistemological position (Ritchie and Spencer, 2002), we took a post-positivist contextual constructionism stance. The results of the analysis were considered subjective from the position of both participants and the researcher, and specific to their context and to individuals (Madill et al., 2000). We report our qualitative analysis as per the COREQ checklist (Appendix 2.6.).

We used an inductive thematic framework analysis (Braun and Clarke, 2006, Ritchie et al., 2003) to examine patterns of categories across our participants. As stated, the interview schedule framework was based upon the MRC Complex Interventions process evaluation framework (Moore et al., 2015). Ritchie and Spencer (2002) suggest that framework analysis is a useful approach for questions of context (e.g. 'what is the context of Sleepio implementation?') and strategy (e.g. 'how can Sleepio be implemented in this FEP service?'). This approach allowed us to meet our aim of capturing expectations for Sleepio dCBTi intervention and its implementation, whilst allowing additional themes to inductively expand the framework (Ward et al., 2013).

Video recordings of interviews and transcriptions were iteratively reviewed alongside reflective notes to familiarise researcher FR to the data. Initial indexing to the thematic framework and inductive coding of emergent themes was undertaken by FR (see Appendix 2.7.). Themes were reviewed and refined through interaction with the raw data and discussion with co-investigators at research meetings. Categories and subcategories were charted and mapped into a framework matrix. The final phase of analysis was to select representative quotes to illustrate the subcategories and synthesise the results.

Researcher FR (PhD) is a female trainee clinical psychologist, trained in qualitative methodology specifically Interpretative Phenomenological Analysis. At the time the

interviews were undertaken, she worked in the FEP service and had existing professional relationships with some keyworker participants. The field researcher for the project works for the service as a principal clinical psychologist and the chief investigator collaborates frequently with the service to undertake research. This provided the research team with additional insight into barriers and facilitators to Sleepio implementation, but also acts as a source of bias in interpretation, influencing the results. Reflective notes kept during the data collection process helped the researcher FR reflect on sources of bias.

As the service has a small staff group, we report limited summary demographic information about keyworker participants (gender and professional group only) to reduce the risk of deanonymization. However, researcher FR was familiar with keyworkers, their professional role in the team, and relative experience when undertaking and analysing interviews.

2.4.10. Preliminary Logic Model

A logic model of Sleepio implementation in FEP services is being developed. A preliminary version is presented and discussed, aiming to shape the ongoing implementation of Sleepio in the service.

2.5. Results

2.5.1. Process of Implementation

The service population includes ~250 service users, with ~150 new service users per year. Around 80% would be expected to experience clinically significant sleep difficulties and around 50% to experience Insomnia Disorder (Reeve et al., 2018). Ten service users expressed interest in the study and were sent participant information. These referrals originated from three of four FEP area teams (five from the north east team, two from the north west team, and three from the south team) and seven individual keyworkers. Three declined to participate for the following reasons: involved in too many interventions, did not want their GP to be notified, and sleep improved. One potential participant did not engage with assessment processes. Five participants completed screening and met criteria for participation (SCI-02 mean score 1.4, range 0-2; Table 6.). Four participants intended to use Sleepio on a computer or laptop and one intended to use an iPhone. Five participants completed study initial assessment (sleep assessment and completion of measures) and were set up with the intervention (age range 21-33, mean 28.4yrs, 3/5 male, all White British).

At present, four service users have started using Sleepio (one paused their use of the intervention after starting, due to losing access to a suitable device). Two have not begun the intervention.

2.5.2. Characterising Service User Participants

Clinical assessment of sleep indicated that all consenting service users were experiencing insomnia (Table 5). Additionally, some participants described narcolepsy symptoms, nightmares or sleep paralysis.

Table 5. Sleep difficulties reported in clinical sleep assessment.

Sleep Difficulty	Component	n Participants
Insomnia		5
	DIS	5
	DMS	5
	EMA	4
Nightmares		2
Narcolepsy		1
Sleep Paralysis		1

DIS = difficulty initiating sleep, DMS = difficulty maintaining sleep, EMA = early morning awakening

All consenting service users (n=5) completed assessment measures (Table 6). Participant scores on the ISI indicated that all were experiencing moderate or severe clinical insomnia. SPEQ-H scores indicated that participants were experiencing low levels of hallucinations. On the R-GPTS, three participants scored in the average range and two in clinical ranges for ideas of reference. Three participants scored in the average range and two in clinical ranges on persecutory beliefs. On the DASS-21, two participants scored in normal to mild ranges and whilst three others reported some moderate to extremely severe mood difficulties. Fear of Covid19 Scale scores demonstrated low levels of anxiety about Covid19.

Table 6. Participant scores and allocated descriptive categories on assessment measures.

Measure	n Participants	Subscale	Median score	Range	IQR		
Sleep Condition Indicator	*5*		2	0 to 2	1		
			No Insomnia (n)	Probable Insomnia (n)			
			0	5			
			Median score	Range	IQR		
Insomnia Severity Index	*5*		19	18 to 26	3		
			No Insomnia (n)	Subthreshold (n)	Clinical Insomnia - Moderate (n)	Clinical Insomnia - Severe (n)	
			0	0	3	2	
			Median score	Range	IQR		
Revised Green et al. Paranoid Thoughts Scale	*5*	*Reference*	8	1 to 25	6		
	5	*Persecution*	4	0 to 31	21		
			Average (n)	Elevated (n)	Moderately Severe (n)	Severe (n)	Very Severe (n)
			3	1	0	1	0
			3	0	0	1	1
			Median score	Range	IQR		
Specific Psychotic Experiences Questionnaire	*5*	*Hallucinations*	8	1 to 16	3		
			Median score	Range	IQR		
Depression, Anxiety and Stress Scales - 21	*5*	*Depression*	16	0 to 28	12		
		Anxiety	8	4 to 20	12		
		Stress	18	8 to 30	6		
			Normal (n)	Mild (n)	Moderate (n)	Severe (n)	Extremely Severe (n)
		Depression	1	0	2	1	1
		Anxiety	2	1	0	1	1
		Stress	1	2	1	1	0

IQR = interquartile range.

2.5.3. Expectations of Sleepio Intervention

The qualitative sample was 8 keyworkers (KW, 4 female, 4 male), covering each area team. No keyworker dropped out. Keyworkers were community psychiatric nurses or occupational therapists. No service user chose to complete a pre-intervention interview.

Table 7. summarizes the 6 categories and sub-categories developed from thematic framework analysis and specifies how many participants contributed to each sub-category. These categories and subcategories contributed to the preliminary logic model (see 2.5.4.).

Table 7. Categories and subcategories from framework analysis.

Category	*Subcategory*	KW1	KW2	KW3	KW4	KW5	KW6	KW7	KW8
Sleep Difficulties	*Awareness of the Need*	Y	Y	Y	Y	Y	Y	Y	Y
	Symptomatology and Sleep	Y	Y	Y	Y	Y	Y	Y	Y
	Diverse Sleep Difficulties	Y	Y	Y	Y	Y	Y	Y	Y
	Contributing Factors	Y	Y	Y	Y	Y	Y	Y	Y
	Impact of Covid19	Y	Y	Y	Y	N	N	Y	N
Existing Interventions	*Keyworker Interventions*	Y	Y	Y	Y	Y	Y	Y	Y
	Medication	Y	Y	Y	N	Y	N	N	Y
Beliefs about Sleepio	*Helpful*	Y	Y	Y	Y	Y	Y	Y	Y
	Safe	Y	Y	Y	Y	N	N	Y	Y
	Concerns	Y	Y	Y	Y	Y	Y	Y	Y
	Tool in Toolbox	N	Y	N	Y	Y	Y	Y	Y
	Anticipated Mechanism	Y	Y	Y	Y	Y	Y	Y	Y
	Interaction with the Service	Y	Y	Y	Y	Y	Y	Y	Y
Service User Facilitators and Barriers	*Comfort with Technology*	N	N	Y	Y	Y	Y	Y	Y
	Digital Access	Y	Y	Y	N	Y	Y	Y	Y
	Stage and Stability	Y	Y	Y	Y	Y	Y	Y	Y
	Priorities for Care	Y	Y	Y	Y	Y	Y	Y	N
Service Facilitators and Barriers	*Talking or not Talking about Sleep*	Y	Y	N	Y	Y	Y	Y	Y
	Sleepio and Resource Restrictions	N	Y	Y	Y	Y	Y	Y	Y
	The Role of a Keyworker	N	Y	N	Y	N	Y	N	Y
	Active Engagement and Connection	N	Y	Y	Y	Y	N	Y	Y
	Embracing Research and Innovation	N	Y	Y	Y	N	Y	Y	Y
	Familiarity Needs	Y	Y	N	N	N	Y	N	N

Categories are elucidated below. Quotation clarifications are represented by square brackets [ ]. Where material is omitted, we indicate this with ellipses [...]. Page and line number are provided for quotes.

Category 1. Sleep Difficulties

Category 1.1. Awareness of the Need

Keyworkers spoke about the high prevalence of sleep disorder in the FEP population, "*I think within our specialty service for psychosis sleep is... You know, a huge issue*" (KW3, pg.1, L.12).

They felt that addressing sleep was important for recovery, "*as a service, we all understand the impact that sleep can have in terms of someone's recovery, in maintaining their health and wellbeing*" (KW3, pg.5, L.214-215).

Category 1.2. Symptomatology and Sleep

Keyworkers recognised a relationship between sleep and psychosis, "*in turn [after sleep dysfunction] seeing people presenting with, I suppose, sort of like early signs of, you know, a psychotic presentation. That [relationship] is probably the, the most common […] when people are first presenting*" (KW5, pg.1, L.12-14). Some keyworkers felt that sleep was more related to negative symptoms, "*it's not as if people are kinda more, more psychotic if you like, more positive symptoms, I've not really seen that that much, but I think more like it... If you think of the syndrome, the negative kinda syndrome […] is that kinda linked?*" (KW7, pg.3, L.116-118). Mood was also characterised as related to sleep, "*it might be, the, you know the person is not depressed, but we don't want to get to the point where these sleep problems are, are becoming to the point where they're having a negative impact on their mental health*" (KW2, pg.2, L.85-87). One keyworker felt that Covid19 impacted the relationship between sleep and psychosis symptomatology "*I don't know, is it [sleep problems], because kinda covid and the stress, the kinda flipping your sleep pattern, the impact that has on your, you know, kinda biological physical health and stuff? Or is that part of the negative kind of syndrome of psychosis or… Is it partly kinda mood or affecting mood, you know, or is it a combination of all that together?*" (KW7, pg.3, L.118-122).

Category 1.3. Diverse Sleep Difficulties

Insomnia was not always the primary sleep difficulty reported. Keyworkers spoke about service users experiencing hypersomnia, nightmares, sleep paralysis, and circadian rhythm dysfunction. They felt that a variety of sleep disorders other than insomnia may impact on the implementation of the intervention, "*[where there are] no specific issues with falling asleep or staying asleep, just more maybe that their routines maybe not the most established... Maybe the Sleepio study wouldn't be particularly helpful for that*" (KW3, pg.7,

L.280-282). Other keyworkers felt that Sleepio would be useful for a diverse range of difficulties, "*to be honest near enough everybody would benefit from that type of intervention. 'Cause I think even using a CBT type model for sleep, I think it's just such a good tool for life […] there are lots of people who are maybe not having severe issues but still getting times where sleep is disturbed, so I don't necessarily think it would just be something that I would be thinking about the, the worst-case insomnia. You know, I think everybody can benefit from the intervention*" (KW6, pg.8, L.325-330)

Category 1.4. Contributing Factors

Keyworkers had an awareness of behavioural, environmental, biological and psychological factors contributing to poor sleep, "*a lot of the caseload is I feel, lack of structure and routine is causing people, they're like, always staying up late at night and then kinda sleeping till afternoon during the daytime*" (KW4, pg.1, L.19-21). These factors were linked to **4.3. Stage and Stability** of the service user, "*often sort of what you find, if people, in early stages of recovery, aren't doing particularly much, em, there, there's a good chance they're not going to be overly tired when they go to bed*" (KW5, pg.2, L.56-58).

Category 1.5. Impact of Covid19

Keyworkers felt that Covid19 had impacted on service user sleep, "*Absolutely yeah [Covid19 has had an impact]. I'd say yeah for a number of reasons. I'd say partly because the, the, maybe the usual structure and routine is not there. So, groups and activities or work, em, that's been taken away, so that lack of structure and routine. And again, I think, I've noticed a lot of people talking about sort of a more vivid dreams and things since lockdown. So yeah, that, that's been quite a common theme. Actually, having this is, lots of people talking about quite vivid dreams*" (KW4, pg.2, L.66-70).

Category 2. Existing Interventions

Category 2.1. Keyworker Interventions

Keyworkers reported using sleep hygiene and diaries, "*Finding out a wee bit more about their sleep patterns first, so, sleep diaries, sleep hygiene and get some leaflets that I would refer to as well. There's a booklet on sleep that often give to some patients. Em, we, it tends to be basic, trying to do basic interventions*" (KW8, pg.2, L.61-64). They felt existing interventions were limited, "*I don't think we have a lot of interventions though. I mean, I think we've got. Some… I think we've all got a couple of things up our sleeve that will use. That are, you know, very simple things. And then you've got medication. But other than that, there's not a great deal to be honest*" (KW2, pg.3, L.119-121), and variable in their delivery and keyworker confidence, "*every keyworker is probably a bit different in what they offer and what they're comfortable and confident in offering. So, I think that's something that's really important, to consider, because it's not without intention of helping somebody, but I don't think there's necessarily a consistent approach because everybody's got different levels of experience and maybe... compete-confidence in delivering certain interventions*" (KW6, pg.2, L.55-60).

Category 2.2. Medication

Keyworkers identified beliefs that medication was efficacious in the short term but was not effective longer term. This belief strengthened their appetite for Sleepio intervention, "*CBT is so effective, is more effective than medications [in changing sleep]. Better than medication, because medication is just a short-term intervention. It's, you know, they can't, it's not the long-term solution*" (KW1, pg.3, L.97-77). Keyworkers seemed to prefer a non-drug intervention, "*if we can [improve sleep] without, em, giving them chemical interventions, then, that's a good sign*" (KW2, pg.7, L.270-271) and felt that service users would appreciate a non-drug intervention, "*I think a lot of our young people would really, ah, you know, value that and appreciate that [alternative to medication]*" (KW3, pg.4, L.136).

2. Existing Interventions was linked closely to **5.2. Resource Restriction**, as there was a view that sleep intervention resources were limited.

Category 3. Beliefs about Sleepio

Category 3.1. Helpful

Keyworkers held positive views about the helpfulness and efficacy of digital intervention, "*I have not read up on anything or research, but I really do think [digital interventions] work. I've got belief in them. From time to time I use them myself. You know, family members use them. They do work. I hear people saying positive things about them, so I just say that to patients as well. These things, do help. Try and encourage people to kinda pull them out and use them*" (KW7, pg.5, L.201-204). They felt Sleepio specifically would be helpful, "*I think it be fantastic [to have access]… Obviously CBT is so effective*" (KW1, pg.3, L.96-97).

Category 3.2. Safe

Keyworkers identified believing that Sleepio intervention was safe, "*I don't think it's going to do any harm for anybody*" (KW2, pg.7, L.266). They also spoke about Sleepio as 'Covid19-safe', "*I think especially during Covid's times, people might feel safer accessing something digitally rather than having that kind of face-to-face contact […] could offer some more safety and security if it was digital*" (KW3, pg.3, L.94-99).

Category 3.3. Concerns about Sleepio

Keyworkers expressed some concerns about Sleepio implementation in FEP services. Despite belief in its safety, they were worried that it may increase distress and paranoia about technology and being monitored, "*It would be maybe more traumatic for them if they're on their own trying to do this from home and maybe not fully understanding it, and the app's talking to them, and thinking about somebody who's going through psychosis, that could possibly be problematic*" (KW4, pg.6, L.211-213). Some keyworkers thought that face-to-face interventions may be superior, "*I think face-to-face CBT would probably be more effective*" (KW1, pg.3, L.106). Other concerns mentioned by only one keyworker were the ease of disengagement, increased worry about sleep, and the remote nature of monitoring feeling anxiety-provoking to keyworkers, as they may not be able to respond quickly.

Category 3.4. Tool in the Toolbox

Keyworkers conceptualised Sleepio as an additional tool in the toolbox for both keyworkers and service users, "*I hope [Sleepio] would give them another tool, as I say, in their toolkit, something that they can go to as and when they need it*" (KW8, pg.4, L.142-143). They indicated a relaxed approach to using the intervention, "*I feel sort of like you're not gonna use every single intervention under the sun with a patient. But the more that you've got, I guess, sort of like 'in your locker', to be able to sort of, like, discuss or offer, the better. It is nothing but a good thing*" (KW5, pg.6, L.210-212).

Category 3.5. Anticipated Mechanisms

Keyworkers explored anticipated features of Sleepio. These included education and knowledge about sleep and behaviour change, reducing distress around sleep disturbance, reduced fear of relapse, service user autonomy, and flexibility of access to the app. Autonomy was seen as differentiating Sleepio from other interventions offered by the service, "*I suppose the good thing is […] it gives the patient ownership over their own care... It's something that, I think, yeah, I think our patients could probably do with a bit more of. Em, I think they maybe lean a wee bit more heavily on keyworkers in particular, rather than maybe having taken on that responsibility for their own care*" (KW8, pg.3-4, L.122-130).

Category 3.6. Interaction with the Service

Keyworkers believed there was a role for service professionals in promoting the application, supporting engagement, helping with any difficulties, checking on progress via the Sleep Clinic interface, and providing additional input where needed. This was linked to **5.4 Engagement and Connection**, "*I suppose the keyworker tends to be the person that has the most contact with the person? So just, so I know how that person is been getting on, not just in terms of the sleep? How they've been, been engaging with this? Are we noticing in it, any improvements are noted or are things getting worse and it gives us the opportunity to bring that to an appointment and see, you know, I notice you've not been sleeping as well this week. Is there*

anything going on? Is there anything you're worried about? And I suppose it just breaks down every barrier in terms of starting those conversations with someone" (KW3, pg.8, L.332-338). Keyworkers spoke about the importance of all professionals providing a unified message in implementation, "*I think having access to the support of the different professionals as well... would be helpful, because we all sing from the same hymn sheet in a way so they would be able to, em, ask questions of who ever seen them*" (KW8, pg.6, L.229-230).

Category 4. Service User Facilitators and Barriers

Category 4.1. Comfort with Technology

Keyworkers felt that FEP service users were generally comfortable with technology and digital interventions like Sleepio would be suitable, "*I actually think this is quite exciting, this app, because it's the way things are going these days. And again, our, the age group of the people we support are proper, like, so tech savvy, and I think it will be a lot of people will be keener to do that than possibly… it's obviously it's not for everybody, but I do think a lot of people will be keener to, to, or more receptive to a sort of digital thing as opposed to face to face sort of intervention*" (KW4, pg.3, L.109-116).

Category 4.2. Digital Access

Digital literacy and access were identified as crucial factors in accessing Sleepio, "*I think the biggest issue with it is a-accessibility for everyone. There are some people who perhaps don't have a smartphone, smartphones for instance, and you won't be able to access it that way. I guess that's probably the biggest thing for me... The only kind of real barrier I guess, like, is everyone being able to access it*" (KW5, pg.4, L.141-144). Keyworkers linked this theme to **4.3. Stage and Stability**, noting that social factors were related to lack of digital access, "*Some people don't have access to technology. Most younger folk will have access to technology, I think, but, uh, I see a lot of people with really chaotic lifestyles. I don't, you know, they don't have, you know they may have a smartphone one week, but the next week it is in the pawn shop and they don't have internet in the house*" (KW2, pg.5, L.174-175).

Category 4.3. Stage and Stability

Keyworkers spoke about factors they thought would exclude service users from Sleepio. They thought that service users at an early stage of recovery or with continuing psychosis symptoms would not be appropriate, "*I wonder if people who are still pretty, or still kinda experiencing symptoms and still pretty kinda, em, suspicious, or paranoid, or whatever, or distracted [may not be suitable]... Em, so I guess people in early recovery or in recovery ... they're gonna participate more than people who are in early stages, starting to develop relationships with the team, are gonna be more kinda difficult for those reasons. You know, kinda, building up trust and, em… so I guess where they are at on their journey in terms of recovery, you know? Will impact on whether they take part*" (KW7, pg.7, L.274-281). Keyworkers said they consider substance misuse an exclusion criterion for participation, "*What I wonder about, maybe like drug use if somebody's heavily into substances, how? You know, how's that's maybe, gonnae, it's gonna go. Because if, they will have been given a lot of that information and education and I guess I could see that the substances would maybe be a real barrier to actually engage in and make any benefits from it*" (KW6, pg.6, L.234-236). Both factors were closely related to **4.4. Priorities for Care** as keyworkers thought sleep may not be a priority and to **5.4. Engagement and Connection**, as these factors may impact on engagement.

Category 4.4. Priorities for Care

Keyworkers believed that service users would have to be in a position to prioritise sleep in order to engage with the intervention, "*I suppose you can only bring a horse to water. You can't make it drink. Like you can only provide them with the advice and I suppose it is good to know. Em, If you know, I suppose when we're referring for psychology there is a level of their commitment required in order to get help [like for Sleepio]*" (KW1, pg.6, L.209-212). They thought that keyworkers may believe sleep to be a priority when service users do not, "*sometimes you know you, with certain interventions that can feel that way, like you know, I can see that this would benefit you, but you know, for them it's you know. It's not on the radar*

at all […] because there may be other people who, even though you think they've sleep concerns it doesn't really seem on their radar. They don't bring it up. They don't seem that bothered about it. Uh-huh, yeah, it's not something that we're willing or wanting to address just now. It's not a priority" (KW5, pg.7-8, L.291-303).

Category 5. Service Facilitators and Barriers

Category 5.1. Talking or not Talking about Sleep

Keyworkers reported that speaking about sleep is something they do routinely, and they did not anticipate any reluctance in bringing it up, "*Any difficulties asking people [about sleep]? None. [Sleep is] something we talk about quite a lot and it's just like talking about the weather, really*" (KW1, pg.5, L.197). However, in concert with **5.2. Resource Restrictions** they thought that the resource constraints in the service can mean sleep is not discussed, "*I think as a Keyworker sometimes […] it's the last thing on your mind. Em even when you go in with the intention of taking information and saying here we go […] it's just not on your radar when you're going in to see somebody*" (KW6, pg.8, L.310-315).

Category 5.2. Sleepio and Resource Restrictions

Keyworkers felt the demands being placed upon the service and the resource constraint in keyworkers would act as a barrier to Sleepio implementation, "*Again [barriers to the intervention] just comes down to workload again. […] I've never, knowing what the caseload sizes were like then, they're much, much higher now. With probably less resources. So again, just comes down to workload and pressure on keyworkers*" (KW7, pg.11, L.441-444). Keyworkers felt that Sleepio could lessen the demands on keyworkers by providing a sleep intervention which did not require heavy input from them, "*So it kind of feels like. It's an intervention, but it's not necessarily all on the key worker to deliver that*" (KW6, pg.5, L.176-177). However, they were concerned that they would struggle to monitor service users' use of the application due to resource, "*I wonder how that would be because I could imagine*

myself being outside somebody's house about to get into a visit and trying to log on and go right. What's going on? What've they actually done?" (KW6, pg.10, L.408-410).

Category 5.3. The Role of a Keyworker

Several keyworkers felt that the way service users viewed their role and the variety in their role was a barrier to implementing Sleepio, "*as a keyworker you can kinda get separated. There's like 'no, I want to talk to psychology about that', or we'll just do the housing just now. So that could... That's a kind of barrier, because you've got lots of hats on as a key worker*" (KW4, pg.7, L.275-277). This related to the theme of **5.2. Resource Constraint**, as a limited resource was split across many demands in the role.

Category 5.4. Active Engagement and Connection

Keyworkers believed that a strength of the FEP service was the active approach to engagement that professionals take to build a connection with service users. They thought that this would positively impact implementation of Sleepio and service user engagement with it, "*because we use quite an assertive outreach approach with all our young people, I think that the keyworkers would have a really proactive part in supporting someone to engage in this study*" (KW3, pg.5, L.209-211).

Category 5.5. Embracing Research and Innovation

Keyworkers felt the service embracing innovation and research would aid implementation of Sleepio, "*Yeah, I think, I think with [service] it's been part and parcel of… My time at [service], there's always been different things and it's always to improve the service*" (KW8, pg.8, L.328-330), and service user engagement with Sleepio, "*people do, like, we've got kinda, a lot of people previously in research. So, people have kinda, people do take part in it. You know they do want to, and they do want to help themselves and they do want to help others through research ... So, it's how you kinda sell research to them. Not only would it help them, it would*

also help other people. A lot of folk like that notion" (KW7, pg.8, L.327-331). Keyworkers felt that Sleepio was consistent with innovation in digital delivery during the Covid19 pandemic, "*A lot of our contacts, I guess over the last year have moved to a bit of a digital platform, I'm, I guess that ties in with that, em … I guess it allows you to be more supportive for things like that*" (KW5, pg.5, L.188-191).

Category 5.5. Familiarity Needs

Keyworkers felt that they would require increased familiarity and training in use of the application and Sleep Clinic interface in order to fully implement it, "*is it possible for us to be able to get access to it as key workers to, you know, have a try or even. The position of using it ourselves? Yeah, I mean that's, that's maybe just maybe just me, but I would like to be able to talk to somebody as if I've experienced it as well, you know?*" (KW6, pg.11, L.427-429). One identified that the anxiety they felt about the application (**3.3 Concerns about Sleepio**) was related to their lack of familiarity with it, "*[I feel] Anxious {laughs} [about using the Sleep Clinic] … Just 'cause it's something that I've never done before. So, its fear of the unknown, really*" (KW2, pg.9, L.347).

2.5.4. Preliminary Contributions to Logic Model

Whilst a full logic model cannot be elucidated, initial and hypothesised contributions can be mapped onto a working logic model for Sleepio implementation (Figure 6). The model's features include contextual factors, the intervention inputs, known and theorised facilitators and barriers acting upon the implementation of the intervention, anticipated intervention mechanisms, and potential outcomes of Sleepio implementation in FEP services.

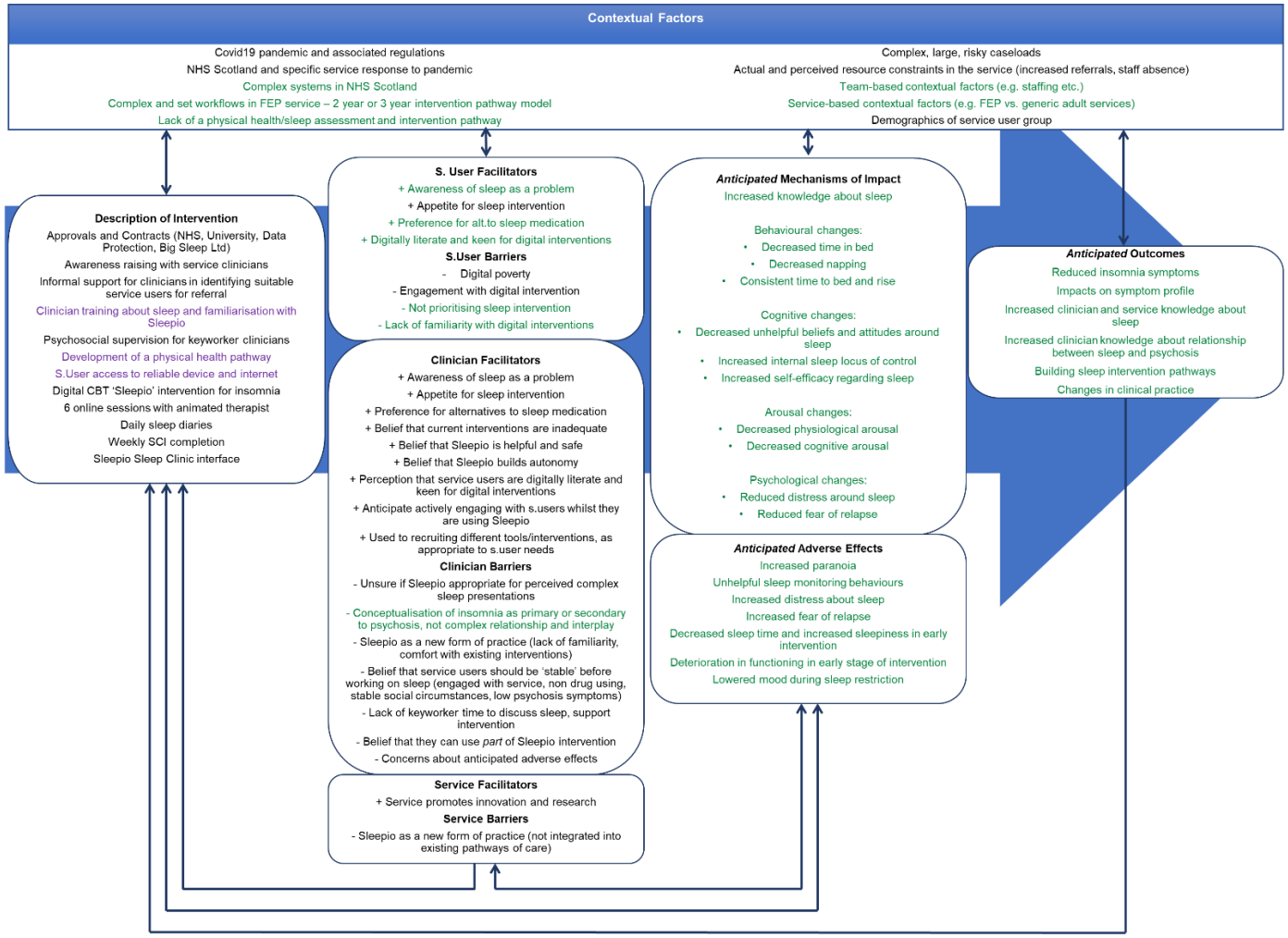

Figure 6. Preliminary logic model describing the initial implementation of Sleepio.

Black text represents elements arising from preliminary data. Green text represents hypothesised elements. Purple text represents elements not yet in place.

2.6. Discussion

2.6.1. Implementation of Sleepio

This study presents preliminary data arising from a process evaluation of the implementation of dCBTi intervention in a FEP service in NHS Scotland. There were significant impacts to the study implementation timeline due to required approvals and contracts across the three contributing organisations. With efforts to advertise the study and integrate it into the service, the rate of referral was ten referrals in 11 weeks.

Qualitative data suggests that service resource constraints may have impacted on sleep issues being explored and referrals made. Staff's concerns about the complexity of sleep difficulties and their understanding of the relationship between sleep difficulties, psychosis, and mood symptoms may have also limited referrals. Clinicians identified applying additional referral criteria related to service user stability (e.g. considering substance misuse an exclusion criteria). Initial quantitative data suggest that referred service users were experiencing relatively mild symptoms of psychosis. Five of ten referred service users consented to participate to the study. These service users all self-identified as White British, which may not be representative of people experiencing psychosis (Cantor-Graae and Selten, 2005). The demographics and symptomatology characteristics of referred service users may present a basis for concern. Health inequalities based on protected characteristics including race and ethnicity may widen if digital health interventions are not equitably offered or adapted for all groups (Latulippe et al., 2017; Zhang and Walsham, 2021). Digital health innovations are known to increase the risk of health inequality for people experiencing severe mental ill-health (Spanakis et al., 2021). In this, the use of digital methods compounds the health divide already experienced by people who lack access to devices, of minority ethnicity and/or who experience severe mental ill-health in an intersectional manner (Zhang and Walsham, 2021). It is therefore imperative that Sleepio implementation is considered with individuals of minority ethnicity and who are experiencing severe mental ill-health.

All consenting participants were eligible for inclusion. Consenting service users reported moderate to severe insomnia, the presence of other sleep disorders, and a range of mood symptomatology from non-clinical levels to extremely severe depression and anxiety. However, psychosis symptomatology was reported to be low. Taken together with findings from framework analysis, this suggests that clinicians primarily referred service users who are

considered more stable in psychosis presentation, and for whom they consider sleep to be the outstanding difficulty or the driver of mood difficulties. Participating service users reported low levels of anxiety about Covid19. These measures were collected >1 year after initial Covid19 regulations and scores may have been different if the study was undertaken earlier in the pandemic.

Currently no participants have reached the end of the 10-week intervention timeline. Preliminary application usage data suggests that service users have a mixed response to the application, with some using it on a weekly basis and others not starting the intervention. One participant stopped using Sleepio due to losing access to a device. People attending mental health services are disproportionately affected by digital poverty and exclusion (Tobitt and Percival, 2019; Spanakis et al., 2021). We did not provide a device nor data to participants, which is likely to induce inequalities in access and increase the impact of digital poverty, as represented in the working logic model. Furthermore, we are aware that there is a synergistic relationship between poverty, race and ethnicity and mental ill-health in promoting digital exclusion (Zhang and Walsham, 2021). It is critical that we monitor indicators of exclusion in ongoing data collection and consider the impacts this has on the applicability and limitations of the resulting logic model.

2.6.2. Expectations for Sleepio

We elucidated keyworkers' perceived barriers and facilitators impacting on the process of Sleepio implementation. Overall, keyworkers recognised the importance and variety of sleep difficulties in the FEP population (Reeve et al., 2019b), and the relationship sleep has to psychosis and mood symptomatology (Freeman et al., 2009, Freeman et al., 2012, Reeve et al., 2015). They identified the limitations of current offered sleep interventions and the need for additional interventions (Waite et al., 2020). Keyworkers described their beliefs and concerns about Sleepio. Allan et al. (2019) found that clinicians expressed similar concerns about the EMPOWER digital intervention for relapse management in psychosis as potentially increasing paranoia. Increased paranoia is one possible outcome of digital intervention for psychosis (Eisner et al., 2019). Keyworkers anticipated service user autonomy to be an important mechanism in Sleepio intervention. Other studies of digital interventions in

psychosis have found that improved self-management is an outcome of digital applications (Berry et al., 2019, Eisner et al., 2019, Huerta-Ramos et al., 2016).

Keyworkers suggested service user facilitators and barriers to the intervention. They identified applying their own eligibility criteria when considering referrals; for example perceived stability and likelihood of engagement. Kingdon and Kirschen (2006) found that beliefs about service user engagement impact on whether psychological interventions are offered to people affected by psychosis. The impact of service user comfort with technology and service user stability that were considered in our study were also identified as facilitators and barriers to the implementation of the EMPOWER digital intervention (Allan et al., 2019).

Lastly, we developed an understanding of service level facilitators and barriers to implementation of Sleepio. Similarly to themes resulting from our analysis, clinicians in the EMPOWER implementation trial expressed concerns that the application was not sufficiently person-centred and believed that restricted resources would impact on its implementation (Allan et al., 2019). Palmier-Claus et al. (2013) also found that service user participants were concerned that a digital monitoring application would reduce the person-centred elements of their care.

2.6.3. Preliminary Logic Model

Our preliminary logic model incorporates findings from our data with theorised mechanisms and outcomes. As the model was largely informed by clinician perspectives, the preliminary model should be understood as being through this lens rather than being from the perspectives of multiple stakeholders. Certain features are therefore likely to be underdeveloped, for example implementation facilitators and barriers, hypothesised mechanisms, and outcomes from the perspective of service users.

The hypothesised mechanisms of the intervention were developed from CBTi literature and qualitative data. Qualitative data suggested that keyworkers anticipate reduced distress around sleep and reduced fear of relapse. Known CBTi mechanisms include increased knowledge about sleep, behavioural changes such as decreased time in bed, decreased napping, and consistent sleep scheduling (Maurer et al., 2021, Schwartz and Carney, 2012), cognitive changes, such as decreased unhelpful beliefs and attitudes around sleep, increased internal sleep locus of control, and increased self-efficacy regarding sleep (Chow et al., 2018,

Eidelman et al., 2016, Schwartz and Carney, 2012), and changes to physiological and cognitive arousal levels (Schwartz and Carney, 2012). Interviews also revealed hypothesised adverse effects represented in the model, including increased paranoia, unhelpful sleep monitoring behaviours, increased distress about sleep, and increased fear of relapse. From the literature, we can also hypothesise that decreased sleep time, increased sleepiness, deterioration in functioning, and poorer mood may occur for some people during intervention (Kyle et al., 2011).

2.6.4. Strengths and Limitations

One strength of the presented work is its design. Process evaluations have been used previously to consider the implementation of digital interventions in psychosis (Allan et al., 2019, Berry et al., 2019). The MRC process evaluations framework for complex interventions highlights the importance of integrating mixed-methods results from process evaluations to better understand what is observed within clinical trials (Moore et al., 2015). Deaton and Cartwright (2018) argue that randomised clinical trials are neither sufficient in understanding the implementation of a complex intervention nor to lead to practical clinical implementation, and should be supplemented by the use of implementation methodology. Our methodology allows us to fully understand the implementation of Sleepio and inform future clinical efficacy trials (Greenhalgh, 2017).

As above, one crucial limitation was that qualitative data included only clinicians' perspectives. This limits the logic model to representing only facilitators and barriers through the clinician stance and lens and as such is inherently incomplete in its understanding of the factors and stakeholders influencing implementation. In the planned overarching study, we plan to incorporate service user and keyworker perspectives prior to and following Sleepio intervention. Berry et al. (2019) noted the importance of qualitative investigations taking place prior to and during the implementation of a complex intervention, as opposed to only afterwards, as this allows the implementation to be guided by findings. The outcomes of our study could, for example, guide training in FEP services regarding sleep and Sleepio. We also contribute to the wider understanding of how digital interventions can be implemented in psychosis services (Ben-Zeev et al., 2012). Stakeholder perspectives on implementation of digital interventions in psychosis are currently underrepresented in the research (Bucci et al.,

2018) and are critical to the implementation of optimised interventions (Biagianti et al., 2017). At present, we provide data from only one stakeholder group.

The presented work comprises preliminary data of implementation factors and characterisation of service users. We recruited from a single healthboard FEP service. As a result of this and of our contextual constructionism stance the resulting qualitative framework and logic model may not be generalisable. The use of non-probablistic sampling is likely to bias our qualitative dataset; as those who volunteered may hold particular views about Sleepio implementation. Additionally, consenting service users were limited to people with devices and internet access. This is likely to exclude people in the FEP population from participation, and biases the participant sample. At present, consenting service users are homogenous in their self-identified ethnicity and do not represent the underlying population of people experiencing FEP (Bresnahan et al., 2007). This limits the applicability of the resulting logic model in the service and generally, as this may not take into account symptomatology, usage characteristics, facilitators and barriers experienced by people of minority ethnicity.

Our qualitative sample was relatively small, as it was limited by keyworker uptake. Results should be interpreted carefully, particularly considering the epistemological stance taken. Hennink et al. (2017) concluded that conventional saturation in qualitative data is reached at nine participants, but 16-24 provide comprehensive saturation. However, Young and Casey (2019) have suggested that our sample size is sufficient in capturing themes. Crucially, no service user consented to take part in qualitative interviews. This limits the scope of the preliminary logic model and restricts its interpretation to representing the factors acting upon the implementation of Sleepio through the lens of clinicians and the service. It is also likely that researcher FR's position as a clinician within the service biases the dataset and interpretations made. As such, these limitations are explicitly considered in our analysis methodology and epistemological position. Researcher FR conducted the majority of qualitative analysis. Whilst this could be considered adequate in the context of the doctoral project, the study would benefit from an iterative analysis of this data using a team approach. Such an approach would allow for a mix of experiences and perspectives to shape the resulting categories and sub-categories, increasing reflexivity and reducing bias in the results.

2.6.5. Implications

This project has led to development of a preliminary logic model of the implementation of Sleepio in an NHS Scotland FEP service, which will inform the ongoing process evaluation. Planned further work will fully characterise implementation and provide outcome signals for the impacts of Sleepio intervention on symptomatology. Qualitative work will elucidate keyworker and service user perspectives on the Sleepio intervention prior to and following its use. It will be particularly important to recruit service users to interview, to develop the resulting logic model more fully from service users' viewpoints.

We can recommend that further awareness-raising about sleep difficulties, the project, and its inclusion/exclusion criteria are undertaken. Training should be provided; with a focus on diverse sleep difficulties and the relationship between sleep and psychosis. Keyworkers may benefit from sessions familiarising them with the Sleepio application. Opportunities should be given for keyworkers to meet with study researchers and informally discuss referrals. Referrals to the project are likely to fluctuate with service resource. This project will provide important information which may guide future clinical trials of Sleepio efficacy in the context of first episode psychosis.

Future work should consider incorporating the views of other stakeholders including; family and friends, persons with lived experience of first episode services, and multidisciplinary professionals. Our understanding of Sleepio implementation would be greatly improved if similar research were undertaken in other first episode services across the United Kingdom. This would allow us to examine which parts of our findings are context-specific and which are generalisable.

2.7. Conclusions

To our knowledge, this is the first exploration of the implementation of Sleepio in a first episode of psychosis service. We provide a preliminary and working logic model of this implementation which will be used to guide the development of the ongoing project and may contribute to future efficacy trials.

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Appendices

Appendix 1.1. Submission Guidelines for Sleep Medicine

SLEEP MEDICINE

Official Journal of the World Sleep Society and International Pediatric Sleep Association

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AUTHOR INFORMATION PACK

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DESCRIPTION

Sleep Medicine aims to be a journal no one involved in clinical **sleep medicine** can do without.

A journal primarily focussing on the human aspects of **sleep**, integrating the various disciplines that are involved in sleep medicine: neurology, clinical neurophysiology, internal medicine (particularly pulmonology and cardiology), psychology, psychiatry, sleep technology, pediatrics, neurosurgery, otorhinolaryngology, and dentistry.

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Article Types

The primary emphasis of the journal will be clinical and to this end, a number of different types of articles will be published. Each type will be aimed to provide clinically important information needed to keep up to date with the practice of sleep medicine, written in a way to foster interdisciplinary understanding and make clinical information accessible to all practitioners.

Sleep Medicine publishes the following types of articles:

• **Original Articles** dealing with diagnosis, clinical features, pathophysiology, etiology, treatment (by all relevant modalities, including pharmacological, instrumental, surgical, behavioral, nutritional), genetics, epidemiology, natural history and prognosis of human sleep disorders will be considered for publication, provided these have not been previously published except in abstract form or have not been submitted simultaneously elsewhere. Reports may also include technical aspects of sleep medicine, which are relevant for diagnosis, pathophysiology, etiology, treatment and natural history. Basic research articles will also be published where they have a direct impact on or shed considerable light on clinical aspects of sleep. Submission of original articles based on animal or human experimental studies are encouraged, and these articles should include a comment in the abstract and discussion about the potential clinical relevance of the study.

• **Review articles** on all aspects of clinical sleep medicine and related basic science that contribute to understanding clinical sleep medicine will be published. Reviews will be timely, emphasize areas undergoing new development, and include both state of the art reviews and multi-author discussion of controversial areas.

• **Editorials** on manuscripts published elsewhere in the journal or on a timely and controversial topic will be published occasionally. Editorials may contain up to 1000 words and 20 references.

Use of inclusive language

Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Content should make no assumptions about the beliefs or commitments of any reader; contain nothing which might imply that one individual is superior to another on the grounds of age, gender, race, ethnicity, culture, sexual orientation, disability or health condition; and use inclusive language throughout. Authors should ensure that writing is free from bias, stereotypes, slang, reference to dominant culture and/or cultural assumptions. We advise to seek gender neutrality by using plural nouns ("clinicians, patients/clients") as default/wherever possible to avoid using "he, she," or "he/she." We recommend avoiding the use of descriptors that refer to personal attributes such as age, gender, race, ethnicity, culture, sexual orientation, disability or health condition unless they are relevant and valid. These guidelines are meant as a point of reference to help identify appropriate language but are by no means exhaustive or definitive.

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If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.
Divide the article into clearly defined sections.

Figures and tables embedded in text
Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.

Article structure

Subdivision - numbered sections
Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Introduction
State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods
Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

Results
Results should be clear and concise.

Discussion
This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Conclusions
The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Appendices
If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

For Original Articles and Brief Communications a structured abstract should be provided of not more than 250 words. The abstract should be organized by: Objective/Background, Patients/Methods, Results and Conclusions. No abstract is required for Images in Sleep Medicine or Video-Clinical Corners.

Graphical abstract

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

Authors can make use of Elsevier's Illustration Services to ensure the best presentation of their images and in accordance with all technical requirements.

Appendix 1.2. Proposal Outline for Systematic Review

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

*Fields that have an **asterisk (*)** next to them means that they **must be answered. Word limits** are provided for each section. You will be unable to submit the form if the word limits are exceeded for any section. Registrant means the person filling out the form.*

1. * Review title.

Give the title of the review in English

The Prevalence of Insomnia in Non-Affective Psychosis and its Relationship to Positive and Negative Symptoms: A Systematic Review

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

31/03/2021

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/07/2021

5. * Stage of review at time of this submission.

Tick the boxes to show which review tasks have been started and which have been completed. Update this field each time any amendments are made to a published record.

Reviews that have started data extraction (at the time of initial submission) are not eligible for inclusion in PROSPERO. If there is later evidence that incorrect status and/or completion date has been supplied, the published PROSPERO record will be marked as retracted.

This field uses answers to initial screening questions. It cannot be edited until after registration.

The review has not yet started: Yes

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Fiona Robb

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Dr Robb

7. * Named contact email.

Give the electronic email address of the named contact.

[redacted]

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

Institute of Mental Health and Wellbeing, Gartnavel Royal Hospital Administration Building, 1st floor 1055 Great Western Road, Glasgow, G12 0XH

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

07742367822

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Glasgow

Organisation web address:

https://www.gla.ac.uk/researchinstitutes/healthwellbeing/research/mentalhealth/

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Dr Fiona Robb. University of Glasgow
Professor Andrew Gumley. University of Glasgow
Dr Louise Beattie. University of Glasgow
Dr Mairi Spanswick. NHS Greater Glasgow and Clyde

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

This systematic review will be undertaken as part of the principal investigator's thesis for the award of a doctorate in Clinical Psychology at the University of Glasgow.

Grant number(s)

State the funder, grant or award number and the date of award

N/A

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

1) What is the estimated prevalence of insomnia in those with a diagnosis of non-affective psychosis?

What is the estimated prevalence of insomnia in those experiencing a first episode of psychosis?

What is the estimated prevalence of insomnia in those at ultra high risk for developing psychosis?

2) What is the relationship between insomnia and psychosis symptomology in these groups?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

MEDLINE (Ovid), EMBASE, PsycINFO, CINAHL. From database beginning - March 2021. English language

texts.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Non-Affective Psychosis: 'Psychosis' is the experience of loosing touch with reality. Positive symptoms of psychosis include hallucinations and delusions. Negative symptoms include apathy, alogia, avolition and anhedonia. 'Non-affective' describes psychosis occurring in the absence of major mood disruption. Formal psychiatric diagnoses falling into this category include schizophrenia, schizophreniform disorder, brief psychotic disorder, delusional disorder, schizoaffective disorder, and psychotic disorder not otherwise specified. We will also review papers focusing on those experiencing early psychosis or a first episode of psychosis, and those who are in prodromal stages or considered at ultra high risk of developing psychosis.

Insomnia: Insomnia describes a significant difficulty with falling asleep or staying asleep. Symptoms of insomnia are thought to act as a modulatory and causal factor in experiences of mental ill-health. Here we examine insomnia symptoms in addition to formally diagnosed Insomnia Disorder.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion

Participant groups affected by non-affective psychosis, based on standardised clinical assessment or diagnosis of a schizophrenia spectrum disorder.

Participant groups described as recently experiencing a first episode of psychosis based on standardised clinical assessment OR a recognised diagnostic system to describe schizophrenia spectrum disorder for retrospective studies.

Participants considered at ultra high risk of developing psychosis defined by the comprehensive assessment for at risk mental states OR structured interview for prodromal symptoms; OR a recognised diagnostic system to describe schizophrenia spectrum disorder for retrospective studies.

Psychosis should not be defined solely by items within an overall measure of another condition.

Exclusion

Studies of only participants where the primary cause of psychosis symptomatology is organic (e.g. brain injury, illness or dementia populations).
Studies of only affective psychosis populations.
Studies recruiting general population participants e.g. which examine atypical experiences as part of a continuum in non-clinical participants.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion

Papers which examine insomnia; where 'insomnia' is identified using self-report questionnaires, clinical assessment, semi-structured interview, actigraphy, polysomnography or any other clinical diagnostic technique.

In which sleep disorder is a primary measurement.

Insomnia should not be defined by items within an overall measure.

Exclusion

Papers which do not examine insomnia.

Where insomnia is not identified using the above techniques.

Where insomnia is reported solely as a secondary outcome (for example studies of drug efficacy).

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

N/A

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Inclusion

Primary studies reporting objective data on insomnia and psychosis.

Exclusion

Studies not written in English

Studies which were not published in a peer reviewed journal

Theses

Case studies

Conference proceedings

Reviews

Meta-analyses

Commentary on other studies

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

Studies will typically examine sleep in people with non-affective psychosis in outpatient psychosis clinics and services, or in inpatient settings.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

1) Prevalence of insomnia in psychosis and ultra high risk populations

2) Relationship to symptoms of psychosis

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

1) prevalence (expressed as percentages and 95% confidence interval)

2) descriptive summaries of the relationship to symptomatology

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state ‘None’ or ‘Not applicable’ as appropriate to the review

N/A

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

N/A

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Titles and abstracts of retrieved studies will be analyzed

Studies considered relevant, which meet inclusion/exclusion criteria will be selected

Full study publication will be reviewed for inclusion/exclusion criteria

Methodological quality will be independently evaluated and scored by two reviewers

Data extracted and coded - title, authors, journal, study design, sample, setting, assessment method for insomnia, estimated prevalence of insomnia, assessment measures for symptomatology, relationship to

Data will be recorded in an excel spreadsheet

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

JBI Critical appraisal checklist for analytical cross-sectional studies

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

Data with prevalence and related tables to symptomatology we will provide a narrative summary

Meta analysis of proportions for point prevalence - using R?

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

If possible given available data, we will pursue analysis by sample subpopulation (e.g. those at high risk of psychosis, first episode of psychosis, confirmed psychosis). We will consider analysis by sample setting (e.g inpatient or community sample)

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Systematic review

Health area of the review

Mental health and behavioural conditions

---

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

Scotland

---

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

N/A

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

N/A

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

Intended publication in relevant journal

Plan to publish work as part of thesis for a Doctorate in Clinical Psychology, University of Glasgow

Presentation to NHS Greater Glasgow and Clyde First Episode Psychosis service

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

insomnia; psychosis; prevalence; sleep; first episode psychosis, ultra high risk

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

N/A

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.
Please provide anticipated publication date

Appendix 1.3. Search Strategy

TI AB used in EBSCOHost syntax (CINAHL and APA PsychInfo)

ti,ab. used in Ovid syntax (MEDLINE R 1946 – Present and EMBASE 1947-Present)

1. TI insomn* OR AB insomn*

2. TI sleep maintain* OR AB sleep maintain*

3. TI sleep initiat* OR AB sleep initiat*

4. TI sleeplessness OR AB sleeplessness

5. TI sleep OR AB sleep

6. S1 OR S2 OR S3 OR S4 OR S5 ('sleep' – APA PsychInfo 74,896; CINAHL 66,220; Ovid MEDLINE R 156,612; Ovid EMBASE 294,485)

7. TI schizo* OR AB schizo*

8. TI Psychos?s OR AB Psychos?s

9. TI psychotic OR AB psychotic

10. TI Delus* OR AB Delus*

11. TI Hallucinat* OR AB Hallucinat*

12. S7 OR S8 OR S9 OR S10 OR S11 ('psychosis' – APA PsychInfo 185,665; CINAHL 45,032; Ovid MEDLINE R 176,523; Ovid EMBASE 286,353)

13. TI "first episode" OR AB "first episode"

14. TI "first-episode" OR AB "first-episode"

15. TI "early psychosis" OR AB "early psychosis"

16. S13 OR S14 OR S15 ('early psychosis' – APA PsychInfo 8,407; CINAHL 4,833; Ovid MEDLINE R 12,211; Ovid EMBASE 24,694)

17. TI Prodrom* OR AB Prodrom*

18. TI “ultra high risk” OR AB “ultra high risk”

19. TI “ultra-high-risk” OR AB “ultra-high-risk”

20. TI “at risk mental state” OR AB “at risk mental state”

21. TI “at-risk-mental-state” OR AB “at-risk-mental-state”

22. TI “clinical high risk” OR AB “clinical high risk”

23. TI “clinical-high-risk” OR AB “clinical-high-risk”

24. S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 (‘prodromal psychosis’ – APA PsychInfo 5,939; CINAHL 3,329; Ovid MEDLINE R 8,934; Ovid EMBASE 19,464)

25. S6 AND S12 (‘sleep and psychosis’ – APA PsychInfo 4,460; CINAHL 1,197; Ovid MEDLINE R 3,772; Ovid EMBASE 9,091)

26. S12 OR S16 OR S24 (‘all psychosis’ - APA PsychInfo 189,290; CINAHL 48,459; Ovid MEDLINE R 182,241; Ovid EMBASE 297,206)

27. S6 AND S26 (‘sleep and all psychosis’ – APA PsychInfo 4,745; CINAHL 1,405; Ovid MEDLINE R 3,839; Ovid EMBASE 9,262)

Appendix 1.4. Data Extraction Proforma

Authors		
Authors Abbrev		
Year		
Title		
Study Type		
Whole or Part Sample		
Country		
Total Sample n		
Psychosis Sample n		
Age	Mean	
	SD	
	Median	
	Range	
Gender/Sex		
Race/Ethnicity		
Diagnoses		
How diagnosis defined		
Participant Care Context		
How Insomnia Identified		
Insomnia Prevalence	Overall	
	DIS Prevalence	
	DMS Prevalence	
	EMA Prevalence	
	ISI Mild	
	ISI Moderate	
	ISI Severe	
How Symptoms Measured		
Relationship to Symptoms		
Statistical Relationship		

Appendix 1.5. Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies

JBI CRITICAL APPRAISAL CHECKLIST FOR STUDIES REPORTING PREVALENCE DATA

Reviewer_____ Date_____

Author_____Year_____ Record Number_____

	Yes	No	Unclear	Not applicable
1. Was the sample frame appropriate to address the target population?	☐	☐	☐	☐
2. Were study participants sampled in an appropriate way?	☐	☐	☐	☐
3. Was the sample size adequate?	☐	☐	☐	☐
4. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
5. Was the data analysis conducted with sufficient coverage of the identified sample?	☐	☐	☐	☐
6. Were valid methods used for the identification of the condition?	☐	☐	☐	☐
7. Was the condition measured in a standard, reliable way for all participants?	☐	☐	☐	☐
8. Was there appropriate statistical analysis?	☐	☐	☐	☐
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

Appendix 1.6. Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Reviewer_____Date_____

Author_____Year_____ Record Number_____

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____

Appendix 1.7. Critical Appraisal of Prevalence Studies

Table 7. Quality ratings based on JBI Checklist for Prevalence Studies.

	Sample frame appropriate to address target population?	Study participants recruited in appropriate way?	Sample size adequate?	Subjects/setting described in detail?	Analysis conducted w sufficient coverage of identified sample?
Batalla-Martin et al., 2020	Yes	Unclear	Yes	Yes	Yes
Freeman et al. 2009	Yes	Unclear	No	Yes	Yes
Hou et al., 2017	Yes	Yes	Yes	Yes	Yes
Mondal et al., 2018	Yes	Yes	Yes	Yes	Yes
Ogbolu et al., 2012	Yes	No	Yes	Yes	Yes
Palmese et al., 2011	Yes	Unclear	No	Yes	Yes
Reeve et al., 2019	Yes	Unclear	No	Yes	Yes
Seow et al., 2018	Yes	No	Yes	Yes	Yes
Subramaniam et al., 2018	Yes	No	Yes	Yes	Yes
Xiang et al., 2009	Yes	Yes	Yes	Yes	Yes

	Valid methods for identification of condition?	Measured in standard, reliable way?	Appropriate statistical analysis?	Response rate adequate/managed?	Quality Rating
Batalla-Martin et al., 2020	Yes	No	Yes	Unclear	0.67
Freeman et al. 2009	Yes	Unclear	No	Unclear	0.44
Hou et al., 2017	No	Yes	No	Yes	0.78
Mondal et al., 2018	Unclear	Unclear	No	Unclear	0.56
Ogbolu et al., 2012	Yes	Yes	No	Yes	0.78
Palmese et al., 2011	Yes	Yes	No	Unclear	0.56
Reeve et al., 2019	Yes	Unclear	No	Unclear	0.56
Seow et al., 2018	Yes	No	No	Unclear	0.56
Subramaniam et al., 2018	Yes	No	No	No	0.56
Xiang et al., 2009	No	Yes	No	Yes	0.78

Authors in grey reflect those co-rated by FR and HL.

Appendix 1.8. Critical Appraisal of Analytical Cross-Sectional Studies

Table 8. Quality ratings based on JBI Checklist for Cross-Sectional Studies.

	Inclusion criteria clearly defined?	Subjects and setting described in detail?	Insomnia measured in a valid and reliable way?	Standard criteria for measurement of condition?
Batalla-Martin et al., 2020	Yes	Yes	Yes	Yes
Freeman et al., 2009	Yes	Yes	Yes	Yes
Freeman et al., 2019	Yes	Yes	Yes	Yes
Grezellschak et al., 2017	Yes	No	Yes	No
Hou et al., 2017	Yes	Yes	No	Yes
Li et al., 2016	Yes	Yes	Unclear	Yes
Li et al., 2017	Yes	Yes	No	Yes
Miller et al., 2019	Yes	Yes	Yes	Yes
Miller et al., 2020	Yes	Yes	Yes	Yes
Miller et al., 2021	Yes	Yes	No	Yes
Palmese et al., 2011	No	Yes	Yes	Yes
Reeve et al., 2018	Yes	Yes	Yes	Yes
Reeve et al., 2019	Yes	Yes	Yes	Yes
Seow et al., 2018	Yes	Yes	Yes	Yes
Subramaniam et al., 2018	Yes	Yes	Yes	Yes
Xiang et al., 2009	Yes	Yes	No	Yes

	Confounding factors identified?	Strategies to deal w. confounding factors stated?	Outcomes measured in valid and reliable way?	Was appropriate statistical analysis used?	Quality Rating
Batalla-Martin et al., 2020	Yes	No	Yes	Unclear	0.75
Freeman et al., 2009	Yes	Yes	Yes	Yes	1
Freeman et al., 2019	No	No	Yes	Yes	0.75
Grezellschak et al., 2017	Yes	No	Yes	Yes	0.625
Hou et al., 2017	Yes	Yes	Yes	Yes	0.875
Li et al., 2016	Yes	Yes	No	Yes	0.75
Li et al., 2017	Yes	Yes	Yes	Yes	0.875
Miller et al., 2019	Yes	Yes	Yes	Yes	1
Miller et al., 2020	Yes	Yes	Yes	Yes	1
Miller et al., 2021	Yes	Yes	Yes	Yes	0.875
Palmese et al., 2011	No	No	Yes	Unclear	0.5
Reeve et al., 2018	No	Unclear	Yes	Yes	0.75
Reeve et al., 2019	No	Unclear	Yes	Yes	0.75
Seow et al., 2018	No	No	Yes	Yes	0.75
Subramaniam et al., 2018	Yes	Yes	Yes	Yes	1
Xiang et al., 2009	Yes	Yes	Yes	Yes	0.875

Authors in grey reflect those co-rated by FR and HL.

Appendix 1.9. Meta Analysis Supplementary Results

1.9.1. Supplementary results for studies aiming to establish prevalence

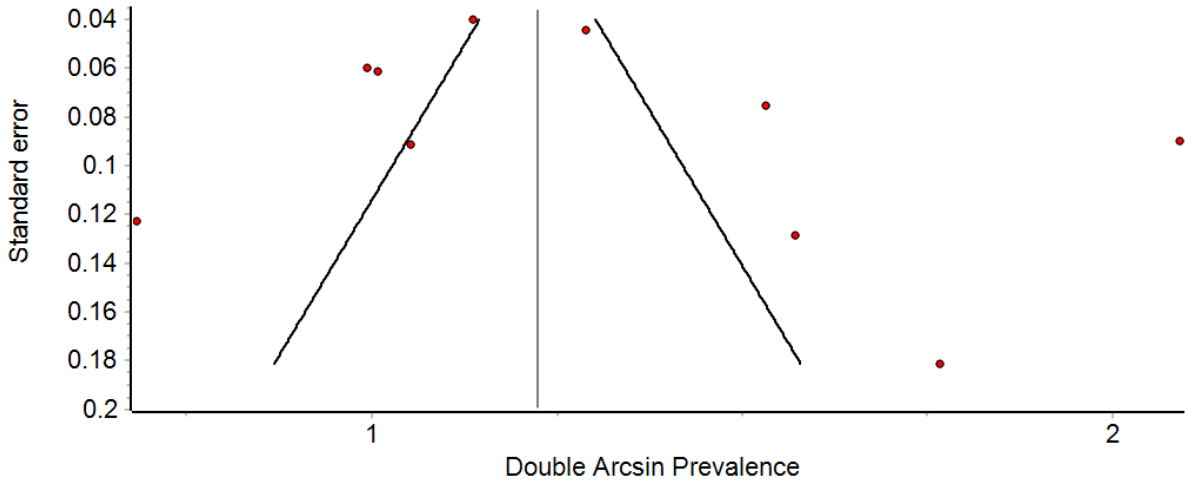

Figure 7. Funnel plot for studies aiming to establish prevalence

1.9.1.1. Random-effects model across studies aiming to establish prevalence

Table 9. Random-effects results for studies aiming to establish prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	10.54347436
Freeman et al., 2009	0.6	0.417766967	0.769627425	8.114914257
Hou et al., 2017	0.288924559	0.253964116	0.32518535	10.78054104
Mondal et al., 2018	0.75	0.669669608	0.822618083	10.09682381
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	9.444086851
Palmese et al., 2011	0.48	0.406154229	0.554283426	10.33481879
Reeve et al., 2019	0.5	0.373295155	0.626704845	9.315879037
Seow et al., 2018	0.25	0.17623746	0.33173089	10.0703334
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	10.56093734
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	10.73819112
Pooled	0.365418577	0.272162144	0.463950503	100
Statistics				
I-squared	95.09782267	92.73784754	96.69087881	
Cochran's Q	183.5918897			
Chi2, p	0			
tau2	0.093326043			

1.9.1.2. Quality-effects model across studies aiming to establish prevalence

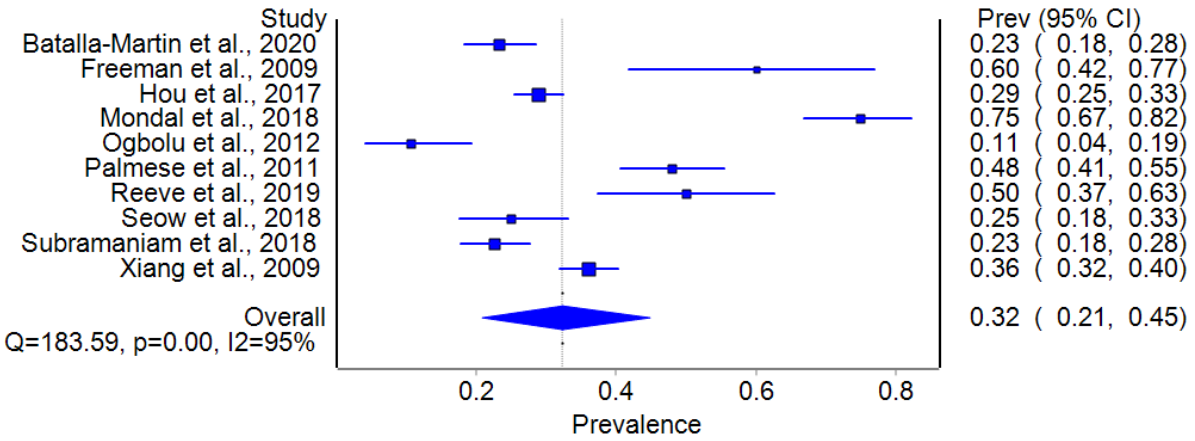

Figure 8. Quality-effects forest plot for studies aiming to establish prevalence

Table 10. Quality-effects results for studies aiming to establish prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	11.44903392
Freeman et al., 2009	0.6	0.417766967	0.769627425	1.624323199
Hou et al., 2017	0.288924559	0.253964116	0.32518535	29.15134998
Mondal et al., 2018	0.75	0.669669608	0.822618083	5.009235282
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	4.439726201
Palmese et al., 2011	0.48	0.406154229	0.554283426	6.625409702
Reeve et al., 2019	0.5	0.373295155	0.626704845	2.981094834
Seow et al., 2018	0.25	0.17623746	0.33173089	4.882476504
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	9.921137932
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	23.91621245
Pooled	0.323547813	0.208698332	0.449884987	100
Statistics				
I-squared	95.09782267	92.73784754	96.69087881	
Cochran's Q	183.5918897			
Chi2, p	0			
Q-Index	11.91532514			

1.9.1.3. Fixed-effects model across studies aiming to establish prevalence

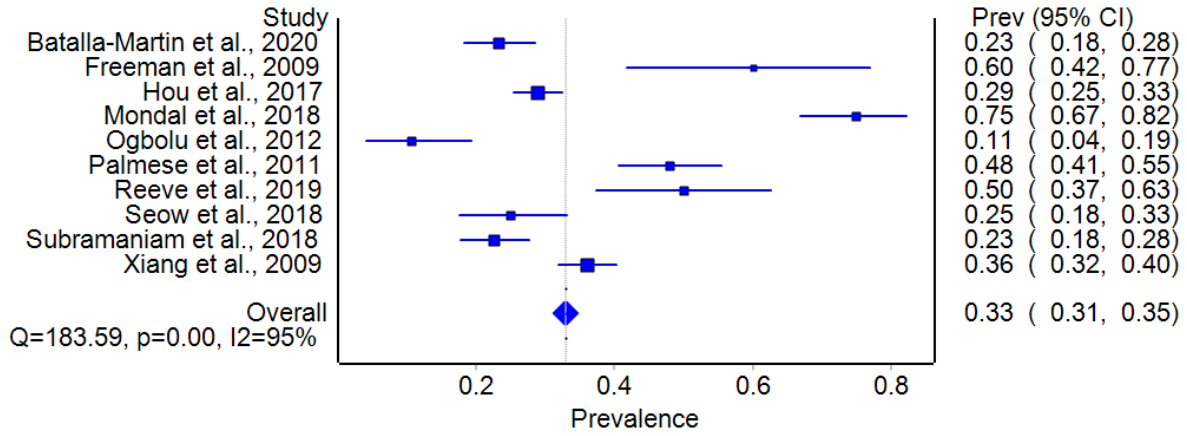

Figure 9. Fixed-effects forest plot for studies aiming to establish prevalence

Table 11. Fixed-effects results for studies aiming to establish prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	11.86779059
Freeman et al., 2009	0.6	0.417766967	0.769627425	1.353149956
Hou et al., 2017	0.288924559	0.253964116	0.32518535	27.66193434
Mondal et al., 2018	0.75	0.669669608	0.822618083	5.523513753
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	2.950310559
Palmese et al., 2011	0.48	0.406154229	0.554283426	7.786157941
Reeve et al., 2019	0.5	0.373295155	0.626704845	2.684117125
Seow et al., 2018	0.25	0.17623746	0.33173089	5.346051464
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	12.40017746
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	22.42679681
Pooled	0.329453848	0.310191312	0.349007002	100
Statistics				
I-squared	95.09782267	92.73784754	96.69087881	
Cochran's Q	183.5918897			
Chi2, p	0			

1.9.2. Supplementary results for all studies reporting prevalence

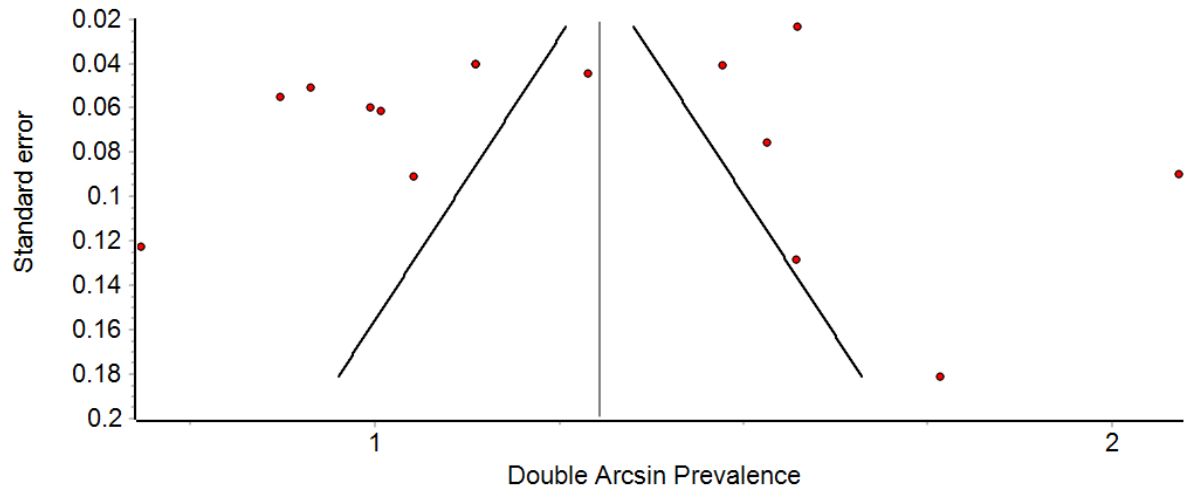

Figure 10. Funnel plot for all studies reporting prevalence

1.9.2.1. Random-effects model across all studies reporting prevalence

Table 12. Random-effects results for studies reporting prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	6.860758982
Freeman et al., 2009	0.6	0.417766967	0.769627425	5.258276514
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	7.097819606
Hou et al., 2017	0.288924559	0.253964116	0.32518535	7.017912034
Li et al., 2016	0.193298969	0.155452031	0.234178213	6.945599922
Li et al., 2017	0.289215686	0.253936375	0.325816872	7.015743408
Miller et al., 2020	0.176829268	0.137327398	0.220109866	6.911090777
Miller et al., 2021	0.449832776	0.410113681	0.489873838	7.012870112
Mondal et al., 2018	0.75	0.669669608	0.822618083	6.565022915
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	6.133657105
Palmese et al., 2011	0.48	0.406154229	0.554283426	6.722546932
Reeve et al., 2019	0.5	0.373295155	0.626704845	6.049044804
Seow et al., 2018	0.25	0.17623746	0.33173089	6.547497506
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	6.872330887
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	6.989828497
Pooled	0.347945741	0.274133262	0.425570642	100
Statistics				
I-squared	97.10706532	96.21809697	97.78707413	
Cochran's Q	483.9376471			
Chi2, p	0			
tau2	0.091579667			

1.9.2.2. Quality-effects model across all studies reporting prevalence

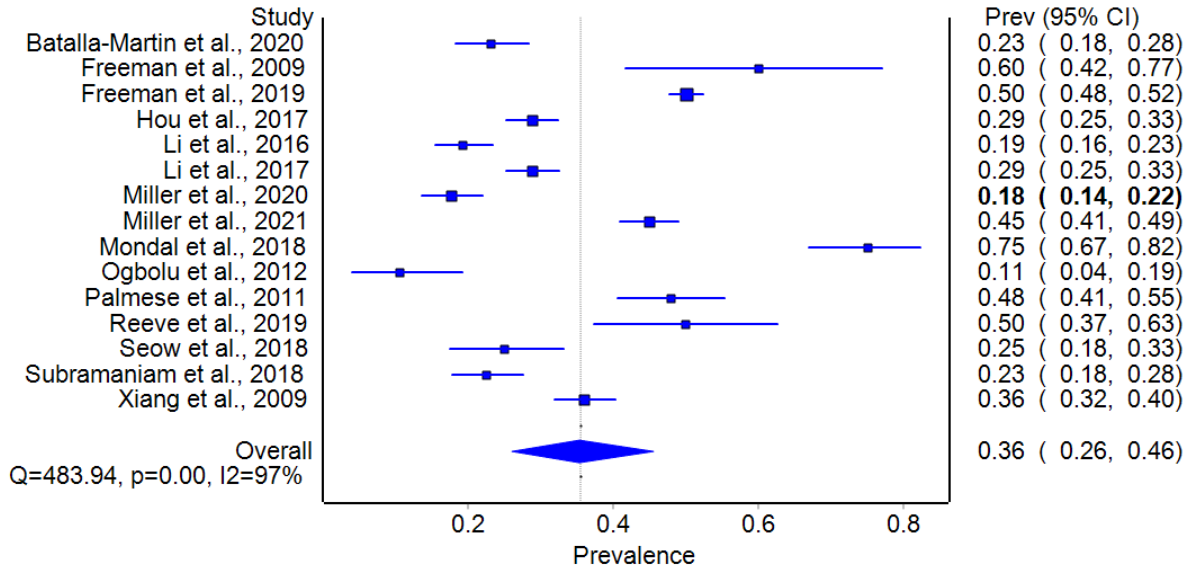

Figure 11. Quality-effects forest plot for all studies reporting prevalence

Table 13. Quality-effects results for all studies reporting prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	4.478649124
Freeman et al., 2009	0.6	0.417766967	0.769627425	1.225663596
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	24.27567635
Hou et al., 2017	0.288924559	0.253964116	0.32518535	9.851857942
Li et al., 2016	0.193298969	0.155452031	0.234178213	6.554897677
Li et al., 2017	0.289215686	0.253936375	0.325816872	10.92250804
Miller et al., 2020	0.176829268	0.137327398	0.220109866	7.737273545
Miller et al., 2021	0.449832776	0.410113681	0.489873838	10.71781257
Mondal et al., 2018	0.75	0.669669608	0.822618083	2.404704146
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	2.612786638
Palmese et al., 2011	0.48	0.406154229	0.554283426	2.878149435
Reeve et al., 2019	0.5	0.373295155	0.626704845	1.810576724
Seow et al., 2018	0.25	0.17623746	0.33173089	2.367571182
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	3.843606495
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	8.318266535
Pooled	0.355218609	0.260323012	0.456096272	100
Statistics				
I-squared	97.10706532	96.21809697	97.78707413	
Cochran's Q	483.9376471			
Chi2, p	0			
Q-Index	23.54253117			

1.9.2.3. Fixed-effects model across all studies reporting prevalence

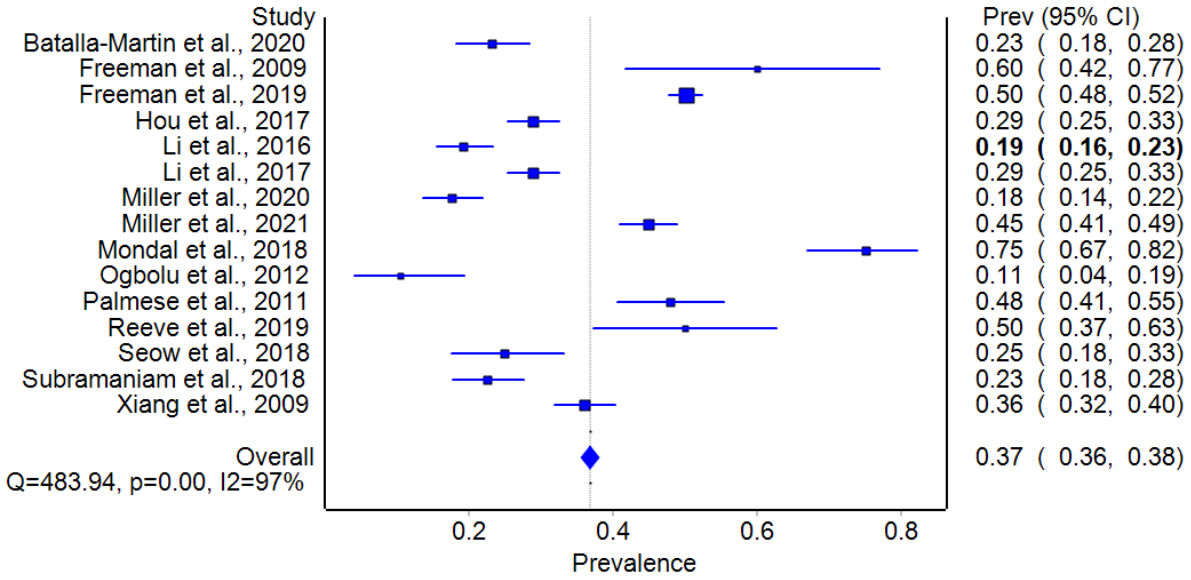

Figure 12. Fixed-effects forest plot for all studies reporting prevalence

Table 14. Fixed-effects results for studies reporting prevalence

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.232209738	0.183390159	0.284874352	4.469880525
Freeman et al., 2009	0.6	0.417766967	0.769627425	0.509649929
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	30.11947531
Hou et al., 2017	0.288924559	0.253964116	0.32518535	10.41858134
Li et al., 2016	0.193298969	0.155452031	0.234178213	6.491770407
Li et al., 2017	0.289215686	0.253936375	0.325816872	10.23477316
Miller et al., 2020	0.176829268	0.137327398	0.220109866	5.489180383
Miller et al., 2021	0.449832776	0.410113681	0.489873838	10.00083549
Mondal et al., 2018	0.75	0.669669608	0.822618083	2.0803743
Ogbolu et al., 2012	0.106060606	0.041447291	0.193520966	1.111203944
Palmese et al., 2011	0.48	0.406154229	0.554283426	2.932575821
Reeve et al., 2019	0.5	0.373295155	0.626704845	1.010944941
Seow et al., 2018	0.25	0.17623746	0.33173089	2.013534965
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	4.67039853
Xiang et al., 2009	0.36039604	0.319036224	0.402816637	8.446820954
Pooled	0.368520024	0.356339272	0.380785169	100
Statistics				
I-squared	97.10706532	96.21809697	97.78707413	
Cochran's Q	483.9376471			
Chi2, p	0			

1.9.3. Supplementary results for studies using the ISI

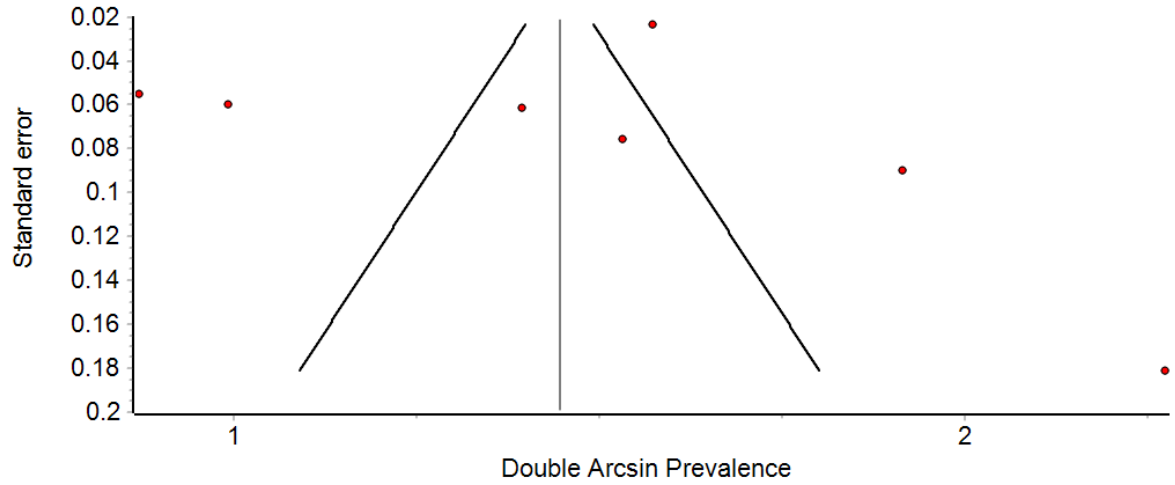

Figure 13. Funnel plot for studies using the ISI

1.9.3.1. Random-effects model across studies using the ISI

Table 15. Random-effects results for studies using the ISI

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.411985019	0.353549191	0.471684552	14.6886887
Freeman et al., 2009	0.833333333	0.675560403	0.948750851	12.08308248
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	15.04422627
Miller et al., 2020	0.176829268	0.137327398	0.220109866	14.76477454
Mondal et al., 2018	0.669354839	0.583788909	0.749696806	14.23495067
Palmese et al., 2011	0.48	0.406154229	0.554283426	14.47806666
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	14.70621067
Pooled	0.456150657	0.319548503	0.596068842	100
Statistics				
I-squared	97.55414498	96.40131481	98.33766877	
Cochran's Q	245.3129872			
Chi2, p	0			
tau2	0.130969772			

1.9.3.2. Quality-effects model across studies using the ISI

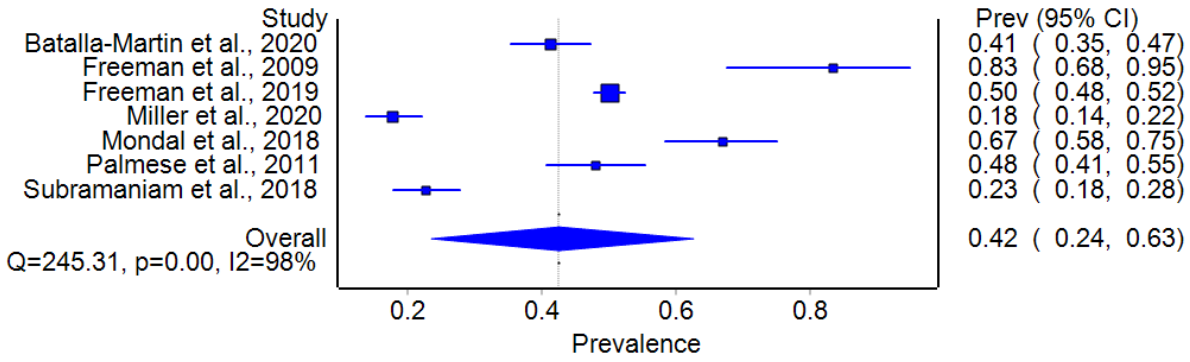

Figure 14. Prevalence of insomnia across studies using the ISI, quality effects forest plot

Table 16. Quality-effects results for studies using the ISI

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.411985019	0.353549191	0.471684552	9.912881464
Freeman et al., 2009	0.833333333	0.675560403	0.948750851	3.107396573
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	49.41856968
Miller et al., 2020	0.176829268	0.137327398	0.220109866	16.8969107
Mondal et al., 2018	0.669354839	0.583788909	0.749696806	5.620068293
Palmese et al., 2011	0.48	0.406154229	0.554283426	6.561844372
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	8.482328925
Pooled	0.424823093	0.235541429	0.625406157	100
Statistics				
I-squared	97.55414498	96.40131481	98.33766877	
Cochran's Q	245.3129872			
Chi2, p	0			
Q-Index	27.06636751			

1.9.3.3. Fixed-effects model across studies using the ISI

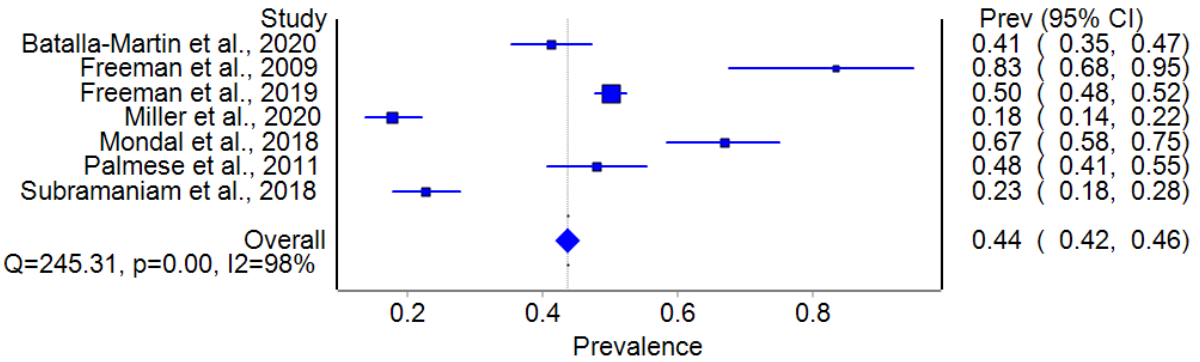

Figure 15. Fixed-effects forest plot for studies using the ISI

Table 17. Fixed-effects results for studies using the ISI

Study	Prevalence	LCI 95%	HCI 95%	weight (%)
Batalla-Martin et al., 2020	0.411985019	0.353549191	0.471684552	8.891474157
Freeman et al., 2009	0.833333333	0.675560403	0.948750851	1.01379425
Freeman et al., 2019	0.501109878	0.478021779	0.524195611	59.9135782
Miller et al., 2020	0.176829268	0.137327398	0.220109866	10.91906266
Mondal et al., 2018	0.669354839	0.583788909	0.749696806	4.138274888
Palmese et al., 2011	0.48	0.406154229	0.554283426	5.83347183
Subramaniam et al., 2018	0.225806452	0.178536133	0.276844743	9.290344025
Pooled	0.437377605	0.419689406	0.455145757	100
Statistics				
I-squared	97.55414498	96.40131481	98.33766877	
Cochran's Q	245.3129872			
Chi2, p	0			

Appendix 2.1. Submission Guidelines for Digital Health

DESCRIPTION | AIMS AND SCOPE | EDITORIAL BOARD | ABSTRACTING / INDEXING | SUBMISSION GUIDELINES

This new interdisciplinary journal provides a unique and dynamic forum to facilitate dialogue between key players in the rapidly emerging field of Digital Health. This dialogue will, in turn, allow the expression digital health to be continually defined by those at its centre - providing a unique, evolving narrative. *DIGITAL HEALTH* is fully peer-reviewed and published on an Open Access basis, to ensure maximum dissemination of content.

DIGITAL HEALTH focuses on healthcare in the digital world, bridging the evolution of advances in informatics and technology in medicine, health and all aspects of health care with the application of these developments in clinical practice, the patient experience, and their social, political and economic implications.

DIGITAL HEALTH covers themes including, but not limited to - e-health, healthcare IT, health informatics, biomedical engineering, connected health, internet health care, social media and online social networks, telemedicine, telehealth, telecare, medical imaging, mobile health, mobile technologies, wearable devices, genomics and personal genetic information, personalised medicine, Big Data and data management, wellness and prevention, gerontology and social care services, simulation and gamification, patient accessibility, acceptability and behaviour, policy and regulation, and the social, political, cultural and ethical implications of advances in the field.

The primary aim of *DIGITAL HEALTH* is to provide universally accessible and digestible content to all stakeholders involved in the digital healthcare revolution. It provides a unique forum for dissemination of high quality content applicable to researchers, clinicians and allied health practitioners, patients, social scientists, industry and government.

DIGITAL HEALTH will be a unique, high impact, international journal encompassing a wide variety of article types and multimedia material (including video articles) on:

- Research results (original research, controlled trials, case studies, feasibility and pilot studies, qualitative and quantitative studies).
- Research protocols and study designs.
- Review articles (literature reviews, systematic reviews, market reviews, critical reviews).
- Educational pieces (tutorials on new methods, best practice, user guides, policy and practice).
- Current topics and opinion pieces (e.g. digests of policy, regulation and legislation), editorials, commentaries, essays and brief communications).

Papers describing both negative and positive results and outcomes will be encouraged, and authors welcomed to supply underlying datasets where appropriate.

All articles will be fully peer-reviewed, published rapidly online within days of acceptance and made available on an Open Access basis.

3. What do we publish?

3.1 Aims & scope

A fully peer-reviewed journal, *DIGITAL HEALTH* presents universally accessible and digestible content on the latest developments in the rapidly emerging field of digital health practices. A unique and dynamic forum, *DIGITAL HEALTH* provides a vital space for the dissemination of, and engagement with, high quality papers for researchers, clinicians and allied health practitioners, patients, social scientists, as well as industry and government.

Before submitting your manuscript to *DIGITAL HEALTH*, please ensure you have read the Aims & Scope.

3.2 Article types

Content Type	Article Types	Abstract word limit	Main Text Word limit
Research Articles	Original research, controlled trials, case studies, feasibility and pilot studies, qualitative and quantitative studies	250	N/A

Appendix 2.2. Approved Proposal for Major Research Project

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. Cognitive Behavioural Therapy is effective in treating insomnia (CBTi). Pilot research suggests that insomnia is a tractable clinical target in psychosis. Digital CBTi reduces both insomnia and paranoia, offering a non-contact intervention during Covid-19 lockdown and its aftermath.

Aims: i) characterise the process of implementing a referrals pathway for Sleepio, ii) consider the expectations of service users and service keyworkers regarding digital sleep intervention and iii) characterise service users beginning sleep intervention.

Methods: People experiencing a FEP and insomnia will be eligible to access Sleepio intervention. Service users and keyworkers will be invited to participate in semi-structured interviews to elicit their views of Sleepio implementation. Recruitment into the study will be monitored. Measures will examine changes in psychosis, insomnia, and mood symptomatology, and Covid-19-related worry at baseline.

Results: We will analyse qualitative interview data of the expectations of service users and keyworkers of the Sleepio intervention. A framework analysis will be used to analyse themes arising from interviews. Recruitment data will be summarised. We will characterise service users' pre-intervention psychosis symptomatology, insomnia, mood, Covid-19-related worry, and the relationships between these. We will consider how these data inform a login model of Sleepio implementation.

Practical Applications: The overarching study aims to develop a logic model to support future implementation of Sleepio in FEP services. The major research project act as an internal pilot and will provide preliminary results to inform the implementation of Sleepio in a first episode psychosis service.

1. Introduction

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. 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.

Quarantine and physical distancing measures in response to epidemics 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). 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 (Brooks 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 Italy, anxiety, poor sleep, and psychological distress were together predictive of Covid-19-related PTSD symptomatology (Casagrande et al., 2020).

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 increased opportunity and need for digital psychological interventions, delivered remotely. 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. 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.

Sleep difficulties, particularly insomnia, are common in people recovering from a FEP (~50% affected; Davies et al., 2017; Reeve, Sheaves & Freeman, 2018a). In people affected by psychosis, severity of sleep disorder is related to flattened affect, increased hallucinations, and paranoia, and mood disorder (Davies et al., 2017; Reeve et al., 2018a; Villa et al., 2018; Reeve et al., 2018b). Models of paranoia development suggest that mood disorder (anxiety, depression and worry) contributes to the development of paranoia, which is then heightened by insomnia (Freeman et al., 2009; Reeve, Sheaves & Freeman, 2015). Insomnia can also occur due to the impact of psychosis symptomatology. In the current context of Covid-19, related worry and governmental regulations based on Covid-19, sleep may deteriorate in this group, impacting on psychosis symptomatology and other mental health variables.

Insomnia is a tractable clinical target in this population, for which intervention shows promising results. Case series and pilot studies investigating CBTi in psychosis populations found it produced

clinically significant reductions in insomnia but mixed impacts on psychosis symptomatology (Freeman et al., 2015; Myers, Startup & Freeman, 2011). Cognitive Behavioural Therapy targeting Insomnia Disorder can be effectively delivered using digital applications (dCBTi), with a comparative efficacy to 1-1 CBTi (Espie et al., 2012). Sleepio, a dCBTi application has been shown to reduce hallucinations and paranoia in a large non-clinical population (Freeman et al., 2017). Additionally, digital application-based interventions have been increasingly used in FEP populations (Rus-Calafell & Schneider, 2020).

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

2. Aims and Questions

Informed by the Medical Research Council process evaluation for complex interventions framework (Moore et al., 2015); the overarching research study aims to develop a logic model of Sleepio implementation in people recovering from FEP, in the context of Covid-19 restrictions and their aftermath. This Major Research Project (MRP) aims to act as an internal pilot; providing initial qualitative and quantitative data towards this implementation study.

We will assess:

2.1. Implementation

1) What is the pathway of approval for researching Sleepio in the context of an early psychosis service?
    i. Data protection approvals
    ii. Ethical approvals
    iii. Management approvals
    iv. Contracting between involved parties
2) How was the referral pathway established and how are recruitment efforts undertaken?
    i. Presentations to the esteem service
    ii. Meetings with local area teams
    iii. Discussion with keyworkers about study design, eligibility, potential participants
3) What is the initial rate of eligibility for the study?
4) What is the initial rate of consent into the study?

2.2. Symptomatology Measures

At baseline:

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?

2.3. 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?

2.4. Logic Model

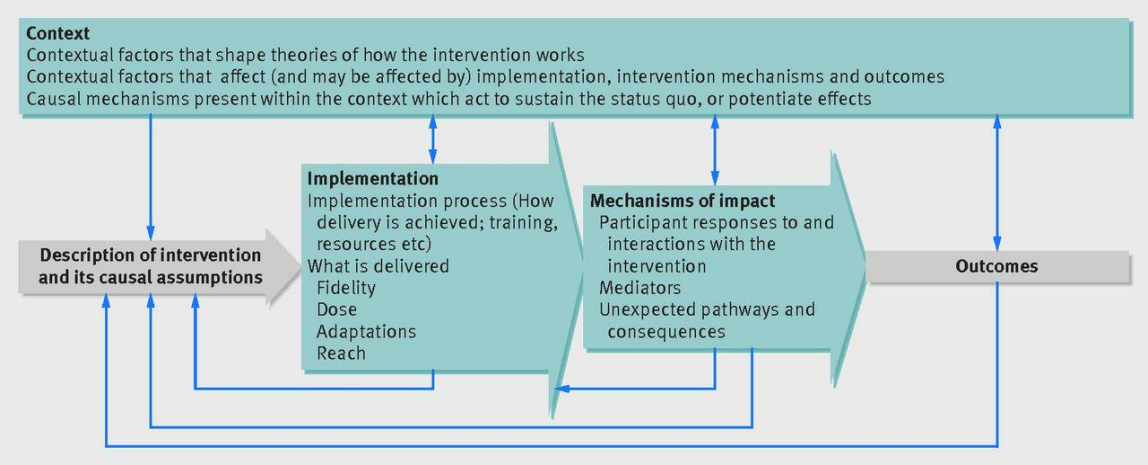

Figure 1. Key functions of process evaluation and relations among them from MRC Complex Interventions guidance.

From these data, we aim to begin to develop a logic model for the implementation of Sleepio intervention in FEP services. This model will graphically represent the hypothesized context and the process of implementing Sleepio in the Esteem service. Further work following this MRP will further elucidate the mechanisms of Sleepio's impact, outcomes and other factors acting upon the model (Moore et al., 2015).

3. Plan of Investigation

3.1. Participants

3.1.1 Service users of the Esteem FEP service, NHS Greater Glasgow and Clyde (NHSGGC).
3.1.2 Esteem keyworkers.

3.2. Inclusion and Exclusion Criteria (Service Users)

3.2.1 *Inclusion:*

3.2.1.1 Service users under the care of Esteem First Episode Psychosis Service in NHS GGC
3.2.1.2 Aged >=16yrs and ≤35 years (service criteria)
3.2.2.3 Potentially affected by Insomnia Disorder (defined by SCI-02 score ≤2)
3.2.2.4 Access to a device to use Sleepio.

3.2.2 Exclusion:

3.2.2.1 Moderate to severe learning disability
3.2.2.2 Acutely unwell (recent contact with crisis team or hospitalization)
3.2.2.3 Incapacity to provide informed consent
3.2.2.4 Insufficient English to access intervention
3.2.2.5 Organic impairment
3.2.2.6 No access to an appropriate device

3.3. Design

The proposed study is a prospective, non-randomised trial of the implementation of Sleepio in the context of an FEP service.

3.4. Study Procedures

Study protocol will be presented at the Esteem journal club and each area multidisciplinary team meeting (FR).

3.4.1. Service User Participants

Keyworkers in Esteem FEP services will be offered the opportunity to meet with researcher FR to learn about the study and consider service users who may benefit (FR).

Service users will be provided with an information leaflet regarding the study. Those who wish to participate can contact the study email address or ask their keyworker to do so on their behalf. They will be sent an easy-read Participant Information Sheet and Consent Form (FR). Participants will complete consenting processes on Attend Anywhere videocall (FR) and will return signed Consent Forms. Participants will then complete the Sleep Condition Indicator-2 item (SCI-02; Espie et al., 2016)

insomnia screening tool (FR). Where their score indicates that they may be affected by insomnia, they will be eligible to participate.

If participants have indicated they would like to participate in an interview, they will be invited to share their expectations of Sleepio intervention at a Microsoft Teams meeting lasting 45 - 60 minutes (FR). Semi-structured interviews will be digitally recorded and transcribed for purposes of analysis (FR). They will be analysed using a framework analysis (FR).

FR and LB will meet with participants and complete baseline measures using Attend Anywhere and Online Surveys (https://www.onlinesurveys.ac.uk/). This appointment will also allow participants to set up the Sleepio application and complete its initial assessment.

The following service user procedures will occur after the timeline of the MRP:

The intervention period will commence. Participant adherence to and attrition from intervention will be collated via the Sleepio application (LB).

10 weeks following baseline assessment, participants will be invited to repeat symptomatology measures at an Attend Anywhere appointment using Online Surveys (LB).

Participants who have consented to being interviewed about their experience of Sleepio will be invited to participate in a further Microsoft Teams meeting (LB). Participants will be purposively sampled to include a range of participants reflecting their engagement with the Sleepio App. Semi-structured interviews will be digitally recorded and transcribed for purposes of analysis (LB). They will be analysed using a framework analysis (LB).

3.4.2. Staff Participants

Keyworkers in Esteem will be provided with an information leaflet describing the study (FR). This will detail i) service user eligibility criteria, and the pathway for recruiting service users into the study and ii) the role of keyworkers as participants.

Keyworkers will be given the opportunity to participate in semi-structured interviews about their expectations of Sleepio, barriers and facilitators via Microsoft Teams meeting (FR). These will take place prior to service users beginning intervention. They will be provided with a Participant Information Sheet and Consent Form. Participating keyworkers will complete consenting processes on this videocall and will return signed Consent Forms (FR).

The following keyworker procedures will occur after the timeline of the MRP:

Following the intervention period, keyworkers will be offered participation in a further interview with another researcher (LB) about their experiences of Sleepio.

Semi-structured interviews will be digitally recorded and transcribed for purposes of analysis and analysed using a framework analysis (FR; LB).

3.5. Intervention and TAU

3.5.1. Sleepio Intervention

Sleepio is a dCBTi application with a strong evidence base (Espie et al., 2019). The application is composed of six 20-minute sessions, unlocked weekly. It can be accessed via web browser or smartphone. Participants complete an initial assessment and choose a goal, which drives personalisation. Sleepio's components are 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 sessions and enter sleep data. Sleepio's algorithm tailors ongoing intervention based on entered data and information about participants' physical and mental health. Sleepio also provides access to online psychoeducation and a moderated user forum.

3.5.2. Treatment as Usual (TAU)

TAU will be free to vary during the study. TAU may comprise elements of sleep intervention. TAU is likely to be significantly different during Covid-19 restrictions.

3.6. Measures

- Demographic data (gender, age, ethnicity).

3.6.1. Implementation Measures

3.6.1.1. Time taken to procure necessary approvals (data protection, ethical, contracts).
3.6.1.2. Number of presentations to Esteem
3.6.1.3. Number of information sessions delivered to Esteem local area teams
3.6.1.4. Number of meetings with service keyworkers
3.6.1.5 Rate of referral
3.6.1.6. Rate of eligibility to participate.
3.6.1.7. Rate of consent to participation.
3.6.1.8. Proportion completing Sleepio initial assessment.

3.6.2. Symptomatology Measures

Insomnia

- Insomnia Severity Index (ISI, Morrin et al., 2011).

Psychosis

- Specific Psychotic Experiences Questionnaire; hallucinations subscale (SPEQ-H, Ronald et al., 2014).
- Revised Green et al Paranoid Thought Scales (R-GPTS, Freeman et al., 2019).

Mood

- Depression, Anxiety, and Stress Scales, 24 item (DASS-24, Lovibond and Lovibond, 1995).

Covid-19 Anxiety

- Fear of COVID-19 Scale (Ahorsu et al., 2020).

3.6.3. Qualitative Data

- Semi-structured interviews exploring staff expectations for dCBTi intervention
- Semi-structured interviews exploring service user expectations for dCBTi intervention

3.7. Settings and Equipment

The study will take place with service users of the NHSGGC Esteem FEP Service. Measures assessment will be undertaken on Attend Anywhere. Interviews will be recorded and transcribed using NHS GGC Microsoft Teams or an encrypted recording device.

3.8. Sample Size

This is a mixed-methods study focused on implementation. Formal sample size calculation would therefore not be appropriate. For the *overall* study, a target sample size of 40 service user participants is proposed, based on recruitment for 12 months. ~nine service users and ~nine keyworkers are hoped to be recruited for interviews.

The MRP will aim to recruit ≥6 keyworkers and ≥3 service users.

3.9. Data Analysis

3.9.1. Quantitative

Summary descriptive quantitative information will be provided for implementation measures.

Symptomatology measurements will be quantitatively detailed (mean, median, range, variance). Our study is not designed nor powered to detect statistical differences in measures over time..

3.9.2. Qualitative

Information arising from qualitative interviews will analysed using a framework analysis based on the MRC Complex Interventions framework (Moore et al, 2016). This will comprise an iterative process of familiarization with the transcribed data, indexing to the thematic framework, identifying other emergent themes, charting and mapping, and summary interpretation.

3.9.3. Modelling

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

3.9.4. Other

A timeline of changes to Scottish government regulations regarding Covid19 will be collated in order to contextualize study data.

4. Health and Safety Issues

4.1. Researcher Safety Issues

Use of Attend Anywhere 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 operation 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.

4.2. Participant Safety Issues

Prior to consenting, participants will be made aware that keyworkers will be informed of their participation. 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. Potential participants will be made aware of this prior to consenting.

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

5. Ethical Issues

Participation will not commence without informed consent, including ensuring participant awareness of confidentiality and limits to confidentiality. It will be made clear that study participation status will have no impact on TAU care. Aspects of the consent process will be optional - to participate in interviews pre- and post-intervention, for researchers to access participant SCI scores, and to discuss the participant's use of Sleepio with their keyworker.

Potential participants will be made aware that the study may comprise 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.

This study uses an application external to NHSGGC. A contract is in place between the University of Glasgow and NHS GGC (joint data controllers) and between the University of Glasgow and Big Health Ltd. The study will request approval from NHSGGC Information Governance, NHSGGC Research and Development and the NHS Research Ethics Committee. The study will analyse anonymised data outwith NHSGGC (at University of Glasgow). Data will be held in accordance with NHS GGC and University of Glasgow policies and GDPR.

6. Financial Considerations

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

7. Dissemination

An internal pilot of the study will be submitted as the Major Research Project for a Doctorate in Clinical Psychology at the University of Glasgow. Results will be presented to Esteem staff. The full project will be submitted for journal publication. Participating service users may receive a plain language summary of results if they wish.

8. 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 NHSGGC FEP services. A logic model of Sleepio implementation will help inform this.

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Appendix 2.3. Research Ethics Committee Approval

WoSRES

West of Scotland Research Ethics Service

NHS Greater Glasgow and Clyde

Professor Andrew Gumley
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Gartnavel Royal Hospital
Glasgow
G12 0XH

West of Scotland REC 4
Research Ethics
Ward 11, Dykebar Hospital
Grahamston Road
Paisley
PA2 7DE

Date 24 March 2021
Direct line 0141 314 0213
E-mail WoSREC4@ggc.scot.nhs.uk

Dear Professor Gumley

Study title: **Implementation of a Digital Cognitive Behavioural Therapy Intervention for Insomnia in First Episode Psychosis in the Context of Covid19: A Mixed Methods Study**
REC reference: **21/WS/0010**
IRAS project ID: **280858**

Thank you for your letter received on 15 March 2021, responding to the Research Ethics Committee's (REC) request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC.
A list of the Sub-Committee members is attached.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants
4. sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

1. The use of the word "Pseudonymized data" especially in the service users PIS should be changed as most patients would not know what that means. A suggested text could be "Data that contains no real names…." It could be emphasized to read 'It means that instead of a comment in an interview being attributed to me I would be given an alter ego throughout the transcript'.

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

If you have not already included registration details in your IRAS application form, you should notify the REC of the registration details as soon as possible.

Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to

confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS/HSC sites (as applicable)

I am pleased to confirm that the favourable opinion applies to any non-NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of materials calling attention of potential participants to the research [280858 - Service User - Information Leaflet - V4.1 - 12.03.2021 - Tracked]	4.1	12 March 2021
Copies of materials calling attention of potential participants to the research [280858 - Keyworker - Information Leaflet - V4.1 - Tracked]	4.1	12 March 2021
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [University of Glasgow Clinical Trials Insurance]		15 July 2020
GP/consultant information sheets or letters [280858 - GP Notification Letter]	2	04 December 2020
GP/consultant information sheets or letters [280858 - Keyworker Notification Letter]	3	18 December 2020
Interview schedules or topic guides for participants [280858 - Service User - Interview Schedule - Pre Intervention]	2	07 November 2020
Interview schedules or topic guides for participants [280858 - Service User - Interview Schedule - Post Intervention]	3	16 December 2020
Interview schedules or topic guides for participants [280858 - Keyworkers - Interview Schedule - Pre-Intervention - V3.1 - 25.02.2021 - Tracked]	3.1	25 February 2021
Interview schedules or topic guides for participants [280858 - Keyworkers - Interview Schedule - Post-Intervention - V4.1 - 25.02.2021 - Tracked]	4.1	25 February 2021
IRAS Application Form [IRAS_Form_28122020]		28 December 2020
Letters of invitation to participant [80858 - Service User - PIS Cover Letter - V4.1 - 12.03.2021 - Tracked]	4.1	12 March 2021
Letters of invitation to participant [80858 - Keyworker - PIS Cover Letter - V4.1 - 12.03.2021 - Tracked]	4.1	12 March 2021
Other [280858 - LBeattie CV]		13 July 2020
Other [280858 - MSpanswick CV]		17 July 2020
Other [280858 - Service Manager Approval]		21 December 2020
Other [280858 - Esteem Service Attend Anywhere Patient Guide]		
Other [280858 - Sleepio Onboarding Questions]	1	22 September 2020
Other [280858 - Keyworker - Interview Appointment Letter - Post Intervention - Tracked]	3.2	13 March 2021
Other [280858 - Protocol - Tracked]	5.1	12 March 2021

Document	*Version*	*Date*
Other [280858 - Service User - Interview Appointment - Pre-Intervention - V3.1 - 12.03.2021 - Tracked]	3.1	12 March 2021
Other [280858 - Service User - Assessment and Questionnaire Appointment - Pre Intervention - V2.1 - 12.03.2021 - Tracked]	2.1	12 March 2021
Other [280858 - Service User - Assessment Appt Letter - Post Intervention - Tracked]	2.1	12 March 2021
Other [280858 - Service User - Interview Appointment - Post-Intervention - V3.1 - 12.03.2021 - Tracked]	3.1	12 March 2021
Other [280858 - Keyworker - Interview Appointment - Pre-Intervention - V3.1 - 12.03.2021 - Tracked]	3.1	12 March 2021
Participant consent form [280858 - Service User Consent Form - Tracked]	4	12 March 2021
Participant consent form [280858 - Keyworker - Consent - V4.1 - Tracked]	4.1	12 March 2021
Participant information sheet (PIS) [280858 - Service User - PIS - V3.1 - Tracked]	3.1	12 March 2021
Participant information sheet (PIS) [280858 - Keyworker - PIS - V5.1 - Tracked]	5.1	12 March 2021
Response to Request for Further Information [Replies to REC Provisional Opinion]		
Summary CV for Chief Investigator (CI) [280858 - AGumley CV]		10 July 2020
Summary CV for student [280858 - FRobb CV]		14 August 2020
Validated questionnaire [280858 - SCI02]		
Validated questionnaire [280858 - Insomnia Severity Index]		
Validated questionnaire [280858 - DASS21]		
Validated questionnaire [280858 - SPEQ-H]		
Validated questionnaire [280858 - RPTS]		
Validated questionnaire [280858 - Fear of Covid19 Scale]		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 280858 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely

On behalf of
Dr Ken James
Chair

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

"After ethical review – guidance for researchers"

Copy to: Dr Colette Montgomery Sardar

West of Scotland REC 4

Attendance at Sub-Committee of the REC meeting

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Wendy Cohen	Speech & Language Therapist	Yes	Chair of Meeting
Mr Jim McHugh	Independent Financial Advisor	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Abibat Adewumi-Ogunjobi	REC Manager

Appendix 2.4. NHS Greater Glasgow Research and Development Approval

Coordinator: Emma Mcdonough
Telephone Number: 0141 314 4011
E-Mail: Emma.McDonough@ggc.scot.nhs.uk
Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/research-innovation

Research & Innovation
Dykebar Hospital, Ward 11
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Paisley, PA2 7DE

20/04/2021

Professor Andrew Gumley
University of Glasgow
Mental Health and Wellbeing
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
G12 0XH

NHS GG&C Board Approval

Dear Professor Andrew Gumley

Study Title:	Implementation of a Digital Cognitive Behavioural Therapy Intervention for Insomnia in First Episode Psychosis in the Context of Covid19: A Mixed Methods Study
Principal Investigator:	Professor Andrew Gumley
GG&C HB site	Esteem Service – Stobhill Hospital & Leverndale Hospital
Sponsor	NHS Greater Glasgow &Clyde
R&I reference:	GN21MH015
REC reference:	21/WS/0010
Protocol no: (including version and date)	V5.1 12.03.2021

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file. Researchers must follow NHS GG&C local policies, including incident reporting.

2. **For all studies** the following information is required during their lifespan.
   a. First study participant should be recruited within 30 days of approval date.
   b. Recruitment Numbers on a monthly basis
   c. Any change to local research team staff should be notified to R&I team

d. Any amendments – Substantial or Non Substantial
e. Notification of Trial/study end including final recruitment figures
f. Final Report & Copies of Publications/Abstracts
g. You must work in accordance with the current NHS GG&C COVID19 guidelines and principles.

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

Emma Mcdonough
Research Co-ordinator

CC: Fiona Robb

Appendix 2.5. Service Manager Approval

Re: IRAS 280858 - Revised documents

Andrew Gumley <Andrew.Gumley@glasgow.ac.uk>
Mon 21/12/2020 17:36

To: Whinnery, Scott <Scott.Whinnery@ggc.scot.nhs.uk>
Cc: Spanswick, Mairi <Mairi.Spanswick@ggc.scot.nhs.uk>; Fiona Robb (PGR)

Dear Scott

That is indeed excellent news! Thank you

Warm regards

Andrew

From: "Whinnery, Scott" <Scott.Whinnery@ggc.scot.nhs.uk>
Date: Monday, 21 December 2020 at 17:35
To: Andrew Gumley <Andrew.Gumley@glasgow.ac.uk>
Cc: "Spanswick, Mairi" <Mairi.Spanswick@ggc.scot.nhs.uk>
Subject: RE: IRAS 280858 - Revised documents

Hi Andrew,

Yes our service is happy to support this MRP, Protocol no. 280858, dated 15th December 2020.

Let me know if I have to send this email to anyone else.

Thanks,

Scott Whinnery
Team Leader
Esteem GG&C
Nevis Building, Stobhill Hospital/ Admin Building, Leverndale Hospital
0141 5313207/ 0141 2116563
Scott.whinnery@ggc.scot.nhs.uk

From: Andrew Gumley [mailto:Andrew.Gumley@glasgow.ac.uk]
Sent: 18 December 2020 19:03
To: Whinnery, Scott <Scott.Whinnery@ggc.scot.nhs.uk>
Subject: [ExternaltoGGC]Fwd: IRAS 280858 - Revised documents

Dear Scott

As you know Fiona will be conducting the Sleepio study in the new year. Are you in a position to provide an email noting managerial support for the study?

Thank you so much and warm regards

Andrew

Get Outlook for iOS

Appendix 2.6. COREQ Checklist

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	60
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	64
Occupation	3	What was their occupation at the time of the study?	64
Gender	4	Was the researcher male or female?	64
Experience and training	5	What experience or training did the researcher have?	64
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	64
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	64
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	64
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	64
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	60
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	60
Sample size	12	How many participants were in the study?	69
Non-participation	13	How many people refused to participate or dropped out? Reasons?	69
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	60
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	60
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	69
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	63
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	N/A
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	60
Field notes	20	Were field notes made during and/or after the inter view or focus group?	60
Duration	21	What was the duration of the inter views or focus group?	60
Data saturation	22	Was data saturation discussed?	84
Transcripts returned	23	Were transcripts returned to participants for comment and/or	N/A

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	64, 85
Description of the coding tree	25	Did authors provide a description of the coding tree?	69
Derivation of themes	26	Were themes identified in advance or derived from the data?	64
Software	27	What software, if applicable, was used to manage the data?	N.A
Participant checking	28	Did participants provide feedback on the findings?	N.A
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	69-79
Data and findings consistent	30	Was there consistency between the data presented and the findings?	82
Clarity of major themes	31	Were major themes clearly presented in the findings?	82
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	N/A

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

Appendix 2.7. Coding of Emergent Themes

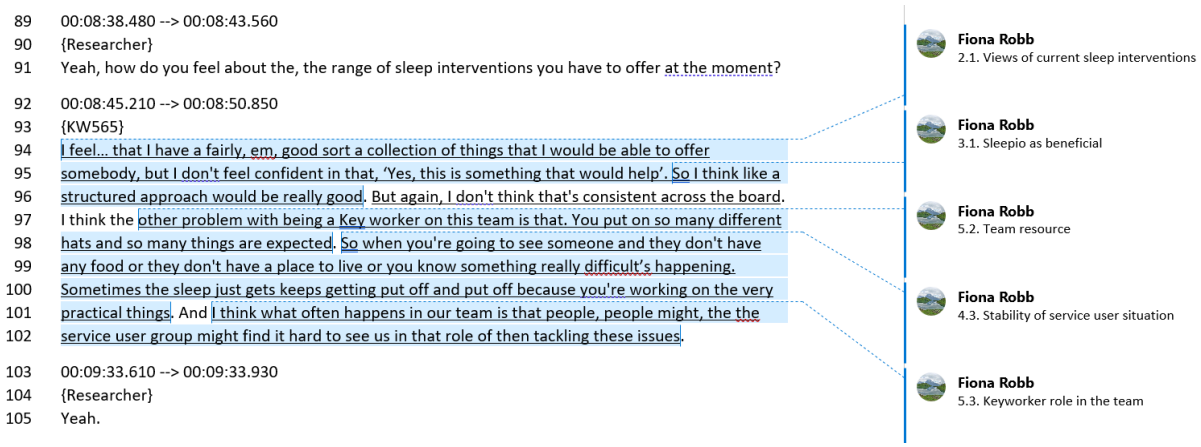

Figure 16. Example of framework analysis coding for categories and sub-categories