Early signs monitoring to prevent relapse and promote wellbeing, engagement and recovery

This merged document (12th April 2019) contains:

File pages 2- 30 EMPOWER Phase I Protocol V1.4 19th December 2016

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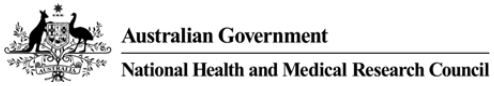

STUDY PROTOCOL

Title: EMPOWER: Early signs Monitoring to Prevent relapse in psychosis and prOmote Wellbeing, Engagement and Recovery

Phase 1 Research Protocol Version Number: 1.4 (19th December 2016)

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2.0 Glossary of Terms

Abbreviation	Description (using lay language)
ACS	Adult Community Service
App	Mobile telephone application
CBT	Cognitive Behaviour Therapy
CI	Chief Investigator
CMHT	Community Mental Health Team
DMEC	Data Monitoring and Ethics Committee
EMPOWER	Early signs monitoring to Prevent relapse and pr0mote Wellbeing, Engagement, and Recovery
EWS	Early warning signs
IP	Intellectual property
JCPs	Joint Crisis Plans
MRC	Medical Research Council
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NIHR	National Institute for Health Research
NPT	Normalization Process Theory
PI	Principal Investigator
PSSUQ	Post-Study System Usability Questionnaire
RA	Research Assistant
RCT	Randomised controlled trial
SSC	Study Steering Committee
WP	Work Package

3.0 Study Synopsis

Title:	EMPOWER: Early Signs Monitoring to Prevent Relapse and Pr0mote Wellbeing, Engagement, and Recover
Short Title:	EMPOWER
Design:	Mixed methods study
Study Centres:	Greater Glasgow and Clyde mental health community services Australian sites - NorthWestern Area Mental Health Service Adult Community Services
Hospital:	NA
Study Question:	NA
Study Objectives:	The objectives of this study phase are to conduct focus group interviews to (i) evaluate the acceptability and usability of mobile symptom reporting using smartphones amongst service users, carers and mental health staff; (ii) identify incentives and barriers to use by service users and carers and implementation by mental health staff; and the identification of pathways to relapse identification and prevention. These interviews will inform modifications to the EMPOWER mobile App which will then be subjected to Beta-testing by interviewing service users, carers and mental health staff regarding acceptability and usability after a 7-day evaluation period.
Primary Objectives:	The development of the EMPOWER intervention
Secondary Objectives	The identification of (i) barriers and enablers to relapse identification and prevention; and (ii) the training needs of teams to enhance relapse detection and prevention.
Inclusion Criteria:	Service user participants: ≥ 16 years of age (no upper age limit) In receipt of CMHT services in NHS Greater Glasgow & Clyde Diagnosis of a relevant DSM-5 schizophrenia spectrum disorder Current presentation does not include severe acute symptoms Carer participants: Regular (i.e., weekly contact) with the consumer participant Professional mental health care staff participants: ≥ 2 months duration of employment All participants will also need to meet the language requirements for participation, and will need to be able to provide informed consent for themselves.
Exclusion Criteria:	< 16 years of age

	Unable to provide informed consent Participation in an existing research study
Number of Planned Subjects:	40 consumers/ service users 40 carers 30 – 45 professional mental health care staff
Investigational product:	EMP0WER mobile telephone Application
Safety considerations:	Risks to personal privacy; Risks to clinical safety
Statistical Methods:	Qualitative Framework Analysis
Subgroups:	NA

4.0 Plain English Summary

The EMPOWER research project is funded by a National Institute for Health Research Health Technology Assessment (NIHR-HTA) and a National Health and Medical Research Council (NHMRC) - Collaborative Research Grant.

The overarching objective of this project is to design and evaluate the novel EMPOWER intervention: a personalized mobile phone based relapse prevention system/ App for individuals with a Schizophrenia Spectrum Disorder. The evaluation comprises two components: (i) evaluation of the system for self-initiated and self-managed early warning signs (EWS) using real time sampling and methods (i.e., phase 1); and (ii) examination of the feasibility of the EMPOWER intervention through a 15-month pilot cluster randomized trail (i.e., phase 2).

Phase 1 will be conducted in NHS Greater Glasgow & Clyde and in NorthWestern Area Mental Health Adult Community Service Teams.

Phase 1 is projected to span 9 months (1st April 2016 – 31st December 2016), and is comprised of three work packages: (WP 1) user and carer engagement, software evaluation and improvement; (WP 2) professional staff engagement, modelling treatment as usual, mapping the relapse prevention pathway, identification of training needs; and (WP 3) software beta-testing. The aims of the first WP are: (a) to evaluate the acceptability and usability of the EMPOWER App amongst service users and their carers, and (b) the identification of incentives and barriers to use. Study endpoints are completion of focus group interviews which will inform design of the EMPOWER App. The aims of the second WP are: (a) to evaluate the acceptability and usability of the EMPOWER App amongst professional care staff, (b) to identify incentives and barriers to implementation by NHS CMHT staff and NorthWestern Mental Health staff (Australian arm), and (c) the identification of relapse prevention pathways and whole team responses. Study endpoints are completion of focus group interviews which will inform design of the EMPOWER App and the identification of training needs to enhance relapse detection and prevention. The aim of the third WP is to finalise the EMPOWER App for implementation in a subsequent pilot cluster randomized controlled trial (i.e., WP 4 of Phase 2), which will compare the EMPOWER intervention to treatment as usual. Study endpoints are to complete interviews with service users, carers and mental health staff to identify preliminary acceptability and usability of the EMPOWER App.

Phase 1 is a 9-month mixed methods study following the UK Medical Research Council's Framework for developing and evaluating complex interventions. For this reason we will draw on Normalisation Process Theory (http://www.normalizationprocess.org/), which provides a conceptual framework for understanding and evaluating the implementation processes by which new health technologies, and other complex interventions, are routinely operationalized and embedded in everyday work, and sustained or integrated into routine practice.

The present study will refine existing smartphone technology (i.e., ClinTouch and CareLoop) to develop the EMPOWER App.

The main features of the EMPOWER App that distinguish it from previous work are:

(i) A stepped care model of relapse detection and prevention managed by the research team,

(ii) Increased empowerment for the service user with greater information on their own symptoms, ownership of their own data, and the ability to self-manage how that information is shared with their treating team.

5.0 Background and Rationale

Schizophrenia is a severe mental illness (SMI) affecting 24 million people worldwide, costing the NHS in the UK £2bn and the Australian Health Sector Aus$1.34bn annually. Costs to the Australian Government are Aus$3.51bn annually and wider societal costs are estimated as Aus$4.9bn annually (Neil et al., 2014). Schizophrenia is a major public health burden and is associated with increased mortality with death occurring 10-15 years earlier than the population at large through both suicide and poor physical health and this differential mortality gap has widened over recent decades (Saha, Chant & McGrath, 2007).

Relapse influences the long-term course of psychosis with rates accumulating following a first episode to 20–35% after one year. In a recent, review the pooled prevalence of relapse of positive symptoms in first episode was 28% (range = 12-47%), 43% (35-54%), 54% (40-63%) at 1, 1.5-2, and 3. years follow-up, respectively (Alvarez-Jimenez et al., 2012). Relapse can occur in up to 80% at five years (Robinson et al., 1999). Relapse is associated with higher inpatient and outpatient costs (Fitzgerald et al., 2009; Ascher-Svanum et al., 2010). The cost of treating relapsing psychosis is four times that of stable psychosis. Despite the rise of community care, 70% of the UK costs of SMI are for unplanned inpatient care for relapse. The 2010 Second Australian National Survey of People Living with Psychotic Illness (Morgan et al 2011) reported that 61.5% of the treated population had a course of illness characterized by multiple episodes of psychotic symptoms with full or partial remission of symptoms between episodes. One-year incidence of hospital admission was 34% of the treated population, with 27.8% of those having one or more further admissions to hospital within the year. In

Australia, almost half (46%) of health sector costs are generated by inpatient care, with psychiatric admissions accounting for 96% of these costs (Aus$609M). Relapsing or unstable psychosis has the greatest impact on these patterns of service utilisation. Raudino et al., (2014) found that psychiatric admissions (including use of emergency services) were associated with higher symptoms, suicidal ideation, poorer functioning and younger age.

5.1 Predictors of Relapse

One important predictor of relapse is lack of acceptance of treatment and unplanned discontinuation of antipsychotic medication (Alvarez-Jimenez et al., 2012). Poorer adherence often signals a lack of engagement with services and failure of services to build a collaborative working alliance (Subotnik et al., 2011). Specifically, non-adherence to antipsychotic treatment is predicted by poorer insight, previous experience of involuntary treatment, poorer premorbid functioning, comorbid substance misuse, forensic history and a poor therapeutic relationship with the prescriber (Day et al., 2005; Lambert et al., 2010). Relapse itself is also an important marker of severity and complexity of illness. Relapse is predicted by previous suicide attempts (Novick et al., 2010), depression, hostility and embarrassment (Rummel-Kulge, Schuster, Peters & Kissling, 2008), poorer premorbid functioning, family criticism, substance misuse, social isolation (Alvarez-Jimenez et al., 2012), negative interpersonal style (probably linked to poorer utilisation of social support) (Gleeson et al., 2005) and greater fear of relapse itself (Gumley et al., 2014).

Birchwood et al (1989) pioneered the development of systematic early signs monitoring for relapse and its integration into routine care. It is now known that relapse is the culmination of a process of change starting days and sometimes weeks before psychosis symptoms re-emerge or are exacerbated. These early warning signs (EWS) include affective changes and incipient psychosis. A recent systematic review (Eisner, Drake & Barrowclough, 2013) to determine the validity of EWS as predictors of relapse in people with non-affective psychosis found that the sensitivity of early signs to relapse (proportion of relapses correctly predicted) ranged from 10% to 80% (median 61%) and specificity (proportion of non-relapses correctly identified) ranged from 38% to 100% (median 81%). Detection of relapse was improved by more frequent monitoring (at least fortnightly) and by the inclusion of both psychotic and affective symptoms.

5.2 Interventions to prevent relapse

Gumley et al., (2003) conducted the first study to evaluate the implementation of cognitive behaviour therapy (CBT) tailored towards the prevention of relapse. CBT delivered on the appearance of EWS lead to a significant reduction in relapse over 12-months. A significant barrier to relapse prevention was service users' fears of help-seeking arising from previous experiences of relapse. For example, service users may avoid calling their key worker in the context of an increase in EWS for fear of being admitted to hospital. In a randomised controlled trial (RCT) of relapse detection, Gumley et al., (2014) found that fear of relapse was as sensitive to the onset of relapse (Sensitivity = 72%, 95% CI = 52–86) as EWS (Sensitivity= 79%, 95% CI = 62–89).

A recent Cochrane Review focused on the effectiveness of interventions targeting recognition and management of EWS of relapse in schizophrenia (Morriss et al., 2013). Significant effects in favour of EWS interventions were found for the number of participants relapsing (15 RCTs, n = 1502, risk ratio (RR) 0.53 95% CI 0.36 to 0.79) and the number of participants being re-hospitalised (15 RCTs, n = 1457, RR 0.48, 95% CI 0.35 to 0.66); however, it was found that the quality of the trials conducted to date was poor in terms of randomisation, concealment and blindness. Therefore, future EWS interventions need to address methodological problems related to trials of EWS interventions that limit their generalizability to usual care. Specifically, these methodological problems (in terms of unclear randomisation, blinding of outcome and incomplete outcome data) mean that EWS interventions cannot be recommended for routine implementation in health services (Morriss et al., 2013).

5.3 Barriers to relapse detection and prevention

There is also significant uncertainty surrounding the prognostic validity of EWS (Eisner et al., 2013), which results in the risk of unnecessary intervention that may sensitise service users and carers to heightened fear of relapse (a potential adverse event related to early signs monitoring; Gumley et al., 2014). Fear of illness and stigma are closely related to emotional dysfunction (Birchwood, 2003) and to poorer insight in schizophrenia (Day et al, 2005). Feelings of fear, depression and helplessness are common emotional experiences prior to full relapse (van Os & Kapur, 2009). Avoidant styles of coping are linked to increased risk of relapse. In an effort to minimise the stigma of illness and prevent relapse, service users can adopt avoidant coping styles (e.g. Birchwood, 2003). These coping styles are associated with greater insecurity in relationships, lower self-esteem, lower levels of adherence and reluctance to seek help in a crisis. Reluctance to seek help may result from greater fear of relapse arising from experiences of involuntary admission. In a recent systematic review, Gumley, Taylor, Schwannauer and Macbeth (2014) found that greater difficulties forming relationships was associated with poorer engagement with services, more problematic relationships with staff, and more frequent and longer hospital admissions. In sum, the detection of and action following these EWS may be constrained by avoidance, stigma, fear of relapse and reluctance to disclose.

In both UK and Australia, an important aspect of service provision for those service users at greatest risk of relapse is having access to an integrated mental health care system that enables clear shared planning for managing risk and relapse prevention. One example of this is the role of Joint Crisis Plans (JCPs) in the UK. The CRIMSON study (Thornicroft et al., 2013) was an individual level RCT that compared the effectiveness of JCPs with treatment as usual for people with schizophrenia. There was no significant impact on the primary outcome (reduced coercion into hospital). It was noted that when faced with crisis, in spite of the considerable effort in developing the JCP with service users, the teams reverted to 'custom and practice' and JCPs were not consulted by staff in planning the team response to a crisis. Furthermore, service users experienced an inability to influence clinicians behaviours and this was interpreted as signalling a lack of respect for their views and opinions. In consequence, they described their interactions as a "playing the game"; that is appearing comply with treatment

decisions. Clinicians themselves experienced their interations with service users as ritualised especially in the context of responding to increase risk (Farrelly et al., 2015). Our work with service users (Gumley & Park, 2010) has highlighted that relapse prevention based on EWS monitoring relies on the service user initiating help-seeking in the context of feeling vulnerable and threatened. Many individuals find help-seeking a challenge and may have had difficult or traumatic experiences of psychosis. Delay in help-seeking narrows the window of opportunity for successful relapse prevention, which in turn increases reliance on coercive measures confirming pre-existing negative expectations. It is therefore essential to develop and evaluate an intervention that can not only change the disclosure of relapsing individuals but one that can radically change the behaviour of mental health teams and the actions of their staff in a crisis.

5.4 Digital Technology

Digital technology offers such a step change that can influence the behaviour of both service users and mental health teams to enhance engagement with the early signs monitoring approach. Smartphones to support healthcare are promising for delivery of interventions that are unconstrained by the limitations of existing treatment settings. Mobile phones are widely available, affordable, and are continuously dropping in cost; there are now over 6 billion mobile phone subscriptions worldwide. Ben-Zeev et al. (2013) have shown that mobile phone usage is similar to the general population in people with serious mental illness including schizophrenia and that these individuals express an interest in engaging with mobile interventions. A recent systematic review concluded that Internet and mobile-based interventions for psychosis seem to be acceptable and feasible and have the potential to improve clinical and social outcomes. Specifically, 74-86% of patients used the web-based interventions efficiently, 75-92% perceived them as positive and useful, and 70-86% completed or were engaged with the interventions over the follow-up. In addition, online and mobile interventions showed promise in improving positive psychotic symptoms, hospital admissions, socialization, social connectedness, depression and medication adherence (Alvarez-Jimenez et al., 2014) In Schizophrenia, acceptability of using mobile phones to monitor symptoms appears to be high with rates of adherence to assessments of EWS estimated at over 80% over 3-months (Granholm et al. 2012) and 1-year (Spaniel et al., 2012). Self-ratings of symptoms using Smartphone demonstrate moderate to strong correspondence with clinician ratings derived from structured clinical interviews (Palmier-Claus et al., 2012). Service users with schizophrenia have also expressed potential benefits to the quality of care from Smartphone EWS monitoring in terms of assisting clinicians to have a better understanding of their service users' mental health, faster and more efficient data exchange, and aiding patient-clinician communication. They felt that mobile monitoring could be integrated easily into daily routines (Palmier-Claus et al., 2012). Mobile interventions enhancing self-management have been associated with rates of 85% adherence and high levels of satisfaction (Ben-Zeev et al., 2014). Members of our team have been at the forefront of this work in developing this approach to 'real time' monitoring and intervention (Palmier-Claus et al., 2011; Alvarez-Jimenez et al., 2013; Palmier-Claus et al., 2012; Ainsworth et al., 2013)

5.5 Digital Technology Development

We will refine existing technology (i.e., ClinTouch and CareLoop) to deliver EMPOWER. The Background intellectual property (IP) has already been well established by researchers and software engineers based at the University of Manchester (Ainsworth, Lewis, Bucci). ClinTouch was developed through an MRC funded project (PI: Lewis) as a mobile phone based monitoring system to record real time data on current symptoms, establish the acceptability of mobile monitoring in this group and compare against conventional and gold standard measures of psychiatric symptoms. CareLoop, was also funded by the MRC (PI: Lewis), and builds on ClinTouch. CareLoop is a personalised mobile phone based system for mental health service users to record ambulant data on current systems, stressors and functioning to be uploaded in real time to a central server in a clinical team base and linked to prototypical management algorithms.

5.6 Alignment with Health Priorities

We will further develop and enhance our ClinTouch and CareLoop mobile applications and build a relapse prevention pathway that enables service users to become more aware of changes in their thinking, physiology, behaviour and feeling, and will seek to enable individuals to respond to these changes positively. The aim of self-management is to enhance acceptance, autonomy, empowerment and behavioural engagement rather than the patterns of fear, demoralisation, withdrawal, avoidance and defeat observed in the phenomenological studies of early signs. If using technology empowers service users to make informed choices in real time about their treatment and to act promptly under their own control, then we believe we have the potential to transform community care for people with SMI. Our proposal aligns with several emerging NHS and Australian health priorities: prevention; early intervention; personalised care; service user involvement/empowerment; social recovery and efficiency. To deliver innovative and effective community-based care, a major shift in the way care is delivered is needed which empowers service users to play an active role in illness management. The Australian Commission on Safety and Quality in Health Care have prioritised the development of effective partnerships between consumers and healthcare providers and organisations at levels of healthcare provision, planning and evaluation. The NHS Quality, Innovation, Productivity and Prevention (QIPP) Framework for long term conditions is to "empower service users to maximise self management including ensuring service users have appropriate information and knowledge about how to manage their condition". QIPP demands a focus on innovation to drive up the quality of care and increase the productivity of healthcare services.

6.0 Study Design

EMPOWER Phase 1 is a 12-month mixed methods study following the Medical Research Council's (MRC) Framework for developing and evaluating complex interventions. For this reason we will draw on Normalisation Process Theory (http://www.normalizationprocess.org/ NPT; May 2013). This theory provides a conceptual framework for understanding and evaluating the implementation processes by which new health technologies and other complex interventions are

routinely operationalized and embedded in everyday work, and sustained or integrated into routine practice. NPT offers a conceptual map for the process evaluation of complex interventions and for the organization of implementation processes. Here, NPT is concerned with identifying and understanding the ways that people make sense of the work of implementing and integrating a complex intervention (coherence); how they engage with it (cognitive participation); enact it (collective action); and appraise its effects (reflexive monitoring). Each Workpackage within the overall project has been designed to address these processes of coherence, cognitive participation, collective action and reflexive monitoring.

7.0 Methodology

7.1 Objectives

The objectives of this study are to conduct focus group interviews to (i) evaluate the acceptability and usability of mobile symptom reporting using smartphones amongst service users, carers and mental health staff; (ii) identify incentives and barriers to use by service users and carers and implementation by mental health staff; and the identification of pathways to relapse identification and prevention. These interviews will inform modifications to the EMPOWER mobile App which will then be subjected to Beta-testing by interviewing service users, carers and mental health staff regarding acceptability and usability after a 7-day evaluation period. The aims of each work package that comprise Phase 1 of the research are outlined below.

- *Work package 1:* (i) To evaluate the acceptability and usability of mobile symptom recording using smartphones amongst service users and their carers; and (ii) the identification of incentives and barriers to use.
    - *Deliverables:* Software and protocol updates in response to feedback from service users and carers.
- *Work package 2:* (i) To evaluate the acceptability and usability of mobile symptom recording using smartphones amongst professional mental health care staff; (ii) to identify incentives and barriers to implementation by Mental Health staff; and (iii) the identification of relapse prevention pathways and whole team responses.
    - *Deliverables:* (i) Software and team protocol updates in response to feedback from professional care staff. We will operationalize protocols for dealing with false positives and activation of relapse prevention pathways. (ii) The development of care pathways, identification of operational barriers and enablers. (iii) Identification of training needs of teams participating in our future pilot cluster randomized controlled trial.
- *Work package 3:* (i) To finalize the EMPOWER App for implementation in a pilot cluster randomized controlled trial that will compare EMPOWER to treatment as usual.
    - *Deliverables:* (i) Software and protocol updates in response to feedback from service users, carers and staff. (ii) Agree on final

modifications to EMPOWER App to enhance usability. (iii) Finalize measurement methods for assessment of self-report of acceptability and usability to be administered in our future pilot cluster randomized controlled trial.

7.2 *Settings*

Parallel arms of data collection for Phase 1 of the research project will take place in the UK and Australia. Data Collection for the UK arm will take place in NHS Greater Glasgow & Clyde. Data collection for the Australian arm of the study will take place across two NorthWestern Adult Community Mental Health Services.

7.3 Methods

7.3.1 *WP1: Task groups with service users and carers*

Task Groups (1 - 2 hours duration) are a type of focus group designed to generate qualitative data and the principles for action, which are grounded in the experience of group members. Task Groups will elicit views about experiences of relapse, incentives and barriers to help-seeking and optimal responses to relapse or the threat of relapse. Task groups will explore: (i) the utility of early signs monitoring, including service users' views about intermittent, low frequency and high intensity EWS monitoring; (ii) views about using self-management messages and what self-management messages would have greatest salience; (iii) the design parameters of the system that could best sustain their involvement; (iv) views about help seeking and activating a relapse prevention pathway; (v) the best way to involve carer stakeholders; (vi) the best way to contact mental health staff; and (vii) how would they like to use their data from EMPOWER. This will build on our initial PPI work and be informed by service users and carers recruited to the Study Steering Group. As part of the Task Groups, participants will have an opportunity to try out the EMPOWER App and system. These data will inform the final design and Beta Testing of EMPOWER to optimise the usability, salience, applicability and overall coherence of the intervention. We recognize that some participants will be unable attend Task Groups (e.g. due to time constraints or difficulties engaging in groups). Therefore in order to maximize engagement and diversity of views we will offer participants unable to attend Task Groups the opportunity to participate in individual interviews. These will utilize the same Topic Guide to facilitate discussion.

7.3.2 *WP 2: Task groups with professional mental health care staff*

The aim of the Task Groups with Mental Health Staff is to clarify the existing support pathways and procedures, systems, and policies in teams participating in usual care, and to clearly differentiate these from our experimental intervention. We will focus on the following questions: (i) What are the strengths and limitations of these existing pathways?; (ii) What are the relevant policies and procedures that guide treatment as usual?; (iii) What are the feasibility, risks and incentives to incorporate mobile phone technology into the monitoring and detection of risk of relapse?; (iv) What are the best methods to deal with false positives?; (v) How can we optimise pathways to relapse prevention?; In line with NPT we will distinguish EMPOWER from current practice; collectively agree about

the purpose of the intervention; enable staff to understand what the intervention would require of them; and construct potential value of the intervention for their work. We recognize that some participants will be unable attend Task Groups (e.g. due to time constraints of engaging in groups). Therefore in order to maximize engagement and diversity of views we will offer participants unable to attend Task Groups the opportunity to participate in individual interviews. These will utilize the same Topic Guide to facilitate discussion.

7.3.3 *WP 3: Software beta-testing*

In each team, the software will be beta-tested with 10 service users, their carers, and mental health care staff (i.e., key workers and medical practitioners) over 7-days. Following the software beta-testing, we will follow up at a time and location mutually convenient to the researcher and participants. During this interview service user participants will be asked about the benefits and problems of using the EMPOWER App, including investigating their views about the user interface, the number and frequency of questions, wording of items, omissions, fit with everyday life and other suggestions for improving usability. Consumer participants will also complete the Post-Study System Usability Questionnaire (PSSUQ) to test the usability of the application. The PSSUQ has been used previously in respected studies testing the usability of Apps in healthcare (e.g., Sheehan, Lee, Rodriguez, & Schnall, 2012). In addition we will conduct an in-depth interview exploring participants experiences of using the App and their perspectives on its acceptability and utility.

Carer participants who partake in the follow up interview with consumers will be asked for their views of the usability and usefulness of the EMPOWER App. Professional mental health care staff will also be asked for their perspective on the usability and usefulness of the EMPOWER App in a separate follow up interview.

7.4 Procedure List

Work Package	**Information to be collected**
WP 1	Information pertaining to eligibility Focus group contributions
WP 2	Information pertaining to eligibility Focus group contributions
WP 3	Information pertaining to eligibility Initial and follow-up interview contributions App adherence data (consumer participants only) PSSUQ answers (consumer participants only)

8.1 Study Population

8.1.1 Recruitment Procedure

8.1.1.1 WP 1

Potential service user participants will be identified and approached by key workers, who will ask them if they would be interested in meeting with the study RA to discuss the study. If the service user expresses an interest in participating their preferred contact details will be passed on to the study RA in order to make arrangements for providing the Participation Information Consent Form (PICF). Staff can also provide potential participants with a Leaflet (Attachment E) so that individuals can directly contact a member of the study team for additional information. In addition, we will use Posters (Attachment F) that can be placed in the waiting areas of participating CMHTs.

Finally, we will engage with the Mental Health Network (Greater Glasgow & Clyde) and ACUMEN to support engagement of potentially eligible participants. Both these organizations work directly with NHS Greater Glasgow & Clyde promote the wider involvement of service users and carers in shaping mental health services and facilitate collaboration through support and networking. In addition we will engage with Support in Mind Scotland who have a strong engagement with carers of people diagnosed with Schizophrenia. These organisations have expressed a strong interest to engage with EMPOWER to highlight the study with members of their respective constituencies.

Following the provision of informed consent, service user participants will be invited to nominate a carer to participate. Once a carer has been identified the study RA will make arrangements via telephone to provide information about participation and seek informed consent. The latter will occur in a face-to-face setting. Should insufficient carers be recruited by this method, focus group participation will be opened to any carer associated with a participating site, and the opportunity made known though Carer Consultants employed within the service and flyers and/or posters at the service. Copies of any flyer, or poster, to be used will be lodged with the ethics committee prior to use.

NB. service user participants are still eligible for participation if they choose not to nominate a carer, if there is no individual that meets the inclusion criteria for a carer participant, or if their nominated carer does not wish to partake.

8.1.1.2 WP 2

Professional mental health staff will be identified through service managers and presentations at staff meetings by the study RA. Staff members will be invited to take part in a focus group and will be given a Participant Information Sheet/ Consent Form. They will be advised that participation is voluntary, and will sign the consent form before being interviewed. Should insufficient professional mental health staff be recruited by this method, focus group participation will be opened to any clinician associated with a participating site, and the opportunity will be made known through email announcement from the relevant service manager. Copies of any flyer, or poster, to be used will be lodged with the ethics committee prior to use.

8.1.1.3 WP 3

In the first instance, service users who partake in WP 1 will be invited to partake in the software beta-testing. If an inadequate number of service users are recruited via this method, potential service user participants will be recruited in a manner akin to work package 1.

Service user participants will be asked of their preference regarding carer participation. Those who express interest will be asked to share their carer's contact details with the study RA. The study RA will then make arrangements to contact the nominated carer, so as to provide information about participation and obtain informed consent for participation.

The corresponding key workers and medical practitioner/ doctor for each service user participant will be invited to partake and provide information/ feedback regarding their experience of having a consumer utilize the program. If an inadequate number of professional mental health staff participants are recruited via this method, participants will be recruited in a manner akin to WP 2.

NB. Service user participants are still eligible for participation if they choose not to nominate a carer, if there is no individual that meets the inclusion criteria for a carer participant, or if their nominated carer does not wish to partake. Service user participants are also eligible for participation if their key clinician/ case manager chooses not to partake.

8.2 Eligibility Criteria

8.2.1 Service users

Service users will be eligible for participation in work packages 1 and 2 if:

(i) they are adults (16 + years of age),
(ii) in contact with a local community based service,
(iii) who have either
  a. been admitted to a psychiatric in-patient service at least once in the previous two years for a relapse of psychosis;
  b. or received crisis intervention (e.g. via a crisis intervention service; re-engaged with a CMHS) in the previous two years for a relapse of psychosis have been admitted to a psychiatric in-patient service at least once in the previous two years for a relapse of psychosis,
(iv) have a diagnosis of a relevant DSM-5 schizophrenia related disorder (i.e., schizophrenia, schizoaffective disorder, or substance/ medication induced psychotic disorder).
(v) their current presentation Current presentation does not include severe acute symptoms,
(vi) they are able to provide informed consent as adjudged by their care coordinator/ case manager, or if in doubt the responsible consultant, and
(vii) they are able to manage the language requirement of participation.

Service users will be eligible for participation in work package 3 if:

(i) they are adults (16 + years of age),
(ii) in contact with a local community based service,
(iii) have a diagnosis of a relevant DSM-5 schizophrenia related disorder (i.e., schizophrenia, schizoaffective disorder, or substance/ medication induced psychotic disorder).
(iv) their current presentation Current presentation does not include severe acute symptoms,
(v) they are able to provide informed consent as adjudged by their care coordinator/ case manager, or if in doubt the responsible consultant, and
(vi) they are able to manage the language requirement of participation.

8.2.2 Carers

Following the provision of service participant's informed consent, they will be asked to nominate a carer with whom they regular (i.e., weekly) contact. The frequency of contact is the only eligibility criterion for carer participation. Carers who are nominated by eligible service users who provide informed consent will also be approached for their inclusion in the study.

8.2.3 Professional mental health care staff

Professional mental health care staff will be eligible for participation if they have been working for the service for $\geq$ 2 months, so as to ensure that they have had an orientation to and are familiar with the service system.

8.2.4 Exclusion Criteria

Individuals will not be eligible for participation if they do not meet the inclusion criteria outlined above. Ownership of a mobile phone will not be an inclusion criterion as we will provide mobile phones for WP3.

8.3 Consent

Written consent for participating in this research will be sought from all participants. Participants will have capacity to give informed consent for themselves. In order to provide informed consent, all participants will meet face-to-face with the study RA, who will present in written and verbal form the aims and procedures of the study, and the processes for withdrawal and for making enquiries or complaints.

8.4 Sample Size

The numbers projected for the WPs 1 and (i.e., 30 service users, 30 carers, and 20 – 30 professional mental health care staff) and WP 3 (i.e., 10 service users, carers, and professional mental health care staff) will provide sufficient data to create the framework of analysis. No formal sample size calculation (e.g., power analysis) was considered appropriate for these WPs, as they are not aimed at evaluating

treatment effects. The number of participants recruited into each of the WPs will provide adequate information and insights to inform the design and size of a future definitive, pragmatic, multi-site, and multi-national pilot cluster randomized controlled trial.

8.5 Statistical Methods

Task groups (WPs 1 and 2) and follow-up interviews (WP 3) will be digitally recorded, transcribed and anonymized before being entered onto N-VIVO (a computer assister qualitative software package) to organize the data and enable progression to analysis. Analysis will draw upon Framework Analysis, which is a qualitative approach specializing in pragmatic, generalizable qualitative method designed for real world implementation (Richie et al., 2013). The framework approach has been developed specifically for applied or policy relevant qualitative research in which the objectives of the investigation are typically set in advance and shaper by the information requirements of the funding body. The timescales of applied research tend to be short and there is often a need to link the analysis with quantitative findings. For these reasons, although the framework approach reflects the original accounts and observations of the people studied (that is, "grounded" and inductive), it starts deductively from present aims and objectives. The data collection is more structured than would be the norm for much other qualitative research and the analytical process tends to be more explicit and more strongly informed by an a priori approach (Pope, Ziebland, & Mays, 2000).

9.0 Participant Safety and Withdrawal

9.1 Risk Identification

9.1.1 Risks associated with WPs 1 and 2

The potential risks of harm or discomfort to service users, carers, and professional mental health staff who participate in the focus groups (i.e., WPs 1 and 2) include:

(i) Risks to personal privacy associated with the dissemination of personal information by other participants,

(ii) Distress resulting from inappropriate, abusive, or offensive interaction/s with other participants,

(iii) Increased paranoia resulting from participation, especially in the event of deterioration in the mental wellbeing of service-user participants,

(iv) Talking about experiences of relapse could also be potentially distressing.

The anticipated likelihood of these risk eventuating is considered low based on the past experiences of the investigators. For example, Professor Gumley has conducted group-based research previously with service users meeting similar

inclusion criteria, and problem behavior in group has been rare and no privacy breaches have been identified.

9.1.2 Risks associated with WP3

The potential risks of harm or discomfort to service users who participate in the software beta-testing (i.e., WP 3) include:

(i) Risk to personal privacy associated with the unlawful dissemination of personal information by unauthorized hackers, and

(ii) Risks to the clinical safety of service user participants (i.e., true and false positive detections of relapse).

The anticipated likelihood of personal privacy being breached by the unlawful dissemination of personal information by unauthorized hackers is considered low given the past experiences of the investigators. For example, previous research that PI Prof Lewis has undertaken has included the development and/ or evaluation of technology, which have involved the hosting of participant information on servers (e.g., ClinTouch and CareLoop) and no such breaches have occurred. Moreover, the risk is largely mitigated due to the small scale/ short duration of the study, and the standards of data storage and server security at the host institution.

The anticipated likelihood of clinical safety being comprised (i.e., service user participants' wellbeing deteriorating and the system flagging a true positive detection of relapse, or the system flagging a false positive detection of relapse) is low given the short duration of the software beta-testing.

A further risk to the research team and the organizations involved associated with WP 3 is the potential unlawful dissemination of information regarding the research tool by unauthorized hackers. The anticipated likelihood of this risk eventuating is low, as no such breaches have occurred in previous research projects that the investigators have undertaken. This risk is also largely mitigated due to the small scale of the study.

9.2 Risk Management

The potential risks of harm or discomfort to service users, carers, and professional mental health staff who participate in the focus groups (i.e., WPs 1 and 2), which are outlined above, will be negated/ minimised/ managed via the following processes:

(i) All focus groups will be co-facilitated by two individuals. Key facilitator responsibilities will include advising participants of rules of engagement with the group (e.g., confidentiality, respectful communication), and upholding the same.

(ii) Facilitators will also monitor participants' degree of distress, and take action accordingly. Participants who display or report distress will be offered a debriefing session.

The potential risks to system and personal privacy, and clinical safety associated with WP 3 will be negated/ minimised/ managed via a rigorous safety protocol has been developed by the research team, and experts from the information systems discipline. The safety protocol is comprised of 2 levels of security including system and privacy protection, and clinical safety.

9.2.1 System Safety and Privacy Protection

Three general principles of information security (confidentiality, integrity and availability) will be followed in the design and implementation of EMPOWER. All data transmitted to and from EPOWER servers will be encrypted over https with strong ciphers as detailed in the Approved Cryptographic Algorithms Good Practice Guidelines (NHS, 2012). Cipher suites will be implemented in compliance with Section 6 ("Preferred uses of cryptographic algorithms in security protocols") of the Good Practice Guidelines. In cases where participant data are downloaded from the EMPOWER sites, these data will be securely encrypted with a pass phrase of appropriate length and complexity. Data transfers are secured by using standards web security protocols. Uploading data to a central server in real time enables study data to be captured and so protects against data loss such as a phone, which can be lost or stolen. This removes the need for personal data storage on the device. The purpose of the server in this case is secure data storage.

9.2.2 Clinical Safety

A range of measures are also in place to ensure participant's clinical safety. Changes in early warning signs will be observable by the researchers, and responses will be manual rather than automated. Information related to clinical safety (i.e., early warning signs, idiosyncratic signs, etc.) will be screened 3 times per week by the study RA, and specific attention will be paid to deterioration of early warning signs. Any detected increase will activate the protocol, which includes a number of potential actions. The study RA will 'push' self-management strategies (including the participant's pre-identified idiosyncratic wellness management tools), and will advise the clinical team of any significant change to the participant's mental health.

In the case that a participant contacts the study RA, or other members of the research team, communicating distress, the study RA/ member of the research team will provide immediate support, and will then contact the participant's treating team.

In the case that a participant stops using the system (i.e., misses more than 2 scheduled prompts). The following protocol will be adopted: (i) after two missed prompts an SMS will be sent reminding the service user to log on and use the App, and (ii) after subsequent instances/ missed prompts, the research team will follow up with a supportive phone call encouraging participation. Information will be passed on to the consumer's treating team if they stop responding to the prompts to monitor their early warning signs, and if they miss the follow up interview with the study RA.

9.3 Risk Monitoring

Risks will be monitored by the study RA. Within their role as interviewer and group facilitator within the various work packages, the study RA will monitor participants' degree of distress, and take action accordingly. All interviewees will be invited to discuss any feelings of distress associated with participating in the interview, and focus group participants will also be invited to speak privately with the study RA and/or co-facilitator at the conclusion of the group if they feel distressed following the focus group. The study RA will also monitor the risks associated with the software beta-testing; information related to clinical safety will be screened 3 times per week.

9.4 Risk Reporting

The study RA will report all incidents of distress that come to her attention, and any potential clinical deterioration in participants' mental health to CI Prof Gumley, and to the participant's treating team. The study RA will also record all incidents in a database, and Prof Gumley will report serious adverse events that are related and unexpected according to International Conference on Harmonisation Guidelines on reporting Serious Adverse Events (Section II B) to the Sponsor and the REC.

9.5 Handling of Withdrawals

9.5.1 Procedures

Participants will be free to withdraw at any time. As a part of the informed consent procedure they will be instructed to let a member of the research team know of their withdrawal ahead of time. Participants who choose to withdraw will be offered debriefing as a matter of course. The treating team overseeing the care of service user participants will also be advised of any withdrawals. Information collected from participants up until the point of withdrawal will be stored in the databank.

9.5.2 Specific Consequences of Withdrawal

There are no specific consequences that individuals should be made aware of prior to giving consent to partake in Work Packages 1, 2, and 3. There will be no change to the treatment/s received by the service user from their treating team, nor will there be any change to their relationship with the service, if a service user participant chooses to withdraw from the research. Withdrawn individuals will not be replaced.

Similarly there will be no change in any aspect of carers' relationships with their loved one's treating team, and mental health staff participants' employment by NHS Greater Glasgow & Clyde will not be adversely affected.

10.0 Data Security and Management

The confidentiality of all study data will be ensured via the following security mechanisms.

10.1 The EMPOWER App

A range of measures are in place to help ensure the security of the EMPOWER App and the data generate by its users. The App is hosted on University of Manchester web server, and has standard measures in place to prevent unauthorized access. All data transmitted to and from EPOWER servers will be encrypted over https with strong ciphers as detailed in the Approved Cryptographic Algorithms Good Practice Guidelines (NHS, 2012). Cipher suites will be implemented in compliance with Section 6 ("Preferred uses of cryptographic algorithms in security protocols") of the Good Practice Guidelines. In cases where participant data are downloaded from the EMPOWER sites, these data will be securely encrypted with a pass phrase of appropriate length and complexity. Data transfers are secured by using standards web security protocols. Uploading data to a central server in real time enables study data to be captured and so protects against data loss such as a phone, which can be lost or stolen. This removes the need for personal data storage on the device. The purpose of the server in this case is secure data storage. We will also incorporate ISO 25010 which provides for safety-in-use and measures satisfaction with security. These security measures correspond closely to the NHS standards with which ClinTouch currently complies.

A number of technical measures will also be employed in order to protect personally identifiable data. Any data stored on the phone by the participant will be encrypted. We will also recommend that service users set a passcode to access their Smartphone. All Smartphones provided by the research team will require a passcode for access. All service users recruited to the study will give their informed consent, and this will include risks to data security. These measures should be sufficient to prevent unauthorized data access, should the phone be lost or stolen.

10.2 Other study data

Each study participant will be assigned a unique trial identification number at the start of the assessment process. This number will be written on all clinical assessment forms/datasheets and databases used to record data on study participants. A hard copy of a record sheet linking patient identity, contact details and trial identification number for all participants will be kept at each site. It will be placed securely in a locked filling cabinet separate from datasheets.

The local study RA will enter the data on to an electronic database, and all such data will be checked for errors before being transferred to the appropriate statistical package. All data will be kept secure at all times and maintained in accordance with the requirements of the Data Protection Act, and archived according to clinical trial GCP regulations.

Audio recordings of the focus groups and participant interviews will also be stored securely on a computer at the University of Glasgow and will be destroyed following transcription and analysis of the data.

Most international collaborators will only have access to de-identified information following the cessation of data collection for work packages 1 – 3. The only exceptions to this will be the CI Prof Gumley, the Trial Manager in Glasgow (to be

appointed), PI Prof Williams, Aus CI Gleeson and Aus PI A/Prof Farhall and, so as to ensure the analyses and implications can be coordinated across UK and Australian arms of the research.

10.3 Type of Information stored

Information from WPs 1 and 2 will be stored in a non-identifiable form. Information from WP 3 will be stored in a potentially identifiable/ re-identifiable (i.e., coded) form. This is necessary so as to ensure that the various types of information that will be collected (i.e., use of the App, feedback provided at the follow up interview) can be linked.

The security arrangements and access for the code will be as follows. Each participant's dataset will have a unique code and will be stored in a password protected database. The unique code will be linked to the participant's name and contact details. The information linking the participant's unique code and contact details will be stored in a document separate from the study database and will also be password protected. Only the principal researchers will know the password and have access to the document linking the code and contact details.

11.0 Research Governance

NHS Greater Glasgow & Clyde is the Sponsor of the Trial in the UK. In accordance with high standards of research governance we will ensure researchers receive training in the International Conference on Harmonisation (ICH) Guidelines - Good Clinical Practice. We will set up a Study Steering Committee (SSC) and an Independent Data Monitoring and Ethics Committee (DMEC) prior to the start of the study. The SSC will comprise study applicants, a representative of the HTA, and representatives of service users and providers, and have an independent chairman. An DMEC will also be established to monitor (1) recruitment of study participants, (2) ethical issues of consent, (3) quality of data (including missing data), (4) the incidence of adverse events, and (5) any other factors that might compromise the progress and satisfactory completion of the trial. This will also have an independent chairman, and include an independent statistician.

11.1 Study Steering Committee (SSC)

The role of the SSC is to provide overall supervision for a project on behalf of the Project Sponsor and Project Funder and to ensure that the project is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice. The SSC will be constituted following NIHR Guidance (Version date: May 2013). The membership of the SSC is described on Page 3 above.

11.2 Data Monitoring and Ethics Committee (DMEC)

The DMEC will have access to unblinded comparative data and monitor these data and make recommendations to the SSC on whether there are any ethical or safety issues on whether the study should continue. The DMEC will be constituted following NIHR Guidance (Version date: May 2013). The membership of the DMEC

is described on Page 3 above.

11.3 Audit

NHS Greater Glasgow and Clyde will retain the right to audit implementation of the trial in the UK context.

12.0 Ethics and Dissemination

12.1 Research Ethics Approval

Before Phase 1 of the study Research Ethics Favourable Opinion will be sought from West of Scotland Research Ethics Service (Glasgow) and NorthWestern Research Ethics (Melbourne).

12.2 Protocol Amendments

The views of the SSC and DMEC will be sought on any proposed amendments to the EMPOWER Protocol. Following this any proposed amendments will be submitted to the Study Sponsor and Research Ethics Committees for approval. Protocol amendments will be added to the EMPOWER Protocol and to the ISRCTN Registry.

12.3 Consent

Only those who agree to provide written informed consent will be included in the study. All potential participants, including Service Users, Carers and Mental Health Staff will be provided with a copy of a Participant Information Sheet and Consent Form that includes a contact number for the study team.

12.4 Dissemination Plan

(i) We will produce an EMPOWER Dissemination Policy. This document will outline a comprehensive list of possible papers with basic descriptions of objectives, contents, authorship, and journals to be targeted.

(ii) Dissemination will occur via a number of methods, which include publication of trial papers, conference presentations, book chapters, and the HTA final report (monograph and trials directory).

(iii) Participants will be informed of the results by being offered written and/ or face-to-face feedback.

(iv) We have an obligation to give the Sponsor and NIHR-HTA notification of an output prior to any publication (whether in oral, written or other form) of data or the results of the project or of matters arising from such data or results. Therefore, the trial manager should be notified of any outputs (oral, written or other form). The trial manager will coordinate notification to the HTA. Research projects are contractually obliged to submit a draft final report for inclusion in the influential Health Technology

Assessment journal series. The journal is indexed on MEDLINE, EMBASE and the ISI Science Citation Index, and assessed for inclusion in the Database of Abstracts of Reviews of Effectiveness. Before a draft final report is published it is peer-reviewed by at least four relevant experts to ensure scientific integrity and quality standards. An editor will review the external reviewers' comments and the draft version of the report, and feedback is given to the author. Ideally, this will take place within two months of receipt of the draft final report. The team is invited to resubmit their revised report within four weeks. There may be a further round of editorial review before the report is sent to the publisher. The NIHR Journals Library ensures that the results of pilot and feasibility studies which have been funded by the participating programmes are published, regardless of outcome or significance of findings in order to ensure that as much information as possible about each study is in the public domain. Authors are encouraged to report everything, be transparent in their reporting, be reflective and avoid overstating their findings.

13.0 Appendices

List of additional Documents

Document Name	Version Number	Date
Project Protocol Attachment A: EMPOWER GANTT Chart	1.0	8th January 2016
Project Protocol Attachment A: Work Package 1 and 2 Task Group Topics	1.0	8th January 2016
Project Protocol Attachment B: Post-Study System Usability Questionnaire; PSSUQ	1.0	8th January 2016
Project Protocol Attachment C: Post-Study Beta-Testing Usability Interview	1.0	8th January 2016

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STUDY PROTOCOL[1]

Title: EMPOWER: Early signs Monitoring to Prevent relapse in psychosis and prOmote Wellbeing, Engagement and Recovery (Phase 2)

Version Number: 1.4 (8th January 2019)

ISRCTN: 99559262

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UK NHS Greater Glasgow & Clyde
Australia Australian Catholic University

Approvals

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[1] Prepared in accordance with **SPIRIT** (Standard Protocol Items: Recommendations for Interventional Trials: Chan et al. 2013)

Contents

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2.0 Glossary of Terms

Term	Description (using lay language)
ACS	Adult Community Service
App	Mobile telephone application
CBT	Cognitive Behaviour Therapy
CI	Chief Investigator
CHaRT	Centre for Healthcare Randomised Trials
CMHS	Community Mental Health Service
CRCT	Cluster Randomised Controlled Trial
CTU	Clinical Trials Unit
Care Coordinator	Key Worker (UK) or Key Clinician (Australia)
DMEC	Data Monitoring and Ethics Committee
EMPOWER	Early signs monitoring to Prevent relapse in psychosis and pr0mote Wellbeing, Engagement, and Recovery
EWS	Early warning signs
IP	Intellectual property
JCPs	Joint Crisis Plans
MHRA	Medicines and Healthcare products Regulatory Authority
MRC	Medical Research Council
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NHSGG&C	NHS Greater Glasgow & Clyde
NIHR	National Institute for Health Research
NPT	Normalization Process Theory
PI	Principal Investigator
PSSUQ	Post-Study System Usability Questionnaire
RA	Research Assistant
RCT	Randomised controlled trial

RMHN	Registered Mental Health Nurse
Service User	Consumer, Patient or person in receipt of mental health services
SOP	Standard Operating Procedure
SSC	Study Steering Committee
TAU	Treatment as usual
WP	Work Package

3.0 Summary in Plain English

BACKGROUND: Relapse in schizophrenia is a major cause of distress and disability amongst patients and their families. Relapse is predicted by changes in symptoms such as anxiety, depression and suspiciousness (early warning signs, EWS) and can be used as the basis for timely interventions to prevent relapse and hospitalization. Research shows that interventions focused on EWS can reduce these negative outcomes and enhance recovery. The quality of research evidence is poor so that it is not possible to estimate whether these can be applied in routine practice.

AIMS: We aim to build a practitioner led and peer informed intervention (EMPOWER) that utilizes digital smartphone technology for the monitoring of EWS; that promotes autonomy, self-management and timely help seeking whilst minimizing the risk of false alarms. Therefore, we will seek to embed our digital technology into a Stepped-Care model that aims to enhance self-management and facilitate timely support from mental health services.

PARTICIPANTS: Eligible service users will be (i) adults (age 16+) (ii) in contact with a local community based services; (iii) who have either been admitted to a psychiatric in-patient service or received crisis intervention at least once in the previous two years for a relapse of psychosis; (iv) a DSM-5 diagnosis of a Schizophrenia-related disorder. Service users will also be invited to nominate a carer to participate.

SETTINGS: The study will take place in Glasgow (UK) and Melbourne (Australia).

DESIGN AND PROCEDURES: We will undertake a pilot cluster randomised controlled trial (CRCT) where we will randomise Community Mental Health Services (CMHS) to EMPOWER or to 'Treatment as Usual' (TAU). We aim to recruit 120 service user participants from 8 Community Mental Health Services and follow them up for 12-months. This pilot will enable us to investigate the feasibility of a larger scale (definitive) trial and the acceptability and safety of the EMPOWER intervention. The study will also constitute a Clinical Investigation of a Medical Device. We will conduct a Health Economic study and we will also undertake wider engagement of service user, carer and NHS stakeholders to facilitate transition to the main study.

INTERVENTION: The EMPOWER intervention involves three levels of stepped care: (i) smartphone based early signs monitoring, (ii) individualised self-management support delivered through smartphone, and (iii) activation of a relapse prevention pathway into secondary care. Service user participants will have access to the EMPOWER App for the full 12-months of the study. EMPOWER will enable service users, their nominated carer and their care coordinator to agree and personalize additional individual EWS items. Wellbeing messages tailored to enhance self-management and autonomy will be delivered and thresholds for activating a team-based relapse prevention pathway will be set.

OUTCOMES: We will identify the feasibility of the main trial in terms of recruitment and retention to the study and the acceptability, usability, safety and

outcome signals of the EMPOWER intervention. We will assess relapse, symptom recovery, emotional recovery, empowerment and engagement. We will determine (a) any changes or enhancements to the smartphone app, and (b) any changes or enhancements to the implementation of the intervention required for optimal operation in the main trial. We will manualise the intervention and establish the methods to deliver the main (definitive) trial.

4.0 Background and Rationale

Schizophrenia is a severe mental illness (SMI) affecting 24 million people worldwide, costing the NHS in the UK £2bn and the Australian Health Sector Aus$1.34bn annually. Costs to the Australian Government are Aus$3.51bn annually and wider societal costs are estimated as Aus$4.9bn annually (Neil et al., 2014), while in the UK societal costs are estimated to be in the region of £11bn (Rethink, 2012). Schizophrenia is a major public health burden and is associated with increased mortality with death occurring 10-15 years earlier than the population at large through both suicide and through poor physical health. Furthermore this differential mortality gap has widened over recent decades (Saha, Chant & McGrath, 2007).

Relapse influences the long-term course of psychosis with rates accumulating following a first episode to 20–35% after one year. In a recent review the pooled prevalence of relapse of positive symptoms following first episode was 28% (range = 12-47%), 43% (35-54%), 54% (40-63%) at 1, 1.5-2, and 3-years follow-up, respectively (Alvarez-Jimenez et al., 2012). Relapse can occur in up to 80% at five years (Robinson et al., 1999). Relapse is associated with higher inpatient and outpatient costs and the cost of treating relapsing psychosis is four times that of stable psychosis. Despite the rise of community care, 70% of the UK costs of SMI are for unplanned inpatient care for relapse (Fitzgerald et al., 2009; Ascher-Svanum et al., 2010). The Second Australian National Survey of People Living with Psychotic Illness (Morgan et al 2011) reported that 61.5% of the treated population had a course of illness characterised by multiple episodes of psychotic symptoms with full or partial remission of symptoms between episodes. One-year incidence of hospital admission was 34% of the treated population, with 27.8% of those having one or more further admissions to hospital within the year. In Australia, almost half (46%) of health sector costs are generated by inpatient care, with psychiatric admissions accounting for 96% of these costs (Aus$609M). Relapsing or unstable psychosis has the greatest impact on these patterns of service utilisation. Raudino et al., (2014) found that psychiatric admissions (including use of emergency services) were associated with higher symptoms, suicidal ideation, poorer functioning and younger age.

4.1 Predictors of Relapse

One important predictor of relapse is lack of acceptance of treatment and unplanned discontinuation of antipsychotic medication (Alvarez-Jimenez et al., 2012). Poorer adherence often signals a lack of engagement with services and failure of services to build a collaborative working alliance (Subotnik et al., 2011). Specifically, non-adherence to antipsychotic treatment is predicted by poorer insight, previous experience of involuntary treatment, poorer premorbid functioning, comorbid substance misuse, forensic history and a poor therapeutic relationship with the prescriber (Day et al., 2005; Lambert et al., 2010). Relapse itself is also an important marker of severity and complexity of illness. Relapse is predicted by previous suicide attempts (Novick et al., 2010), depression, hostility and embarrassment (Rummel-Kulge, Schuster, Peters & Kissling, 2008), poorer premorbid functioning, family criticism, substance misuse, social isolation (Alvarez-Jimenez et al., 2012), negative interpersonal style (probably linked to

poorer utilisation of social support) (Gleeson et al., 2005) and greater fear of relapse itself (Gumley et al., 2014).

Birchwood et al. (1989) pioneered the development of systematic early signs monitoring for relapse and its integration into routine care. It is now known that relapse is the culmination of a process of changes which commence days and sometimes weeks before psychosis symptoms re-emerge or are exacerbated. These early warning signs (EWS) include affective changes and incipient psychosis. More recent data suggests that potential relapse can be detected around 5-weeks before rehospitalisation, with very early changes detectable 8-weeks before (Spaniel et al., 2016). A systematic review (Eisner, Drake & Barrowclough, 2013) to determine the validity of EWS as predictors of relapse in people with non-affective psychosis found that the sensitivity of early signs to relapse (proportion of relapses correctly predicted) ranged from 10% to 80% (median 61%) and specificity (proportion of non-relapses correctly identified) ranged from 38% to 100% (median 81%). Detection of relapse was improved by more frequent monitoring (at least fortnightly) and by the inclusion of both psychotic and affective symptoms.

4.2 Interventions to prevent relapse

Gumley et al., (2003) conducted the first study to evaluate the implementation of cognitive behaviour therapy (CBT) tailored towards the prevention of relapse. CBT delivered on the appearance of EWS led to a significant reduction in relapse over 12-months. A significant barrier to relapse prevention was participants' fears of help-seeking arising from previous experiences of relapse. For example, service users may avoid calling their Care coordinator in the context of an increase in EWS for fear of being admitted to hospital. Our research has also demonstrated that fear of relapse is linked to more traumatic experiences of psychosis and hospital admission and greater fear of symptoms such as voices and paranoia (White & Gumley, 2009). In a randomised controlled trial (RCT) of relapse detection, Gumley et al. (2015) found that fear of relapse was as sensitive to the onset of relapse (Sensitivity = 72%, 95% CI = 52–86) as EWS (Sensitivity= 79%, 95% CI = 62–89). Fear of recurrence was also associated with greater depression, feelings of entrapment, self blame and shame.

A Cochrane Review focused on the effectiveness of interventions targeting recognition and management of EWS of relapse in schizophrenia (Morriss et al., 2013). Significant effects in favour of EWS interventions were found for the number of participants relapsing (15 RCTs, n = 1502, risk ratio (RR) 0.53 95% CI 0.36 to 0.79) and the number of participants being re-hospitalised (15 RCTs, n = 1457, RR 0.48, 95% CI 0.35 to 0.66); however, it was found that the quality of the trials conducted to date was poor in terms of randomisation, concealment and blindness. Therefore, future EWS interventions need to address methodological problems that limit their generalisability to usual care. Until this happens EWS interventions cannot be recommended for routine implementation in health services (Morriss et al., 2013).

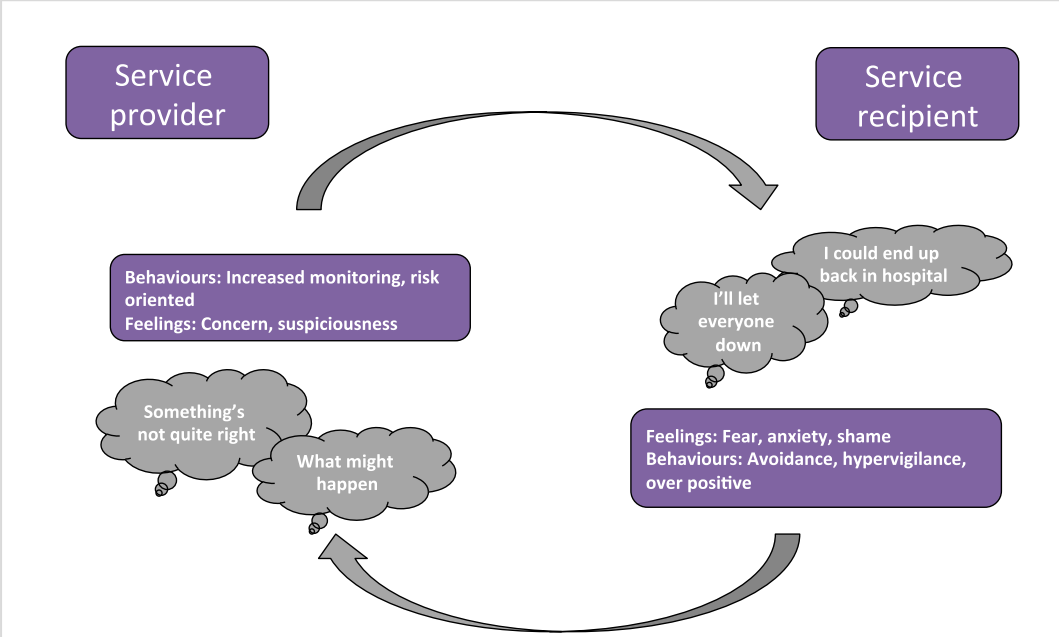
4.3 Barriers to relapse detection and prevention

There is also significant uncertainty surrounding the prognostic validity of EWS (Eisner et al., 2013), which has the potential to result in risk of unnecessary intervention that may sensitise service users and carers to heightened fear of relapse (a potential adverse event related to early signs monitoring; Gumley et al., 2015). Fear of illness and stigma are closely related to emotional dysfunction (Birchwood, 2003) and to poorer insight in schizophrenia (Day et al, 2005). Feelings of fear, depression and helplessness are common emotional experiences prior to full relapse (van Os & Kapur, 2009). Avoidant styles of coping are linked to increased risk of relapse. In an effort to minimise the stigma of illness and prevent relapse, service users can adopt avoidant coping styles (e.g. Birchwood, 2003). These coping styles are associated with greater insecurity in relationships, lower self-esteem, lower levels of adherence and reluctance to seek help in a crisis. Reluctance to seek help may result from greater fear of relapse arising from experiences of involuntary admission. In this sense, avoidance of help-seeking can be understood from the perspective that people with experience of psychosis are attempting to minimise or avert the adverse consequences of help-seeking based on their lived experience. In a recent systematic review, Gumley, Taylor, Schwannauer and Macbeth (2014) found that greater difficulties forming relationships was associated with poorer engagement with services, more problematic relationships with staff, and more frequent and longer hospital admissions. In sum, the detection of, and action following EWS, may be constrained by poor relationships between service providers and people using services, avoidance of help seeking, perceived stigma, fear of relapse and reluctance to disclose EWS.

In both UK and Australia, an important aspect of service provision for those service users at greatest risk of relapse is having access to an integrated mental health care system that enables clear shared planning for managing risk and relapse prevention. One example of this is the role of Joint Crisis Plans (JCPs) in the UK. The CRIMSON study (Thornicroft et al., 2013) was an individual level RCT that compared the effectiveness of JCPs with treatment as usual for people with schizophrenia. There was no significant impact on the primary outcome (reduced coercion into hospital). It was noted that when faced with crisis, in spite of the considerable effort in developing the JCP with service users, the teams reverted to *'custom and practice'*. Staff did not consult JCPs in planning the team response to a crisis. Furthermore, people in receipt of services experienced an inability to influence clinicians' behaviours and this was interpreted as signalling a lack of respect for their views and opinions. In consequence, they described their interactions as a "*playing the game*"; that is appearing to comply with treatment decisions. Clinicians themselves experienced their interactions with service users as ritualised especially in the context of responding to increased risk (Farrelly et al., 2015). Our work with service users (Gumley & Park, 2010) has highlighted that relapse prevention based on EWS monitoring relies on the service user initiating help-seeking in the context of feeling vulnerable and threatened. Many individuals find help-seeking a challenge and may have had difficult or traumatic experiences of psychosis. Delay in help-seeking narrows the window of opportunity for successful relapse prevention, which in turn increases reliance on coercive measures confirming pre-existing

negative expectations. It is therefore essential to develop and evaluate an intervention that can not only change the disclosure of relapsing individuals but one that can radically change the behaviour of mental health teams and the actions of their staff in a crisis.

Figure 1: A Cognitive-Interpersonal Framework for EWS



Our conceptual framework for improving relapse detection and prevention aims to understand how EWS unfold in the context of important caring relationships. Figure 1 provides an illustration of our cognitive-interpersonal framework for EWS. Fear of recurrence drives feelings of fear, anxiety and shame. Coping strategies to regulate emotional distress (e.g. increased hypervigilance, worrying, avoidance etc) shape care providers' own cognitive and emotional responses to perceived increased risk of relapse. For example, care-providers may interpret increased emotional distress or avoidance (e.g. cancelling appointments) as evidence of increased risk prompting changes in clinical care and risk management. These changes may further confirm individuals' negative expectations of services and fear of recurrence. Therefore interventions that can enhance positive emotional awareness, choice and autonomy (through self-management promotion) and improved communication (through increased understanding) could provide a means to disrupt and change negative interpersonal cycles.

4.4 Digital Technology

Digital technology offers such a step change that can influence the behaviour of both service users and mental health teams to enhance engagement with the early signs monitoring approach. Smartphones to support healthcare are promising for delivery of interventions that are unconstrained by the limitations

of existing treatment settings. Mobile phones are widely available, affordable, and are continuously dropping in cost; there are now over 6 billion mobile phone subscriptions worldwide. Ben-Zeev et al. (2013) showed that mobile phone usage is similar to the general population in people with serious mental illness including schizophrenia and that these individuals express an interest in engaging with mobile interventions. A recent systematic review concluded that Internet and mobile-based interventions for psychosis seem to be acceptable and feasible and have the potential to improve clinical and social outcomes. Specifically, 74-86% of patients used the web-based interventions efficiently, 75-92% perceived them as positive and useful, and 70-86% completed or were engaged with the interventions over the follow-up. In addition, online and mobile interventions showed promise in improving positive psychotic symptoms, hospital admissions, socialisation, social-connectedness, depression, and medication adherence (Alvarez-Jimenez et al., 2014). More generally, in a recent systematic review of technology based monitoring of health conditions symptom monitoring practices appeared to be well accepted and may be a feasible complement to clinical practice (Walsh, Golden, & Priebe, 2015). Qualitative feedback suggested that acceptability of monitoring was related to perceived validity, ease of practice, convenient technology, appropriate frequency and helpfulness of feedback, as well as the impact of monitoring on participants' ability to manage health and personal relationships. Interestingly, participants who were diagnosed with schizophrenia had apparently higher rates of adherence compared to other mental health conditions such as anxiety and depression.

In Schizophrenia, acceptability of using mobile phones to monitor symptoms appears to be high with rates of adherence to assessments of EWS estimated at over 80% over 3-months (Granholm et al. 2012) and 1-year (Spaniel et al., 2012). Self-ratings of symptoms using Smartphone demonstrate moderate to strong correspondence with clinician ratings derived from structured clinical interviews (Palmier-Claus et al., 2012). Service users with schizophrenia have also expressed potential benefits to the quality of care from Smartphone EWS monitoring in terms of assisting clinicians to have a better understanding of their service users' mental health, faster and more efficient data exchange, and aiding patient-clinician communication. They felt that mobile monitoring could be integrated easily into daily routines (Palmier-Claus et al., 2012). Mobile interventions enhancing self-management have been associated with rates of 85% adherence and high levels of satisfaction (Ben-Zeev et al., 2014). Members of our team have been at the forefront of this work in developing this approach to 'real time' monitoring and intervention (Palmier-Claus et al., 2011; Alvarez-Jimenez et al., 2013; Palmier-Claus et al., 2012; Ainsworth et al., 2013; Lederman et al., 2013; Lederman & Drefus, 2014; Lederman et al., 2014)

4.5 Digital Technology Development

We will refine existing technology (i.e., ClinTouch and CareLoop) to deliver EMPOWER. The Background intellectual property (IP) has already been well established by researchers and software engineers based at the University of Manchester (Ainsworth, Lewis, Bucci). ClinTouch was developed through an MRC funded project (PI: Lewis) as a mobile phone based monitoring system to record real time data on current symptoms, establish the acceptability of mobile

monitoring in this group and compare against conventional and gold standard measures of psychiatric symptoms. CareLoop, was also funded by the MRC (PI: Lewis), and builds on ClinTouch. CareLoop is a personalised mobile phone based system for mental health service users to record ambulant data on current systems, stressors and functioning to be uploaded in real time to a central server in a clinical team base and linked to prototypical management algorithms.

4.5 Alignment with Health Priorities

We will further develop and enhance our ClinTouch mobile applications and build a relapse prevention pathway that enables service users to become more aware of changes in their thinking, physiology, behaviour and feeling, and will seek to enable individuals to respond to these changes positively. The aim of self-management is to enhance acceptance, autonomy, empowerment and behavioural engagement rather than the patterns of fear, demoralisation, withdrawal, avoidance and defeat observed in the phenomenological studies of early signs. If using technology empowers service users to make informed choices in real time about their treatment and to act promptly under their own control, then we believe we have the potential to transform community care for people with SMI. Our proposal aligns with several emerging NHS and Australian health priorities: prevention; early intervention; personalised care; service user involvement/empowerment; social recovery and efficiency. To deliver innovative and effective community-based care, a major shift in the way care is delivered is needed which empowers service users to play an active role in illness management. The Australian Commission on Safety and Quality in Health Care have prioritised the development of effective partnerships between consumers and healthcare providers and organisations at levels of healthcare provision, planning and evaluation. The NHS Quality, Innovation, Productivity and Prevention (QIPP) Framework for long term conditions is to "empower service users to maximise self-management including ensuring service users have appropriate information and knowledge about how to manage their condition". QIPP demands a focus on innovation to drive up the quality of care and increase the productivity of healthcare services.

4.6 Work leading to current study

We utilised a mixed methods approach during Phase 1 (mainly using qualitative methods). For information regarding Phase 1 please see separate protocol (Version 1.2, 3rd August 2016). Briefly Phase 1 was comprised of three work packages: (WP 1) service user and carer engagement, software evaluation and improvement, (WP 2) professional staff engagement, modelling treatment as usual, mapping the relapse prevention pathway, identification of training needs, and (WP 3) software beta-testing. The aims of each work package that comprised Phase 1 of the research are outlined below.

- *Work package 1:* (i) To evaluate the acceptability and usability of mobile symptom recording using smartphones amongst service users and their carers; and (ii) the identification of incentives and barriers to use.
    - *Deliverables:* Software and protocol updates in response to feedback from service users and carers.
- *Work package 2:* (i) To evaluate the acceptability and usability of mobile EWS recording using smartphones amongst professional mental health

care staff; (ii) to identify incentives and barriers to implementation by mental health staff; and (iii) the identification of relapse prevention pathways and whole team responses.
    - *Deliverables:* (i) Software and team protocol updates in response to feedback from professional care staff. We will operationalise protocols for dealing with false positives and activation of relapse prevention pathways. (ii) The development of care pathways, identification of operational barriers and enablers. (iii) Identification of training needs of teams participating in our future pilot cluster randomised controlled trial.
- *Work package 3:* (i) To finalise the EMPOWER App for implementation in a pilot cluster randomised controlled trial that will compare EMPOWER to treatment as usual.
    - *Deliverables:* Agree on final modifications to EMPOWER App to enhance usability. Finalize measurement methods for self-report assessment of acceptability and usability to be administered in our future pilot cluster randomised controlled trial.

Our methods follow the Medical Research Council's (MRC) Framework for developing and evaluating complex interventions. At the heart of this study we will build upon existing technology (ClinTouch) developed and validated by members of our team at the University of Manchester by designing a study to evaluate real world implementation into routine service settings in the UK and Australia. For this reason we will draw on Normalisation Process Theory (http://www.normalizationprocess.org/ NPT; May 2013). This theory provides a conceptual framework for understanding and evaluating the implementation processes by which new health technologies and other complex interventions are routinely operationalised and embedded in everyday work, and sustained or integrated into routine practice. NPT offers a conceptual map for the process evaluation of complex interventions and for the organisation of implementation processes. Here, NPT is concerned with identifying and understanding the ways that people make sense of the work of implementing and integrating a complex intervention (coherence); how they engage with it (cognitive participation); enact it (collective action); and appraise its effects (reflexive monitoring). Each Workpackage within the overall project has been designed to address these processes of coherence, cognitive participation, collective action and reflexive monitoring.

5.0 Phase 2 (Work Packages 4 to 6)

5.1 Objectives

To establish the feasibility of conducting a definitive Cluster Randomised Controlled Trial (CRCT) comparing EMPOWER against Treatment As Usual (TAU). We will establish the parameters of the feasibility, acceptability, usability, safety and outcome signals of an intervention as an adjunct to usual care that is easily deliverable in the NHS and Australian community mental health service settings and:

(i) enhances the recognition of early warning signs by service users and their carers;
(ii) provides a stepped care pathway, that is either self-activated or in liaison with a carer and / or community healthcare professional, which then
(iii) triggers a relapse prevention strategy which can be stepped up to a whole team response to reduce the likelihood of a psychotic relapse.

Specifically we aim to:

(a) enhance and tailor our mobile phone software application (App) to deliver EWS monitoring, self-management interventions and access to a relapse prevention pathway which is firmly embedded in *whole team* protocols and action;
(b) determine rates of eligibility, consent and recruitment of potentially eligible participants (service users, carers and care co-ordinators) to the study;
(c) assess the performance and safety of the EMPOWER Medical Device;
(d) assess the feasibility, acceptability, and usability of the intervention including feedback on suggested enhancements from consumers, peer support workers and clinicians;
(e) assess primary and secondary outcomes in order to determine preliminary signals of efficacy of the EMPOWER Relapse Prevention Intervention as a basis for the estimation of sample size requirements of a future definitive trial,
(f) undertake a qualitative analysis of relapses to refine intervention in the main trial, and
(g) establish the study parameters and data gathering frameworks required for a co-ordinated health economic evaluation of a full trial across the UK and Australia.

Proposals for additional studies (e.g. qualitative studies exploring service users experiences of the App or the experiences of clinicians and peer support workers) which lie within the scope of the aims and objectives of EMPOWER will be proposed to the Project Management Committee (PMC) and approved by the Study Steering Committee (SSC) and will be subject to local Research Governance and Research Ethics arrangements.

5.2 Trial Design

We will evaluate EMPOWER using a multicentre, two arm, parallel groups CRCT involving eight purposively selected Community Mental Health Services (CMHS) (2 in Melbourne and 6 in Glasgow) with 12-month follow-up. The CMHS will be the unit of randomisation (the cluster), with the intervention delivered by the teams to individual service users and with outcomes assessed within these clusters. The study is planned and implemented in concordance with the Consolidated Standards of Reporting Trials (CONSORT) cluster trial extension (Campbell et al., 2004). We chose this design as the EMPOWER intervention enables a team based response to people in receipt of services whose real time EWS monitoring has activated a relapse prevention pathway. We will recruit participants over a 5-month period. The intervention will last 12 months and over that time the primary and secondary outcomes will be assessed. Individual participant involvement will also last up to 12-months.

5.2.1 Clinical Investigation of a Medical Device

As per ISO 14155:2011(E) the study is also a systematic investigation in one or more human subjects, undertaken to assess the safety or performance of the EMPOWER medical device. The EMPOWER algorithm is a Class 1 Medical Device (see EMPOWER - Interpretation of the Medical Device Directive 93/42/EEC).

5.3 Study Settings

The study will take place in NHS Greater Glasgow & Clyde and NorthWestern Mental Health, Melbourne. In Glasgow there are 21 CMHTs comprising 3246 active service users with a diagnosis of Schizophrenia. Of this group there were 906 hospital admissions between 1st August 2012 and 31st July 2014. Of this group, 558 (17.2%) have had one admission and 216 have had > 1 admission. In the Melbourne sites there are approximately 2150 service users with a diagnosis of Schizophrenia. Service utilisation data here show that, one third (34.8%) of these individuals have had one or more psychiatric inpatient admissions in the previous year.

5.4 Eligibility Criteria

5.4.1 Community Mental Health Services (CMHS)

We will engage CMHS likely to have 5 or more care coordinators willing to participate for a period of 12 months and where potential care coordinators have eligible service users on their case load likely to consider participation. If there are less than target numbers of participants for randomisation, and where resources allowed, we will then check for individuals who have become potentially eligible during the screening period.

5.4.2 Service users

Service users from participating CMHS are eligible for inclusion if

(i) they are adults (age 16+);
(ii) in contact with a local community based services;
(iii) who have either
   a. been admitted to a psychiatric in-patient service at least once in the previous two years for a relapse of psychosis;

b. or received crisis intervention (e.g. via a crisis intervention service; re-engaged with a CMHS) in the previous two years for a relapse of psychosis;

(iv) a diagnosis of Schizophrenia-related disorder (DSM-5) specifically
   a. 295.40 Schizophreniform Disorder (ICD10 = F20.81)
   b. 295.70 Schizoaffective Disorder (ICD10 = F25)
   c. 295.90 Schizophrenia (ICD10 = F20.9)
   d. 297.10 Delusional disorder (ICD = F22)

(v) able to provide informed consent as adjudged by the care coordinator or if in doubt the responsible consultant.

5.4.3 Carers

Carers of service users from participating CMHS will be eligible for inclusion if

(i) they have been nominated by eligible participants (see 5.4.2 above)
(ii) they are in regular contact with the person receiving services
(iii) they provide informed consent to participate in the study.

5.4.4 Exclusion Criteria

Individuals will not be eligible for participation if they do not meet the inclusion criteria outlined above. In addition participants will be excluded if they have suffered a recent relapse operationally defined as been discharged from the care of a crisis team or psychiatric inpatient service within the previous four weeks. Participants will be able to use their own mobile phone if this is compatible with the App (Android). Ownership of a mobile phone will not be an inclusion criterion. We will provide participants with a Smartphone Handset with a monthly usage allowance over the 12-months participation in the CRCT.

5.4.5 Withdrawals

Participants wishing to withdraw from the study will be free to do so at any time. Participants who are in receipt of services will be informed that their usual care will not be affected by their withdrawal. Withdrawing participants will be able to request deletion of personally identifying data from the dataset if they wish and will be informed that any anonymised research data will be retained for analysis purposes. There are no *a priori* criteria to withdraw participants from the research.

5.4.6 Changes to participants' CMHS

In the event that a participant's care coordinator leaves the study service user participation in the research will continue.

5.4.7 Participants discontinuing services from participating CMHS

If a participant discontinues receiving services from participating CMHS it will no longer be possible to continue to use the EMPOWER App. Where appropriate and with the participants' agreement, we will support the transfer of care by providing details of their EWS. The likelihood of this event occurring is deemed to be low. In this event, participants will continue their participation in research assessments and feedback on participation.

If the participant's care is transferred to another CMHS within a participating site (NHSGG&C or NorthWestern Mental Health) and the participant expresses a wish to continue to use the App during the study period, then the Research Team will contribute to the transfer of care process and liaise with the new CMHS to facilitate continued App use according to the approved protocol.

5.5 Interventions

5.5.1 EMPOWER Relapse Prevention

The EMPOWER App has been developed through consultation with people using services, their carers and mental health professionals. The EMPOWER App provides a mobile technology monitoring system that enables (See Figure 2 below):

(i) daily monitoring of EWS
(ii) delivery of Wellbeing Messages aimed at enhancing self management
(iii) a pathway to relapse prevention facilitated where appropriate by sharing up to date EWS data with participating CMHS.

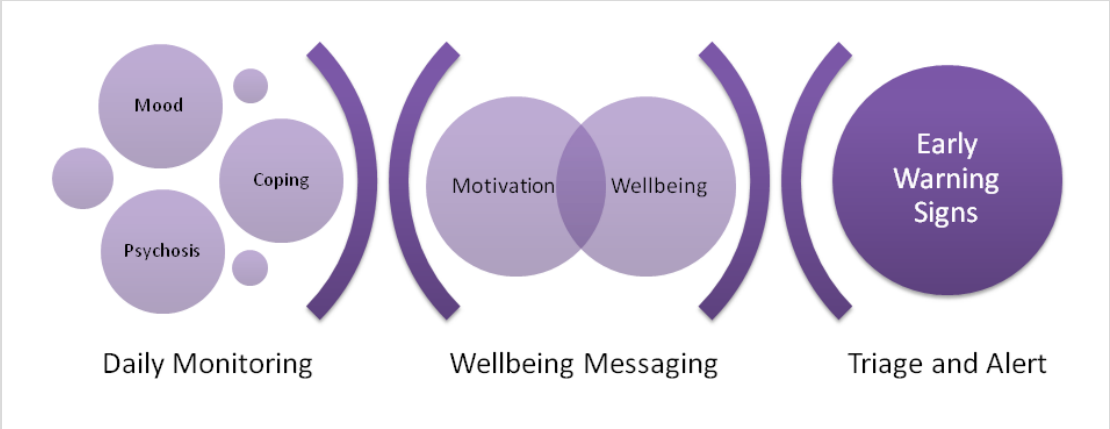
The EMPOWER Medical Device is specifically the algorithm which calculates changes in participants' individual EWS and generates responses to these (see section 5.5.4).

CMHSs who are randomised to EMPOWER will be offered up to two days training which will include orientation to our theoretical model of EWS, familiarisation with the App and support in responding to conversations with service users and carers around sharing and responding to data. We will provide ongoing support to CMHSs over the course of the study.

Service user participants will have access to the EMPOWER App for the full 12-months of the intervention period. EMPOWER will be developed as a flexible user-led EWS monitoring tool that incorporates (i) daily EWS monitoring; (ii) personalised EWS items; (iii) delivery of self management messages directly to service users; (iv) development of a user interface enabling service users to review their own data. These IT characteristics mean that we can design a flexible stepped care model to relapse identification and prevention. This functionality permits a number of steps in a care pathway towards relapse detection and prevention.

Throughout participation in EMPOWER, TAU is free to vary in participating CMHSs and no constraints are placed on participating teams on their practice. Similarly, people in receipt of services and their carers will be encouraged to continue to access their CMHS according to their local care coordinator, psychiatrist and other care planning arrangements. In addition, there are no requirements from EMPOWER for participating teams to change or modify their existing practice in response to alerts from EMPOWER communicating the presence of increased EWS.

Figure 2: EMPOWER App Summary



5.5.2 Procedures for set up and daily monitoring of EWS

A Peer Support Worker will meet with service users, carers and their care coordinators on a number of occasions to:

(i) introduce the people in receipt of services (and their nominated carers) to the EMPOWER stepped care well-being self-management and EWS monitoring as a wellness strategy;
(ii) collaboratively set up the App and
(iii) support the service user's familiarisation with the handset.

During these meetings they will be invited to identify up to 3-personalised early warning signs in addition to the standard EWS list. Participants, their carers and care coordinators will also be able to note specific EWS that are considered to be highly salient to relapse and thus strong risk indicators. Participants will also be invited to monitor their EWS daily for a period of 4-weeks to provide a baseline score for later comparison.

We will offer to meet the carer to discuss their participating in the project. Carers have an important role as allies in supporting effective EWS monitoring. This will provide an opportunity to share the EMPOWER model of EWS, familiarise carers with the App and support them in responding to EWS.

Baseline monitoring will commence at the completion of the set up session(s). The EMPOWER software will emit pseudo-random invitations once per day, between 12 noon and 6pm, 7-days a week over 4-weeks. The Peer Support worker will phone participants at least fortnightly to check in to remind them of the monitoring and will offer support in solving any practical problems.

Following baseline a further meeting, ideally including the participant, their nominated carer and the care coordinator, will be arranged to review monitoring and discuss:

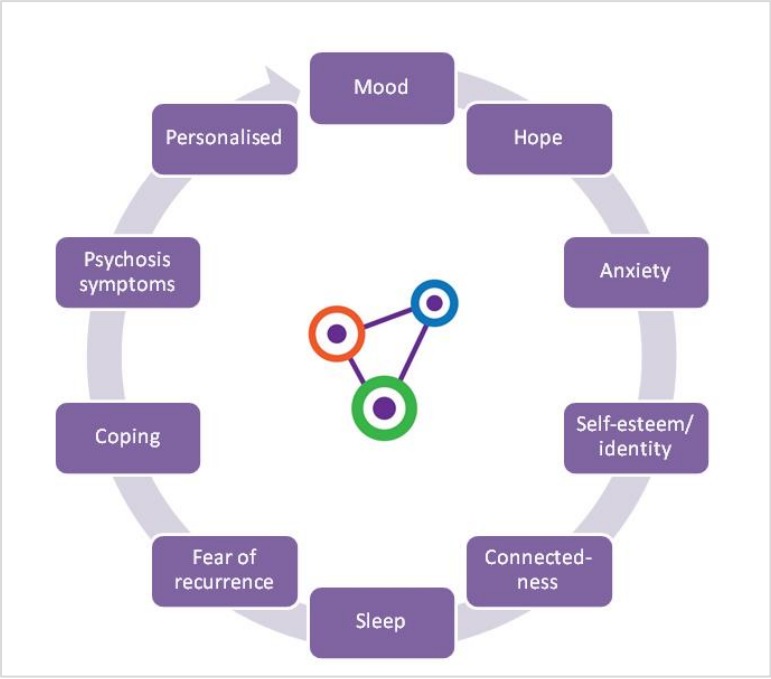
(i) data collected over the previous 4-weeks;
(ii) role and function of Wellbeing messages;
(iii) encourage continued use of the EMPOWER App;
(iv) supplementary assessment of changes in early signs;
(v) the importance of continuing to utilise local CMHS.

Regular use of the App for daily monitoring will then commence, as described in the following section. Participants and the research team will be able to view patterns of EWS by domain (e.g. anxiety, see Figure 3) and over specified time periods. Phone contact from the Research Team will support maintenance of monitoring, troubleshooting technical problems and discussions regarding activating the relapse prevention pathway. In addition the Research Team will produce reports summarising in graphical form the ebb and flow of participants daily monitoring for participants so they can share these data with family and care co-ordinators if they wish to.

5.5.3 The EMPOWER Questionnaire

Daily monitoring of EWS is initiated by pseudo-random mobile phone invitations to complete an EWS Questionnaire. The questionnaire contains 22-items reflecting 13-domains (See Figure 3 below). Items include both positive (e.g. "I've been feeling close to others") and negative content (e.g. "I've been worrying about relapse"). Each item is completed using a simple screen swipe, which enables quick and efficient completion by users. Each item is automatically scored on a scale of 1 to 7. Where particular items score >3, users are invited to complete supplementary questions to enable more fine-grained assessment of that domain.

Figure 3 EMPOWER Questionnaire Domains



All entries into the EMPOWER Questionnaire are automatically uploaded to a Server based at the University of Manchester or, in the event where a data connection is not available, cached in the phone's memory for later upload when that connection is re-established. These data are subject to our algorithm for generating Wellbeing Messages and further assessment to trigger the local relapse prevention pathway.

5.5.4 The EMPOWER Medical Device

The EMPOWER Medical Device is the alert algorithm that forms one part of a broader system that is designed to identify and respond to EWS. Other components include self-management support and access to a relapse prevention pathway with Community Mental Health Services (CMHS). Figure 4 provides a graphic representation of the system's high-level components and data flow.

Participants use a mobile phone App that prompts them to answer a daily questionnaire about potential early warning signs of psychosis. The data are then submitted to the EMPOWER server and analysed by the alert algorithm. The algorithm establishes a delta (for detailed description see 5.5.4.1 below) by comparing participants' latest data entry against an established baseline. If changes exceed pre-defined thresholds, an alert is generated for the participant. The consequences of the alert are that the research team, which includes a registered mental health nurse (UK only), clinical psychologists (UK & Australia) and general psychologist (Australia only), are emailed about the participant and the participant's status is set to 'ALERT.' This is highly visible in the researcher interface (see Figure 6).

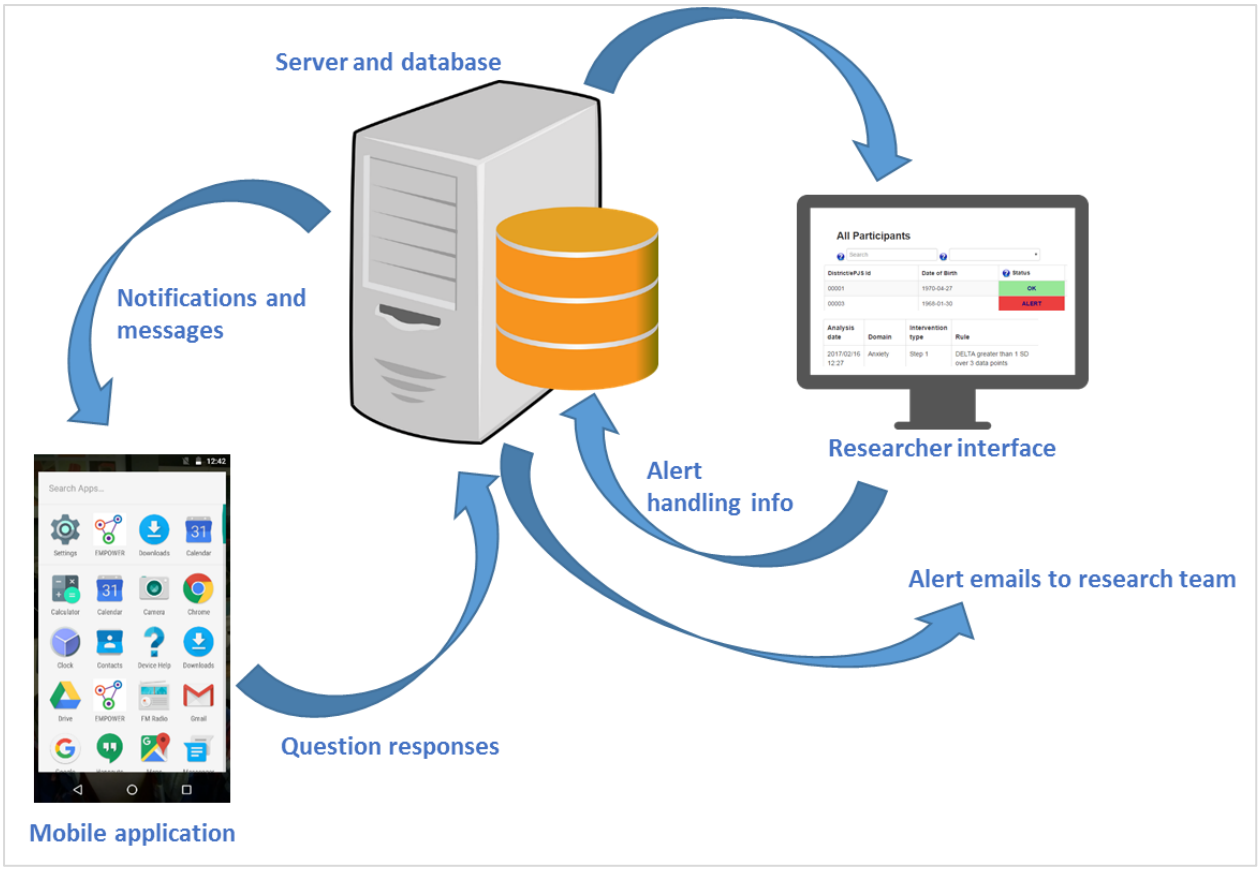
At the same time the alert algorithm runs a separate process scan for EWS changes against the baseline. Based on these changes, the logic selects a message from the most appropriate of several content-based message pools (i.e. one message pool contains helpful messages about 'mood', another about 'anxiety and coping', etc.). This message is delivered back to the participant's mobile App and displayed there. Messages are intended to help people have a greater sense of control over their mental health and wellbeing and to support self-management.

In addition to the aforementioned features, the EMPOWER system also allows participants to use the App to:

- View periodic graphs of their reported data,
- Keep a diary of how they are feeling, and why (stored locally only).

In addition to viewing and handling alerts, researchers can also view longitudinal graphs of their participants' EWS, filtered by question or by domain (group of questions).

Figure 4 EMPOWER System



5.5.4.1 Algorithm description

Based on the variance of EWS observed during users' Baseline period of 4-weeks we will be able to set personalised thresholds for responding to modest increases in EWS across domains (>1 standard deviation) or clinically significant increases or decreases in EWS across domains (>2 standard deviations). We chose 2 standard deviations as an index of reliable clinical change, which is unlikely to happen by chance. Our Algorithm (summarised in Figure 4 below) means that:

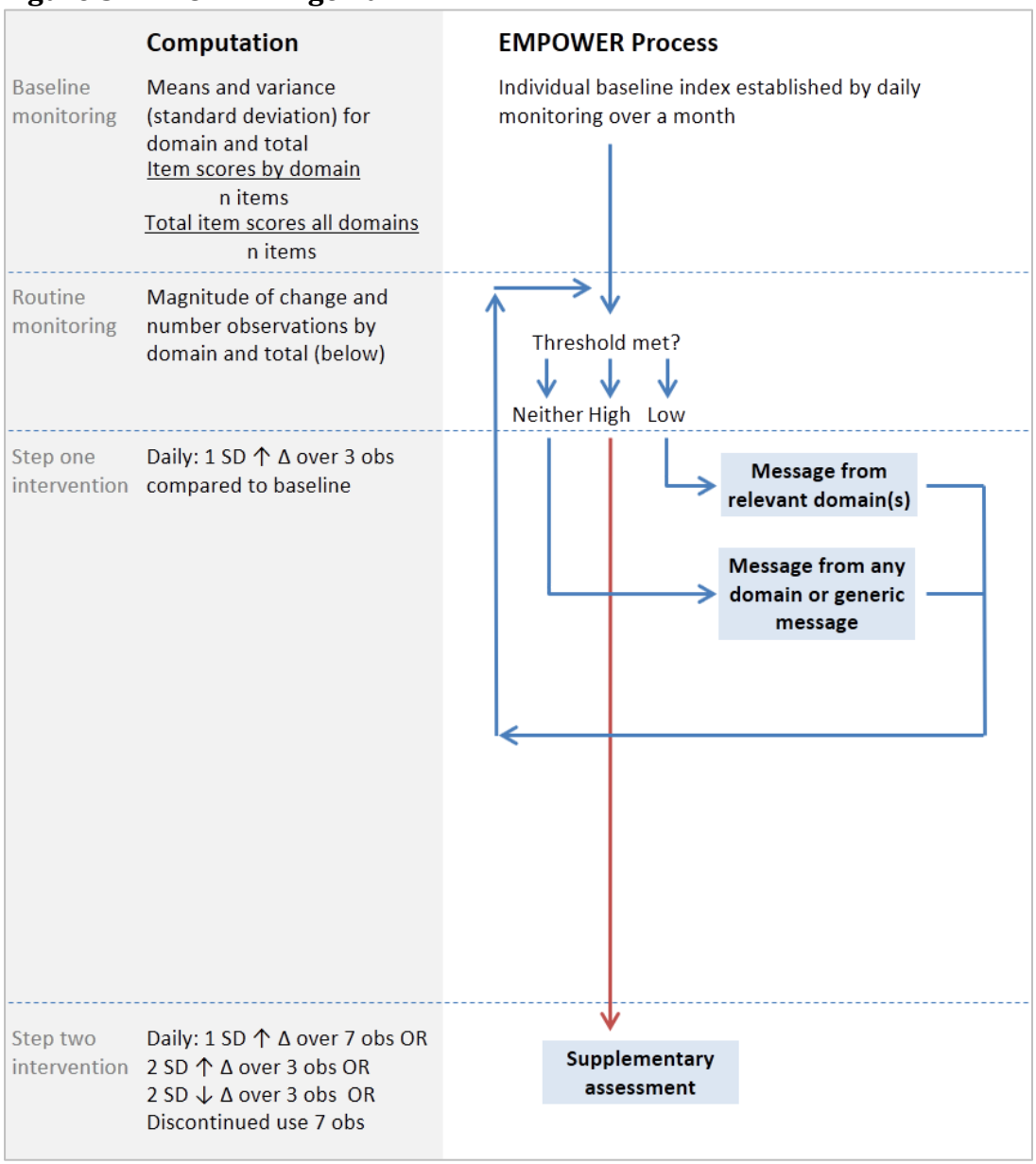
(i) All users receive a generic Wellbeing Message upon completion of the EMPOWER Questionnaire;

(ii) Changes of > 1 standard deviation increase over 3 consecutive observations in any domain will trigger a Wellbeing Message tailored to that breached domain;

(iii) Changes that will trigger a further assessment of EWS and potential sharing with CMHTs of

a. > 1 standard deviation increase over 7 consecutive observations in one or more domains or overall OR
b. >2 standard deviation increase over 3 consecutive observations in one or more domains or overall OR
c. >2 standard deviation decrease over 3 consecutive observations in one or more domains or overall OR
d. discontinued use for 7 consecutive observations.

Figure 5 EMPOWER Algorithm



5.5.5 Monitoring of Users EWS and responding to EWS Alerts

The EMPOWER App will also enable routine monitoring by a Research Mental Health Nurse (RMHN) in Glasgow and Research Assistant (RA) in Melbourne who will have access to all participants data including (a) patterns of EWS (b) patterns of completion and non-completion of EWS (c) patterns of 1 standard deviation increases in EWS and (d) patterns of 2 standard deviation increases or decreases in EWS. When there is a change of > 2 standard deviations an alert will appear on the EMPOWER system. This will result in the following:

- An email will be sent to the researcher,
- The participant's status will be set to ALERT, which is highly visible in the researcher interface.

This alert will be available to the RMHN or RA and their clinical supervisors on the Research Team. The alert can be switched off by completing an action

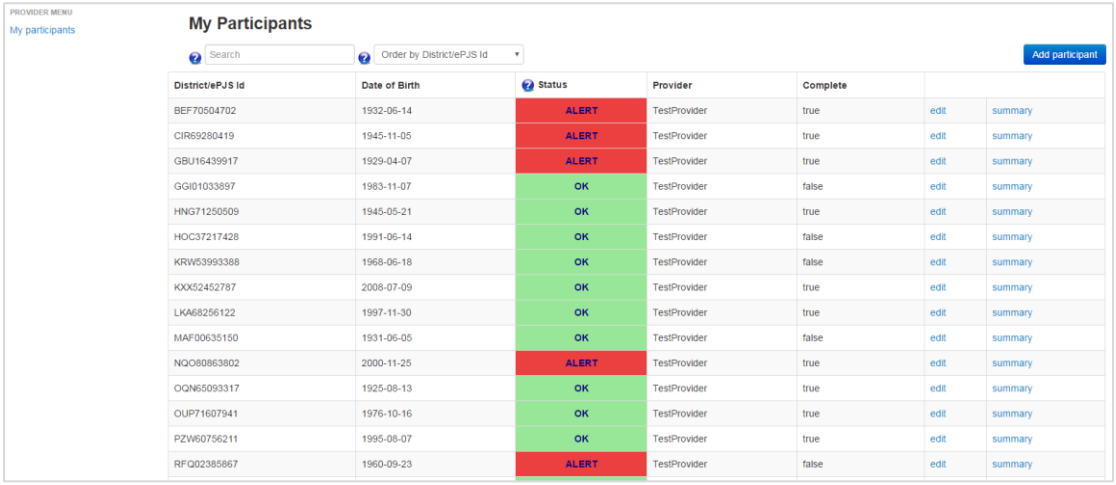
(recorded on a drop down menu with space for more detailed notes). These actions are:

(i) EWS reviewed – no further action taken
(ii) EWS reviewed with participant – no further action taken
(iii) EWS reviewed with participant – action as per individualised plan
(iv) EWS reviewed with participant – information shared with care coordinator / CMHS
(v) EWS reviewed with participant – information shared with CMHS Duty Worker / Crisis Intervention Service
(vi) EWS reviewed – participant unavailable – contact with nominated carer - no further action taken
(vii) EWS reviewed – participant unavailable – contact with nominated carer - information shared with care coordinator / CMHS
(viii) EWS reviewed – participant unavailable – contact with nominated carer - information shared with CMHS Duty Worker / Crisis Intervention Service
(ix) EWS reviewed – participant unavailable – no nominated carer - no further action taken
(x) EWS reviewed – participant unavailable – no nominated carer - information shared with care coordinator / CMHS
(xi) EWS reviewed – participant unavailable – no nominated carer - information shared with CMHS Duty Worker / Crisis Intervention Service
(xii) EWS reviewed - information shared with CMHS Duty Worker (Australia)

Note: Actions (i) – (xi) refer to RMHN actions (UK); action (xii) refers to the RA action (Aust).

Any supplementary information can be added by free text in the system to allow for follow up of any actions sitting with a local CMHS. Figure 6 below illustrates the summary alerts screen accessed by the RMHN / RA to identify current alerts. The action taken is recorded on the server, and the participant's status is reset to 'OK.'

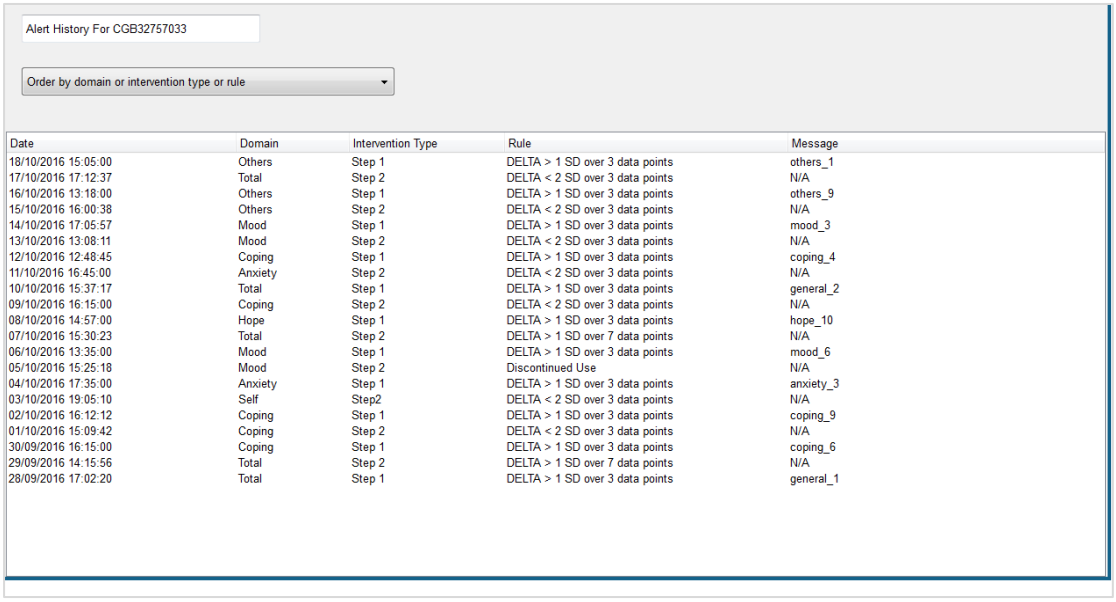
Figure 6 Participant Alerts



District/ePJS Id	Date of Birth	Status	Provider	Complete		
BEF70504702	1932-06-14	ALERT	TestProvider	true	edit	summary
CIR69280419	1945-11-05	ALERT	TestProvider	true	edit	summary
GBU16439917	1929-04-07	ALERT	TestProvider	true	edit	summary
GGI01033897	1983-11-07	OK	TestProvider	false	edit	summary
HNG71250509	1945-05-21	OK	TestProvider	true	edit	summary
HOC37217428	1991-06-14	OK	TestProvider	false	edit	summary
KRW53993388	1968-06-18	OK	TestProvider	false	edit	summary
KXX52452787	2008-07-09	OK	TestProvider	true	edit	summary
LKA68256122	1997-11-30	OK	TestProvider	true	edit	summary
MAF00635150	1931-06-05	OK	TestProvider	false	edit	summary
NQO80863802	2000-11-25	ALERT	TestProvider	true	edit	summary
OQN65093317	1925-08-13	OK	TestProvider	true	edit	summary
OUP71607941	1976-10-16	OK	TestProvider	true	edit	summary
PZW60756211	1995-08-07	OK	TestProvider	true	edit	summary
RFQ02385867	1960-09-23	ALERT	TestProvider	false	edit	summary

Figure 7 below illustrates how the RMHN can access details of the participants' alert history to determine to pattern of changes that have characterised the alert.

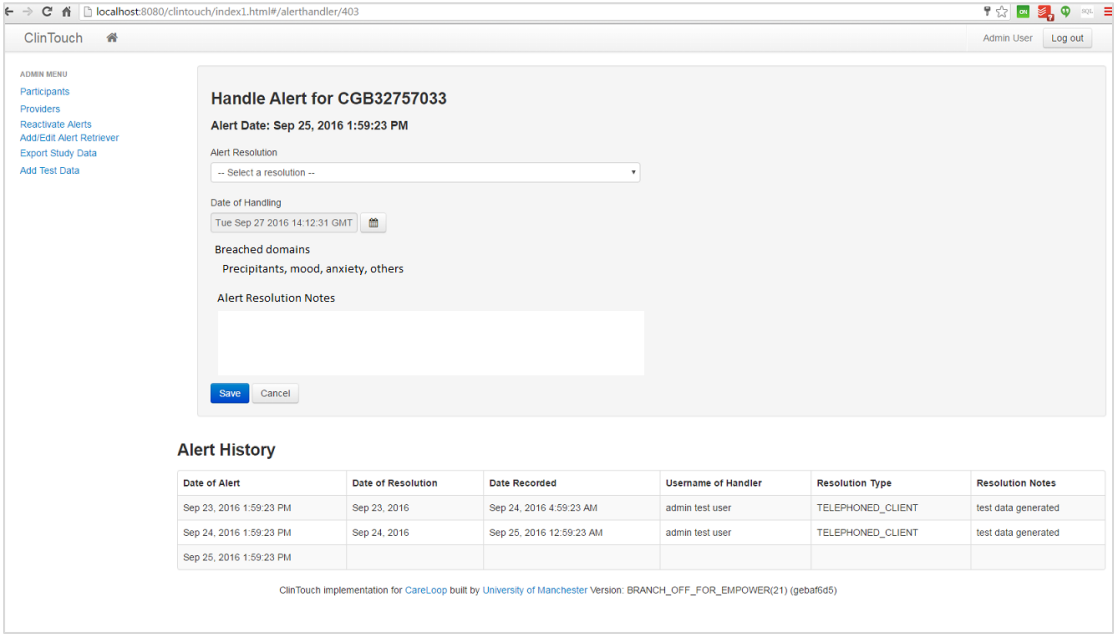
Figure 7 Alert History



Date	Domain	Intervention Type	Rule	Message
18/10/2016 15:05:00	Others	Step 1	DELTA > 1 SD over 3 data points	others_1
17/10/2016 17:12:37	Total	Step 2	DELTA < 2 SD over 3 data points	N/A
16/10/2016 13:18:00	Others	Step 1	DELTA > 1 SD over 3 data points	others_9
15/10/2016 16:00:38	Others	Step 2	DELTA < 2 SD over 3 data points	N/A
14/10/2016 17:05:57	Mood	Step 1	DELTA > 1 SD over 3 data points	mood_3
13/10/2016 13:08:11	Mood	Step 2	DELTA < 2 SD over 3 data points	N/A
12/10/2016 12:48:45	Coping	Step 1	DELTA > 1 SD over 3 data points	coping_4
11/10/2016 16:45:00	Anxiety	Step 2	DELTA < 2 SD over 3 data points	N/A
10/10/2016 15:37:17	Total	Step 1	DELTA > 1 SD over 3 data points	general_2
09/10/2016 16:15:00	Coping	Step 2	DELTA < 2 SD over 3 data points	N/A
08/10/2016 14:57:00	Hope	Step 1	DELTA > 1 SD over 3 data points	hope_10
07/10/2016 15:30:23	Total	Step 2	DELTA > 1 SD over 7 data points	N/A
06/10/2016 13:35:00	Mood	Step 1	DELTA > 1 SD over 3 data points	mood_6
05/10/2016 15:25:18	Mood	Step 2	Discontinued Use	N/A
04/10/2016 17:35:00	Anxiety	Step 1	DELTA > 1 SD over 3 data points	anxiety_3
03/10/2016 19:05:10	Self	Step2	DELTA < 2 SD over 3 data points	N/A
02/10/2016 16:12:12	Coping	Step 1	DELTA > 1 SD over 3 data points	coping_9
01/10/2016 15:09:42	Coping	Step 2	DELTA < 2 SD over 3 data points	N/A
30/09/2016 16:15:00	Coping	Step 1	DELTA > 1 SD over 3 data points	coping_6
29/09/2016 14:15:56	Total	Step 2	DELTA > 1 SD over 7 data points	N/A
28/09/2016 17:02:20	Total	Step 1	DELTA > 1 SD over 3 data points	general_1

In the first instance the research team will always aim to contact the participant (UK) or the Duty Worker (Aust.). Professor Andrew Gumley will supervise the RMHN in Glasgow. John Farhall and John Gleeson will supervise the RA in Melbourne. Regular contact by the senior researchers and RMHN/RA with the local teams using EMPOWER will facilitate engagement with local systems and communication of risk information. Actions arising from the alert are recorded on the Alert Handling Screen (Figure 8)

Figure 8 Alert Handling Screen



5.5.6 Wellbeing Messaging

Our approach to Wellbeing Messaging is informed by our intention that these messages are experienced by users of the EMPOWER App as engaging, friendly, and empowering. We have worked closely with people with lived experience of psychosis to formulate a framework to guide the design of Wellbeing Messages. There are four methods we have applied to attempt to achieve this:

(i) Throughout the study we will survey multiple stakeholders in exploring their preferences and recommendations for Wellbeing Messages through our twitter feed (@EMPOWER_EWS) or via an online survey (University of Glasgow MVLS Research Ethics Number 200150190) https://empower.onlinesurveys.ac.uk/empower-wellbeing-messages-survey.

(ii) Given that we cannot truly know what a person is experiencing at the time they complete an EMPOWER Questionnaire we have designed the structure of our messages to stimulate reflection and curiosity. For example *"When people feel down they find it hard to get motivated. Some people try to plan at least one pleasurable experience each day – what activities do you usually enjoy?"*

(iii) Our framework for determining content of messages is guided by designing messages that reflect
   a. Compassion
   b. Acceptance
   c. Connectedness
   d. Hope and optimism
   e. Identity
   f. Meaning
   g. Empowerment

(iv) Wellbeing Messages are available within the App providing users with the opportunity to explore message content that is relevant and appealing to them at their convenience.

5.5.7 Community Mental Health Services

Following randomisation of CMHSs to EMPOWER we will provide training to those mental health staff in teams based on our model of relapse prevention which emphasises (i) therapeutic alliance; (ii) barriers to help-seeking; (iii) familiarisation with App; (iv) developing an individualised formulation of risk of relapse and (v) developing a collaborative relapse prevention plan. Following this we will aim to meet with care coordinators on a fortnightly basis to provide supervision in the implementation of EMPOWER. This will also enable us to escalate stepped care procedures where EWS fail to resolve following self management or whether they escalate to such a level that necessitates immediate delivery of crisis care.

5.5.8 Treatment as Usual Control

We have chosen to use a treatment as usual (TAU) control condition in both the Glasgow and Melbourne Centres, as this provides a fair comparison with routine clinical practice. In Glasgow and Melbourne secondary care is delivered by adult Community Mental Health Services, which largely involve regular, fortnightly or monthly, follow-up with a care coordinator and regular review by a psychiatrist.

5.6 Outcomes

Outcomes will be measured by self-report, objective assessments and face-to-face interviews. All participants will be assessed at the following time points: baseline pre-randomisation and at 3, 6 and 12-month follow-up.

5.6.1 Feasibility Outcomes

5.6.1.1 Service user-centred

The proportion of eligible and willing service users who then consent; proportion continuing for 12-months to the end of the intervention; number completing >33% EWS datasets; number of times data accessed and number of times data shared with mental health staff and carers. We will also assess self reported acceptability and usability using an adapted version of the Mobile App Rating Scale (Stoyanov et al. 2016).

5.6.1.2 Mental Health Staff

The number of times data discussed with service-user; number of times service user has sought help; number of times EMPOWER triggered a change in management (e.g. appointment brought forward, medication change).

5.6.1.3 Carer

The number of times data discussed with person cared for; number of times person cared for sought help; number of times EMPOWER triggered a change in management (e.g. appointment brought forward, medication change).

5.6.1.4 Safety

Adverse events will be recorded according to the following categories:

- Adverse events (AE)
- Adverse Device Effect (ADE)
- Serious Adverse Device Effect (SADE)
- Serious Adverse Event (SAE)
- Anticipated Serious Adverse Device Effect (ASADE)
- Unanticipated Serious Adverse Device Effect (USADE)
- Device Deficiencies

Details of recording and reporting of all adverse events is contained in our Standard Operating Procedure for Adverse Events in the EMPOWER Trial, v1 15th May 2017.

5.6.1.5 Performance

The following performance endpoints have been identified.

a) Each participant has App successfully uploaded on a Mobile Phone
b) Each participant has personalized early warning signs included in the EMPOWER Questionnaire
c) Each participant receives a daily prompt to complete their questionnaire
d) Participants receive an EMPOWER message each time they complete the questionnaire
e) Following 4-weeks of usage each the EMPOWER Algorithm calculates participants' individualized baseline of symptoms and experiences.
f) Participants can access charts of their symptoms and experiences covering 1-week and 1-month time intervals
g) Following completion of the questionnaire, participants data are transferred to the Manufacturer's server
h) Researcher accesses participants' questionnaire responses and generate charts to observe changes over time
i) Researcher receives a record of alerts for each participant and is able to record actions in relation to these alerts.

Table 1 below provides a summary of each endpoint and also includes how these performance endpoints are monitored, identification of potential performance problems and actions to address these.

Table 1 Performance of the EMPOWER App

Performance Endpoint	Device related	Monitoring and recording of Performance	Performance problems	Actions to address performance
Each participant has App successfully uploaded on a Mobile Phone	No	Peer Support Worker (UK and Aus) and Research Nurse (UK) / RA (Aus)	Participant's Mobile Phone isn't compatible and they are unable to use App	Research Team supplies Mobile Phone
Each participant has personalized early warning signs included in the EMPOWER Questionnaire	No	Peer Support Worker (UK and Aus) and Research Nurse (UK) / RA (Aus)	No risks identified	Mobile App continues to function without personalization
Each participant receives a daily prompt to complete their questionnaire	No	EMPOWER generates alert for discontinued monitoring after 7 missed observations	Questionnaire is not delivered to participant and no data are recorded	Peer Support Worker (UK and Aus) routinely follows up users' to support use of Mobile App Alert would trigger additional contact with user Report to Manufacturer, fix and reinstall and appropriate
Participants receive an EMPOWER message each time they complete the questionnaire	No	Peer Support Worker (UK and Aus) routinely follows up participants to support use of Mobile App	No messages received by participant	Peer Support Worker (UK and Aus) routinely follows up users' to support use of Mobile App Report to Manufacturer, fix and reinstall and appropriate
Following 4-weeks of usage each the EMPOWER	Yes	Research Nurse (UK) and RA (Aus)	If no baseline of participant's symptoms and experiences	Research Nurse (UK) and RA (Aus) reviews acceptability of

Performance Endpoint	Device related	Monitoring and recording of Performance	Performance problems	Actions to address performance
Algorithm calculates participants' individualized baseline of symptoms and experiences.		routinely monitors use	calculated. This means that the EMPOWER Alerts algorithms would not operate.	using the Mobile App with participant
Participants can access charts of their symptoms and experiences covering 1-week and 1-month time intervals	No	Peer Support Worker (UK and Aus) routinely follows up participants to support use of Mobile App	User unable to review their Charts	Peer Support Worker (UK and Aus) routinely follows up participants to support use of Mobile App Report to Manufacturer, fix and reinstall and appropriate
Following completion of the questionnaire, participants data are transferred to the Manufacturer's server	No	Peer Support Worker (UK and Aus) and Research Nurse (UK) / RA (Aus)	Data not transferred	Alert generated after 7 missed observations. Research Nurse (UK) RA (Aus) responds to Alert by contacting participant. Report to Manufacturer, fix and reinstall and appropriate
Researcher accesses participants' questionnaire responses and generate charts to observe changes over time	No	Research Nurse (UK) / RA (Aus)	Software failure meaning that data and Charts are unavailable to Research Nurse (UK) / RA (Aus)	Report to Manufacturer
Researcher receives a record of alerts for each	Yes	Research Nurse (UK) / RA (Aus)	Software failure meaning that data and Charts are	Report to Manufacturer

Performance Endpoint	Device related	Monitoring and recording of Performance	Performance problems	Actions to address performance
participant and is able to record actions in relation to these alerts.			unavailable to Research Nurse (UK) / RA (Aus)	

5.6.2 Primary Outcomes

We will measure relapse over the 12-months following introduction of the EMPOWER Relapse Prevention. There is a lack of agreement with respect to definitions of relapse and many studies fail to utilise standardised and validated observer-rated instruments (Gleeson et al., 2010). Bebbington et al. (2006) have developed reliable and valid criteria for relapse and remission that have strong clinical applicability. Independent and blind observer ratings are applied to detailed extracts taken from clinical notes. Ratings are based on changes in positive psychotic symptoms. Evidence is required of improvement in (for partial remission) or absence of (for full remission) positive psychotic symptoms continuing for at least 4 weeks. Relapse ratings are based on evidence of the re-emergence of, or significant deterioration in, positive psychotic symptoms of at least moderate degree persisting for at least 2 weeks. We will establish reliable and valid criteria for assessing severity of relapse. Following each relapse we will conduct an audit trail exploring help-seeking attempts and service responses to help-seeking as reflected in the participant's clinical case notes. The identification of relapse detection "failures" will enable refinement of the intervention for the main trial. In order to ensure blinded assessment of primary outcomes in the context of a CRCT, we will establish an adjudication committee comprised of expert clinicians/researchers to make independent blinded anonymised ratings of relapse and exacerbations. These will be made using short vignette transcripts derived from collection of health services usage data.

We will also measure symptoms, service engagement, coercion, empowerment, adverse events, emotional adjustment, and carer burden at baseline (pre-randomisation); 3, 6 and 12-month follow-up.

5.6.3 Mechanisms

Measures have been selected which map directly onto hypothesised mechanisms of change as well as known predictors of relapse. Mechanisms of patient benefit are operationalised as improvements in personal recovery, empowerment, utilisation of social supports.

(i) *Recovery and Self Efficacy:* Questionnaire for Personal Recovery (QPR), General Self Efficacy Scale (GSE) will be completed by service user participants.

(ii) *Social and Interpersonal Context:* Psychosis Attachment Measure (SR) and adapted Perceived Criticism Scale will be completed by service user participants.

5.6.4 Secondary Outcomes

We will also assess changes in symptoms, substance use, emotional distress, carer burden, service engagement and adherence and health related quality of life.

(i) *Mental Health Status:* The Positive and Negative Syndrome Scale (PANSS), Personal and Social Performance Scale (PSP) and the Calgary Depression Scale for Schizophrenia (CDSS) will be completed with service user participants.
(ii) *Substance use measures:* Time Line Follow Back for drugs and alcohol (TLFB).
(iii) *Emotional distress:* Fear of Recurrence Scale (FoRSe), Hospital Anxiety and Depression Scale (HADS), and the Personal Beliefs about Illness Questionnaire-Revised (PBIQ-R).
(iv) *Service Engagement:* The Service Attachment Scale (SAS) and the Medication Adherence Rating Scale will be completed by service user participants.
(v) *Health Economics:* Euro-Qol Five Dimension (EQ-5D-5L) and the Assessment of Quality of Life–Eight Dimension (AQoL-8D) and Resource Use Questionnaire (RUQ).

5.6.5 Carer Outcomes

The Involvement Evaluation Questionnaire will be completed as a measure of carers' worrying, tension, urging and supervision. The Carer Perceived Criticism Scale will be used as a measure of Carers' perspectives on relationship quality.

We will also assess Carer Health Economic Outcomes using a purposively designed Health services use questionnaire, Time cost questionnaire, the EQ-5D-5L and the CarerQol-7D.

5.6.6 Care Coordinator Outcomes

Participants care coordinators will complete the Service Engagement Scale (SES).

5.7 Process Evaluation

In line with recent MRC Guidance on process evaluation of Complex Interventions (Kellogg, 2004; Moore et al., 2015) we will produce a Logic Model for the EMPOWER intervention. The overall aim of this process evaluation is to better understand how and why the intervention was effective or ineffective, as well as practical difficulties in adoption, delivery and maintenance to inform potential upscaling into a full clinical trial. The process evaluation was informed by an extensive Stakeholder Consultation with Service Users, Carers and Mental Health Staff. Twenty-five focus groups were held across Melbourne and Glasgow from 20th July 2016 to 18th October 2017, which comprised 84 mental health staff, 17 service users and 38 carers. In line with our person based theoretical orientation (Yardley *et al.*, 2015), we aim to develop an in-depth understanding

of user experiences. Specifically we will explore how service users, staff and carers experienced the EMPOWER intervention.

5.7.1 Service Users

We will purposively recruit a sub-sample of service users who have provided their informed consent to participate in the EMPOWER study and who have been randomised to the EMPOWER Intervention arm. We will aim to identify participants at different time points (following completion of baseline and during the 12-month follow-up period). This is in order to capture the varied and evolving experiences of participants. Specifically we wish to explore the following domains (as per MRC Guidance).

5.7.1.1 Fidelity

Was the EMPOWER intervention delivered as intended?

5.7.1.2 Exposure

The extent to which participants received and understood the different elements of the intervention and whether these were implemented as intended. The acceptability of the intervention will also considered here.

5.7.1.3 Context

Including information relating to aspects of context in which the intervention was delivered.

5.7.1.4 Mechanisms of Impact

What were the "active ingredients of the intervention?

5.7.2 Carers

We will purposively recruit a subsample of carers who have provided their informed consent to participate in the EMPOWER study and whose relatives have been randomised to the EMPOWER Intervention arm. Specifically we will explore their perspectives in relation to their relatives participation and involvement with the EMPOWER intervention. Specifically:

5.7.2.1 Exposure

How do they understand their relative's access to and use of the EMPOWER App?

5.7.2.2 Mechanisms of impact

What changes have they noticed during the time their relative has used the EMPOWER App?

5.7.3 Care Co-ordinators

We will purposively recruit a sub-sample of Care Co-ordinators who have provided their informed consent to participate in the EMPOWER study and whose service users have been randomised to the EMPOWER Intervention arm. We will specifically recruit Care Co-ordinators who have been involved in responding to EMPOWER App alerts associated with changes in EWS or relapse episodes during their involvement in the study. Specifically we wish to explore mental health staffs' experiences in relation to the EWS/Relapse episode, the role of their broader working context, their relationship with their service user

and the EMPOWER App in influencing how they responded to changes in EWS or actual relapse.

5.7.4 Research Team

In order to more fully understand the implementation process, we will conduct qualitative interviews with members of the research team including principle investigators, research assistants, peer support workers and triage nurses. Specifically, we wish to explore the research team members' experience of recruitment and retention. Research team members will have the option to be telephoned by the process evaluation researcher on an agreed number at an agreed time.

5.8 Participant Timeline

Participation in the study will be for up to 12-months.

	Baseline	**Randomisation**	**3-months**	**6-months**	**12-months**
Service Users	X	X	X	X	X
Carers	X	X	X	X	X
Mental Health Staff	X	X	X	X	X

5.9 Sample Size

No formal sample size calculation is appropriate for this pilot phase. The proposed sample size of 120 service users across 40 care coordinators in 8 CMHTs is sufficient for establishing the feasibility and obtaining parameters (including the relevant ICCs for the cluster design) to inform the design and size of a future definitive, pragmatic, multicentre and multinational CRCT.

5.10 Recruitment and Randomisation

As a CRCT randomisation will take place at the level of the CMHT (the cluster). Participating CMHTs will be randomised to the EMPOWER Relapse Prevention Intervention or to continue their usual approach to care. Randomisation sequence generation and procedures will be undertaken by the study statistician at the Centre for Healthcare Randomised Trials (CHaRT) at the University of Aberdeen.

Researchers will approach each eligible care coordinator and seek their consent to participate in the trial. Prior to randomisation, consenting care-coordinators will provide an anonymised list of their current potentially eligible service user caseload. This list will then be randomly ordered by CHaRT. Researchers will then approach these service users sequentially in blocks of up to 5 potentially eligible participants and seek informed consent to participate in the study. If there are further participants eligible for inclusion at the end of this block, the researcher will move onto the next block of 5 (if applicable). Care co-ordinators will provide participants with an easy to read Information Leaflet regarding the

study to enable potential participants to express interest in finding out more about the study. In Australia, Information Posters will be displayed within staff areas of participating sites to inform care-coordinators of the study and provide contact details of research assistants should they wish to participate.

We aim to approach and consent on average 3 participants per care coordinator (giving a total of 120 potential participants). After completing baseline assessments on all consenting service users in care coordinators' and CMHS' caseload, the Clinical Trials Unit (CTU) at CHaRT will conduct randomisation of the CMHS. For Australia, with just two clusters, this will be by simple randomisation by the CTU. For Glasgow, with six clusters, The CTU will create three pairs of teams based on similarity of the catchment area in terms of social deprivation (Carstairs) score or CMHS type (e.g. early intervention service). The CTU will randomly allocate one member of the pair to the intervention, and the remaining member will be allocated to control.

We will explore in this pilot phase the best method of randomly allocating the clusters in the full trial, specifically to establish what matching factors (if any, and/or if matching at all is appropriate, methodologically) are suitable. Any violations of the study protocol will be recorded and reported to the Research Ethics Committee, Study Steering Committee (SSC) and the independent Data Monitoring and Ethics Committee (DMEC).

5.11 Methods (Data collection, management and analysis)

5.11.1 Data Collection Methods

All outcome measures will be administered at baseline and subsequently at 3, 6 and 12 months by RAs who will have been trained in the use of all the instruments and scales, to achieve a satisfactory level of inter-rater reliability. Regular training sessions including the use of video and role play will be conducted with all research assistants in order to maintain reliability and prevent rater drift. Participants will be offered choices regarding length of assessments, including the option of breaks and multiple occasions. Assessment measures will be clearly prioritised so that the most important will be collected first to avoid missing data. We will have a standard protocol for managing any distress that is associated with the completion of measures, which we have successfully utilised in several trials and has been developed in collaboration with service users; this includes telephone contact within 48 hours of assessments in order to check on participant well-being.

5.11.2 Protection Against Bias

Our assessment of the primary outcome will be blinded. Research Assistants will collect health services data as part of the economic evaluation and also identify potential episodes of relapse and exacerbation. These episodes will provide the basis for individual anonymised case vignettes that can be submitted to our independent adjudication panel. This panel will contain expert clinicians/researchers who will have the necessary knowledge, experience and skills to make independent blinded judgements regarding relapse/exacerbation. Contributors will be identified through existing networks. In the event that the

panel is unable make a decision regarding relapse/exacerbation this will be recorded and considered in sensitivity analyses.

5.11.3 Sources of contamination

We have identified a priori four sources of potential contamination i) staff moving from an EMPOWER intervention CMHS to a TAU CMHS ii) service user moves from an EMPOWER intervention CMHS to a TAU CMHS iii) EMPOWER participant service users meet with TAU participants and share experiences of using EMPOWER iv) EMPOWER carer participants meet TAU carer participants. Although the risk of these four sources of contamination is probably low we will be able to consistently monitor for i and ii. However, it is unlikely we are able to consistently identify iii and iv.

A further source of potential contamination is the routine use of health related Apps by participants in the trial. We will assess participants' mobile App usage as part of participants' demographic information into the study and at follow-up.. Specifically we will ask: Do you own a mobile phone? Do you use Health related Applications? What applications do you use? What frequency do you use these applications?

5.11.4 Data Management

Each study participant will be assigned a unique trial identification number at the start of the assessment process. This number will be written on all clinical assessment forms/datasheets and databases used to record data on study participants. A hard copy of a record sheet linking patient identity, contact details and trial identification number for all participants will be kept at each site. It will be placed securely in a locked filing cabinet separate from datasheets. The local study coordinator will enter the data on to an electronic database, and all such data will be checked for errors before being transferred to the appropriate statistical package. All data will be kept secure at all times and maintained in accordance with the requirements of the Data Protection Act, and archived according to clinical trial Good Clinical Practice (GCP) regulations.

5.11.5 Statistical Methods

The analysis will follow the guidelines of the CONSORT statement for clustered randomised trials and recommendations for the analysis of clustered randomised trials when presenting and analysing the data. Here, we have potentially repeated measures on individual patients nested within care coordinators who are nested within teams (the unit of randomisation) who are nested within region (Australia and UK or possibly to be known as Scotland). The analysis will adjust for these factors using appropriate random (patient, if relevant; and care coordinator; and team) and fixed (region) effects. The trial statistician will remain blind until the main analyses are complete. Baseline characteristics of the study population will be summarised separately within each randomised group. Baseline characteristics will also be presented for dropouts and completers within each treatment group. The analysis will be performed on the basis of the intention-to-treat principle and will utilise all available follow-up data from all randomised participants.

6.0 Health Economics (Work Package 5)

6.1 Objectives

We will focus on the development of economic measures as part of the trial including how to capture resource use and quality of life. We will work between different service systems in the UK and Australia to build comparability and utilise the pilot to refine the measurement and capture of economic data.

6.2 Deliverables

This will lead into the development of an analytic framework (model) for the health economic analysis in the definitive study as well as a protocol for the "within trial" evaluation. This pre-trial model will be used to help provide an economic rationale for the design of the definitive trial.

6.3 Methods

As part of the within trial economic evaluation we propose to test two health-related quality of life measures (which can be used to assess Quality-Adjusted Life Years, QALYs), the Euro-Qol Five Dimension (EQ-5D-5L) and the Assessment of Quality of Life –Eight Dimension (AQoL-8D) in the feasibility trial. While the EQ-5D-5L is very commonly used in the UK & Australian context its sensitivity and appropriateness in people with schizophrenia has been seriously questioned (Brazier et al., 2014). The AQoL-8D is a newer HRQoL measure and was developed to be sensitive to the domains of quality of life, which are important to people with mental health problems. A resource use questionnaire to capture costs incurred will also be tested. This questionnaire will need to be appropriate to both the UK and Australian context but may require some system specific modules for services, which differ between the two settings.

7.0 Research Governance

NHS Greater Glasgow & Clyde is the Sponsor of the Trial in the UK and Australian Catholic University in Australia. In accordance with high standards of research governance we will ensure researchers receive training in the International Conference on Harmonisation (ICH) Guidelines - Good Clinical Practice. We will set up a Study Steering Committee (SSC) and an Independent Data Monitoring and Ethics Committee (DMEC) prior to the start of the study. The SSC will comprise study applicants, a representative of the HTA, and representatives of service users and providers, and have an independent chairman. A DMEC will also be established to monitor (1) recruitment of study participants, (2) ethical issues of consent, (3) quality of data (including missing data), (4) the incidence of adverse events, and (5) any other factors that might compromise the progress and satisfactory completion of the trial. This will also have an independent chairman, and include an independent statistician.

7.1 Project Management Committee (PMC)

Operational management and governance of transitions between Work Packages and implementation of the study with be through the EMPOWER Project Management Committee (PMC) comprising the following individuals:

- Professor Andrew Gumley (Chief Investigator)
- Mr Simon Bradstreet (Trial Manager)
- Professor John Gleeson (Melbourne CI)
- Associate Professor John Farhall (Melbourne CI)
- Professor John Norrie (Study Statistician)
- Professor Andy Briggs (Study Health Economist)
- Professor Alison Yung (University of Manchester)
- Matt Machin (Digital technology)
- Professor Max Birchwood (University of Warwick)
- Professor Matthias Schwannauer (University of Edinburgh)
- Mr Frank Reilly (Scottish Recovery Network)

7.2 Project Advisory Group (PAG)

The PMC Group will report to the wider Principal Investigators Group on a regular basis. The PAG will convene on a three-monthly basis.

7.3 Study Steering Committee (SSC)

The role of the SSC is to provide overall supervision for a project on behalf of the Project Sponsors and Project Funders and to ensure that the project is conducted to the rigorous standards set out in the Department of Health's Research

Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice. The SSC will be constituted following NIHR Guidance (Version date: May 2013). The membership of the SSC is described under 1.0.

7.4 Data Monitoring and Ethics Committee (DMEC)

The DMEC will have access to unblinded comparative data and monitor these data and make recommendations to the SSC on whether there are any ethical or safety issues on whether the study should continue. The DMEC will be constituted following NIHR Guidance (Version date: May 2013). The membership of the DMEC is described under 1.0.

7.5 Audit

NHS Greater Glasgow & Clyde will retain the right to audit implementation of the trial in the UK context.

7.6 Measuring Adverse Events

Details of recording and reporting of all adverse events is contained in our Standard Operating Procedure for Adverse Events in the EMPOWER Trial, v1 27th November 2017 (UK) and v1.1 27th November 2017 (Australia).

In order to comply with Medical Devices Regulations 2002, ISO/FDIS 14155:2011 and Standards for Good Clinical Practice (GCP), it is important that all researchers are aware of the different definitions related to adverse events in research and how to record, report and review each of these specific occurrences. It is essential that all adverse events which occur during the course of the EMPOWER study are recorded and reported appropriately in order to ensure that patient safety is maintained.

Adverse events are reportable from the time of study enrolment. For medical device trials, like EMPOWER, the time of enrolment is defined as the time at which, following recruitment, a participant signs and dates the informed consent form.

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs in participants, whether or not related to the investigational medical device (i.e. the EMPOWER algorithm). This includes adverse events related to the EMPOWER intervention group and to the treatment as usual (TAU) group and also to all research procedures involved. Adverse events may be classified as follows.

<table>
<tr><th>Adverse events</th><th>Non-device related</th><th colspan="2">Device related</th></tr>
<tr><td>Non-serious</td><td>Adverse Event (AE)</td><td colspan="2">Adverse Device Effect (ADE)</td></tr>
<tr><td rowspan="2">Serious</td><td rowspan="2">Serious Adverse Event (SAE)</td><td colspan="2">Serious Adverse Device Effect (SADE)</td></tr>
<tr><td>Anticipated Serious Device Effect (ASADE)</td><td>Unanticipated Serious Device Effect USADE</td></tr>
</table>

Potential adverse events, which are not related to the EMPOWER medical device (i.e. that do not relate to the EMPOWER algorithm) but which are related to study procedures, are described below.

Risk	***Rationale***	***Likelihood***	***Resolution***
Distress associated with completion of assessment measures.	Measures ask people to think about potentially distressing subjects.	Low. Assessments are conducted by trained Research Assistants in an empathic, friendly and supportive manner.	Participants can pause or terminate assessments.
Increased fear of relapse or paranoia associated with responding to questions in the EMPOWER App.	Answering questions may increase vigilance for EWS and trigger worry about relapse.	Low. Previous studies have found people value monitoring their wellbeing.	Peer Support Workers stay in contact with participants and can provide reassurance and support.
Worries about surveillance by psychiatric services.	In Phase 1 task groups some service users expressed concern regarding data being accessible by their mental health service.	Low. Mental health services do not have direct access to data from EMPOWER App.	Peer Support Workers stay in contact with participants and can provide reassurance and support.

An adverse event is defined by the ISO14155:2011 guidelines for medical device trials as serious if it:

a) Results in death or,
b) Is a life-threatening illness or injury or,
c) Requires [voluntary or involuntary] hospitalisation or prolongation of existing hospitalisation or,
d) Results in persistent or significant disability or incapacity or,
e) Medical or surgical intervention required to prevent any of the above,
f) Leads to foetal distress, foetal death or consists of a congenital anomaly or birth defect or,
g) Is otherwise considered medically significant by the investigator.

Investigators assessment of causality and expectedness is of particular importance. The relationship between the investigational medical device and the occurrence of each adverse event will be assessed and categorised. The investigator will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the participant's underlying condition, concomitant therapy, other risk factors etc. will be considered. The

Investigator will also consult the current version of the risk analysis report and/or the investigator's brochure.

Relationship	***Description***
Not related	No relationship with investigational device. Other factor(s) certainly or probably causative.
Related	Temporal relationship of the onset of the event, relative to use of the device, is reasonable and there is no other cause to explain the event.

8.0 Widening Stakeholder Engagement for the Main Trial (Work Package 6)

8.1 Objectives

To engage with key services, and local service user and carer organisations in the additional centres participating in the main trial (Scotland, Manchester and Birmingham).

8.2 Deliverables

We will develop a plan for transitioning from a pilot trial to the full scale main trial.

8.3 Methods

We will host three Knowledge Exchange (KE) Events in Edinburgh, Manchester and Birmingham and invite key representatives of NHS services, professional staff and local service user and carer organisations. In these events we will identify key learning outcomes from the EMPOWER project and work with stakeholders in developing plans for the main study phase. We will follow up these KE Events with active engagement with local NHS services, CMHTs and management, local R&D and Information Governance departments. We will identify potential changes to services that would threaten cluster randomisation in a future trial. We will address the following aims:

(i) What is the latest evidence for relapse prevention in psychosis? What is the relapse rate for established psychosis in your service?

(ii) What is the process of relapse and the role of EWS? What experience do stakeholders have of EWS and importance in relapse?

(iii) Implementing our team based approach to early detection of relapse using mobile technology and showing (a) potential for relapse prevention of the approach, including the 12 month relapse rate in our control arm (to show that further interventions are needed), (b) experience of staff, service users and carers/supporters (c) developing the next stage evaluation.

(iv) Engaging teams for the next stage evaluation: what are the potential benefits, including the identification of the current rate of relapse in target areas for the next stage; what will be involved; how should we engage patients and staff from the teams? Can you help us to enlist teams from your area?

We will record the proceedings and disseminate our outcomes from these events to potential participant trusts/teams/user-groups.

9.0 Ethics and Dissemination

9.1 Research Ethics Approval

Before Phase 1 and Phase 2 of the study Research Ethics approval will be sought from West of Scotland Research Ethics Service (Glasgow) and Melbourne Health Human Research Ethics Committee (Melbourne).

9.2 Protocol Amendments

The views of the SSC and DMEC will be sought on any proposed amendments to the EMPOWER Protocol. Following this any proposed amendments will be submitted to the National Institute of Health Research, Study Sponsor, Research Ethics Committees and the Medicines and Healthcare products Regulatory Agency (MHRA) for approval. Protocol amendments will be added to the EMPOWER Protocol and to the ISRCTN Registry.

9.3 Consent

Only those who agree to provide written informed consent will be included in the study. All potential participants, including Service Users, Carers and Care Co-ordinators will be provided with a copy of a Participant Information Sheet and Consent Form that includes a contact number for the study team.

9.4 Confidentiality

The confidentiality of all study data will be ensured via the following security mechanisms.

9.4.1 Software systems, interface and compliance with UK security standards

Three general principles of information security (confidentiality, integrity and availability) will be followed in the design and implementation of EMPOWER. All data transmitted to and from EMPOWER servers will be encrypted over https with strong ciphers as detailed in the Approved Cryptographic Algorithms Good Practice Guidelines (NHS, 2012 and Australian Equivalence). Cipher suites will be implemented in compliance with Section 6 ("Preferred uses of cryptographic algorithms in security protocols") of the Good Practice Guidelines. In cases where participant data are downloaded from the EMPOWER sites, these data will be securely encrypted with a pass phrase of appropriate length and complexity. Data transfers are secured by using standards web security protocols. Uploading data to a central server in real time enables study data to be captured and so protects against data loss such as a phone, which can be lost or stolen. This removes the need for personal data storage on the device. The purpose of the server in this case is secure data storage.

9.4.2 Software systems, interface and compliance with Australian security standards

A range of measures are in place to help ensure the security of the EMPOWER App and the data generated by its users. The App is hosted on a University of Manchester web server, and has standard measures in place to prevent unauthorised access. These measures are governed by the Australian Government standards contained in the Australian Government "Guide to securing personal information" (Office of the Australian Information Commissioner – Jan 2015) and the Australian National Privacy Principles

(replaced National Privacy Principles March 2014), with regard to design principles for confidentially, integrity, availability and physical security. We will also incorporate ISO 25010 which provides for safety-in-use and measures satisfaction with security. These security measures correspond closely to the NHS standards with which ClinTouch currently complies.

9.4.3 Additional security measures:

There are a number of technical measures we will employ to protect personally identifiable data. Any data stored on the phone by the participant will be encrypted. We will also recommend that service users set a passcode to access their Smartphone. All service users recruited to the study will give their informed consent, and this will include risks to data security. These measures should be sufficient to prevent unauthorised data access, should the phone be lost or stolen.

9.4.4 Other study data

Any hard copy/ paper copy information will be stored in locked filing cabinets at local sites and will only be directly accessible by the CI and the study RA. Directly identifying participant information (e.g., consent forms) and de-identified data will be stored in separate locked filing cabinets. Data will be entered onto a secure web-based portal hosted by University of Aberdeen.

9.4.5 Type of information stored

The security arrangements and access for the code will be as follows. Each participant's dataset will have a unique code and will be stored in a password protected database. The unique code will be linked to the participant's name and contact details. The information linking the participant's unique code and contact details will be stored separately from the study database and will also be password protected.

9.5 Dissemination Plan

We will produce an EMPOWER Dissemination Policy. This document will outline a comprehensive list of possible papers with basic descriptions of objectives, contents, authorship, and journals to be targeted.

Dissemination will occur via a number of methods, which include publication of trial papers, conference presentations, book chapters, and the HTA final report (monograph and trials directory).

Participants will be informed of the results by being offered written and/ or face-to-face feedback.

We have an obligation to give the HTA notification of an output prior to any publication (whether in oral, written or other form) of data or the results of the project or of matters arising from such data or results. Therefore, the trial manager should be notified of any outputs (oral, written or other form). The trial manager will coordinate notification to the HTA. Research projects are contractually obliged to submit a draft final report for inclusion in the influential Health Technology Assessment journal series. The journal is indexed on MEDLINE, EMBASE and the ISI Science Citation Index, and assessed for inclusion in the Database of Abstracts of Reviews of Effectiveness. Before a draft final

report is published it is peer-reviewed by at least four relevant experts to ensure scientific integrity and quality standards. An editor will review the external reviewers' comments and the draft version of the report, and feedback is given to the author. Ideally, this will take place within two months of receipt of the draft final report. The team is invited to resubmit their revised report within four weeks. There may be a further round of editorial review before the report is sent to the publisher. The NIHR Journals Library ensures that the results of pilot and feasibility studies which have been funded by the participating programmes are published, regardless of outcome or significance of findings in order to ensure that as much information as possible about each study is in the public domain. Authors are encouraged to report everything, be transparent in their reporting, be reflective and avoid overstating their findings.

9.6 Strategy for Knowledge Exchange and Impact

Our strategy for Knowledge Exchange and Impact means that we are ensuring service user and carer involvement from the outset of the study (for audit criteria see Ruppertsberg et al., 2014). This is reflected in a number of design features of the protocol.

(i) The Scottish Recovery Network (www.**scottishrecovery**.net/) are active collaborators on the project proposal and have actively been involved in the design of the EMPOWER Relapse Prevention Intervention (led by their Director Frank Reilly). A key impact of this early involvement has been to ensure that service users retain control of their data and can be empowered to make decisions to activate different stages of the relapse prevention pathway and share their data with carers and case coordinators. In addition, the SRN will employ the Research Assistant evaluating the outcomes of the CRCT.

(ii) Peer Support Workers will be employed to engage with and support service user participants randomised to the EMPOWER Relapse Prevention Intervention. The main beneficiaries of the intervention are service users with a diagnosis of schizophrenia and their carers. At the outset of the study we will involve these stakeholders in evaluating the acceptability and usability of ambulant symptom recording using mobile phones and identifying key of incentives and barriers to use.

(iii) Our strategy for Knowledge Exchange and Impact also means that we are ensuring the involvement of professional care staff from the outset of the study. This is reflected in our work packages that explore the acceptability and usability of ambulant symptom recording using mobile phones amongst professional care staff, identify incentives and barriers to implementation by NHS Teams and identification existing relapse prevention pathways.

(iv) In addition, our use of a Cluster Randomised Controlled Trial design maximises our ability to learn how to implement the EMPOWER Relapse Prevention Intervention into routine care. Our inclusion of sites spanning the United Kingdom and Australia maximises the portability of this intervention across different health systems.

(v) We will work with and seek feedback from a Trial Steering Group following each WP phase. This will enable us to report transparently achievement of milestones and inform the next step of project development. The Trial Steering Group will comprise stakeholders including clinical academic, health service managers and clinicians, and service user and carers.

(vi) We will organise a number of events for carers, service users and professional staff in Glasgow, Edinburgh, Manchester and Birmingham to identify and share key learning experiences arising from the study and to facilitate scoping and engagement of stakeholders participating in the main study.

10.0 Progression to Full Trial

We have identified 4 of the most important outcomes that will provide the basis for informing progression to the full trial. As advised these will form the basis of discussion rather than hard criteria.

10.1 Recruitment

Since submitting the full application in September 2014 we have initiated engagement with Community Mental Health Teams all of whom have expressed interest in participating in the study.

a) Each of these teams employ between 8 and 10 care coordinators. In order to recruit sufficient service user participants we anticipate having informed consent from 5 care coordinators in each team (a consent rate of between 50 and 62.5%).

b) In order to achieve a sample size of 120 participants we aim to approach and consent 3 participants per care coordinator (giving a total of 120 potential participants). This means that we anticipate that 3 from 5 potential participants on each care coordinators caseload will consent to participate giving a rate of consent of 60% overall.

10.2 Outcomes

It is well established that in mental health trials with challenging patient participant groups using Patient Reported Outcome Measures loss to follow-up is an important methodological concern. We will employ all evidence-based tactics to minimise loss to follow-up and by convention we would not expect loss to follow-up at 12-months to exceed 20%. We will use established analytic techniques to adjust for missing data.

10.3 Process evaluation

In line with recent MRC Guidance on process evaluation of Complex Interventions (Kellogg, 2004; Moore et al., 2015) we will produce a Logic Model for the EMPOWER intervention. This will provide a clear description of the intended intervention, how it will be implemented, and how it is expected to work. The Logic Model will provide the basis for organising observations of processes and outcomes throughout the study and provide a basis to report and fully discuss intervention components for the main trial and implications for intervention theory and methods.

10.4 Safety

We will monitor all Adverse events (AE), Adverse Device Effects (ADE), Serious Adverse Device Effects (SADE), Serious Adverse Events (SAE), Anticipated Serious Adverse Device Effects (ASADE) and Unanticipated Serious Adverse Device Effects (USADE) carefully to detect if there are differences between randomised groups to ensure that it is safe to expose a greater number of participants to the EMPOWER intervention in the main trial.

11.0 Financial and Competing Interests

None declared

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