



STUDY PROTOCOL

Title: Actissist 2.0: Active Assistance for Psychological Therapy 2.0 (Actissist 2.0): Digital Intervention for Co-producing care in psychosis.

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Local Trust collaborators: Greater Manchester Mental Health NHS Foundation Trust
Pennine Care NHS Foundation Trust

This builds on the Actissist study 14/WM/0118.

ROLES AND RESPONSIBILITIES

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| Principal Investigator: | Professor Sandra Bucci, University of Manchester |
| Project Officer: | Dr Alyson Williams, University of Manchester |
| Trial Methodologist: | Professor Richard Emsley, Kings College London |
| Digital Technology Lead: | Mr Matthew Machin, University of Manchester |
| Co-Investigators: | Professor Gillian Haddock, University of Manchester Professor Katherine Berry, University of Manchester Professor Shôn Lewis, University of Manchester Professor Dawn Edge, University of Manchester Professor John Ainsworth, University of Manchester Mr Matthew Machin, University of Manchester Professor Richard Emsley, Kings College London |
| Researcher Assistant: | Dr Natalie Berry, University of Manchester Ms Rose Dicken Ms Rosa Pitts Ms Orla Gleeson Ms Alaina Chaudhry |
| Sponsor Details | Name: The University of Manchester Sponsor contact: Ms Lynne Macrae Role: Faculty Research Practice Governance Co-ordinator Address: Faculty of Biology, Medicine and Health 1.21a Simon Building University of Manchester M13 9PL Email: FBMHethics@manchester.ac.uk Telephone: 0161 275 5436 |

1.0 INTRODUCTION

Schizophrenia is a severe mental illness (SMI) affecting 24 million people worldwide, with the current cost to society estimated to be £11.8 billion per year in England alone (Penn, Waldheter, Perkins, Mueser & Lieberman, 2005). The early phase of psychosis is a critical period, influencing the long-term course of illness. Up to 80% of patients will relapse within 5-years of initial episode. This is significant, because each relapse increases the risk of developing persistent psychotic symptoms and further disconnection from education, employment, social development and community connections, adversely affecting long-term psychosocial development. Currently, the cost of treating relapsing psychosis is 4-times that of stable psychosis. Despite the rise of community care, 70% of the costs of SMI are on unplanned inpatient care for relapse. As the early course of psychosis is sharply predictive of longer-term course of illness, timely, accessible and ecologically-valid interventions are needed to help prevent the development of persistent psychotic illness.

Our proposal addresses established NHS England priorities in the area of SMI treatment policy. Guidelines set out in the 'Five Year Forward View' document (www.kingsfund.org.uk/) identify a clear direction for addressing mental health challenges, with an overarching objective of harnessing the information technology revolution to help digitise aspects of NHS care by 2020. In addition, self-management in long-term conditions is a cornerstone of NHS policy, with the aim being to enhance acceptance, autonomy, empowerment and behavioural engagement. Both of these objectives can be achieved via expansion of accredited health apps that leverage the latest developments in smartphone technology.

Our smartphone app (Actissist) empowers patients to make informed choice in real-time about their treatment and to act promptly under their own control - we believe we have the potential to transform community care for SMI patients. Our proposal aligns with several further NHS health priorities: secondary care SMI service prioritisation; personalised care; patient involvement and empowerment; social recovery; efficiency. Technology presents opportunities to drive improvements in quality, efficiency and population health and revolutionise patient/user experience by: i) putting SMI patients (a historically disempowered group) in control to take a more active role in their own healthcare; ii) improving quality of care by not only assisting self-management, but also assisting clinicians to have a better understanding of a patient's mental health, faster and more efficient data exchange, and aiding patient-clinician communication by both parties having access to real-time data; iii) support shared decision-making and personalised treatments based on analysis of data on people's symptoms/mood/other distressing experiences gathered by the Actissist app; iv)

giving patients choice about the way healthcare is delivered (e.g. refusal rates for complying with face-to-face appointments suggest not all patients wish to engage in current models of healthcare delivery. Indeed, adapted treatments lend themselves well to this client group, who have difficulty attending traditional appointment schedules. For example, in a CBT patient preference trial carried out by members of our team, self-help plus phone support, not face-to-face therapy, was the most popular treatment option expressed by psychosis patients (Haddock et al., 2016). This finding is also borne out in our own pilot data, where a number of participants said they found conventional service schedules intimidating and restrictive.

In early intervention services at least, the Department of Health set a mandate to address the psychosis treatment gap such that 50% of early psychosis patients must receive a NICE-approved treatment package (including psychosocial interventions such as CBT) within two-weeks of referral (NICE, 2009). Smartphone technology now means that it could be possible to deliver real-time, ecologically-valid therapy that extends the reach of standard healthcare delivery. Smartphones are available any time, in almost any location. A recent review showed that smartphone ownership among psychosis patients is comparable to general population ownership rates (Firth, Cotter, Torous, Bucci, Firth, & Yung, 2015). As such, smartphones offer an unprecedented opportunity to enhance health status by delivering real-time interventions which have the potential to extend the reach of treatment to a patient's own environment, thereby: i) transforming patient experience and how patients engage with services; ii) improving the efficiency and co-ordination of care; and iii) supporting people to self-manage their health and wellbeing.

Supported by a 2-year DPFS grant, we have developed a digital intervention (Actissist) that delivers a theoretical, evidence-based psychological treatment for psychosis. Real-time delivery of theoretically-informed and evidence-based strategies allows for early detection of clinical deterioration and timely, personalised treatment. Grounded in the cognitive model of psychosis, Actissist targets five key psychosis risk factor domains shown to predict early psychosis relapse: expressed emotion (especially perceived criticism), socialisation, substance misuse, psychotic symptoms and medication non-compliance. For each of these risk factors, relapse rates increase 2-4 fold (Alvarez-Jimenez, Piede, Hetrick, Bendall, Killackey, Parker & Gleeson, 2012). Actissist has many benefits: it is unconstrained by the limitations of existing treatment settings; serves as a conduit for interventions anytime in almost any location and facilitates users' self-management at point-of-need in one's own environment, thereby empowering people to make informed treatment choices by way of opportunities to modify behaviour directly via a trusted and ubiquitous interface (smartphone). This approach holds several other advantages over conventional treatment: i) cost efficient; ii)

reduces recall bias and generalisation of problems that often occurs when patients are asked to recall their symptoms over the preceding weeks/months, improving validity of symptom reporting; iii) it allows the content of symptom and behaviour change to be assessed; iv) increases the likelihood that 'homework' (integral to the success of psychological interventions) is completed; v) patients can self-initiate use with the app, providing the flexibility to engage with treatment as required (rather than needing to wait for clinic appointments or clinician visits); and vi) overcomes the stigma associated with accessing mental health services (a major barrier to mental health service attendance).

We have systematically demonstrated the safety, feasibility and acceptability of delivering a 12-week digital intervention using smartphone technology as follows: i) 24 patients used the app for 12-weeks; ii) the 'accept' milestone for compliance, pre-defined as 50% of the sample completing 33% or more of items was exceeded (actual achieved=75% of participants), as was the 'target' milestone for compliance pre-defined as 50% of the sample completing 50% or more of items (actual achieved=63% of sample); iii) the proportion of compliant participants was comparable to people completing either face-to-face CBT or computerised-CBT; iv) uptake was higher and drop-out lower than face-to-face and computerised-CBT; v) no reported safety issues or treatment withdrawals; vi) recruitment completed ahead of schedule, demonstrating engagement of all stakeholders to participate in, and willingness of participants to be randomised to, a trial of this nature (further highlighted by the fact that 63% of eligible patients referred to the trial proceeded to randomisation); vii) significant improvements in psychotic and mood symptoms at the end of treatment; viii) high rates of acceptability and subjective benefit of the intervention to patients (90% participants said they would recommend the app to others in a similar position) and overall satisfaction with digital interventions expressed by staff (see supplementary supporting evidence document). Furthermore, even in our small pilot sample, we found statistically significant improvements in key psychotic post-treatment outcome measures for those in the Actissist group, relative to an active control condition, post-treatment.

Aims and Objectives

We propose to build on our work by: (i) enhancing and further personalising Actissist to increase user engagement; (ii) conducting a fully-powered efficacy study in order to examine whether a real-time digital intervention plus TAU is superior to routine symptom monitoring plus TAU using an analysis that allows the intervention to be updated (and therefore remain at the forefront of technology) during the course of the trial.

Other objectives are to: i) explore whether the intervention has added benefit over routine symptom monitoring on a range of other clinical and functional outcomes (e.g. quality of life, social functioning); ii) refine the Actissist app; iii) evaluate the acceptability of the Actissist app in order to continue to refine and improve the usability and functionality of the app; iv) explore organisational solutions and develop a business strategy to embedding digital interventions into the healthcare pathway.

2.0 STUDY DESIGN

We will use a mixed methods approach following the Medical Research Council's (MRC) framework for developing complex interventions. We have chosen to use both qualitative and quantitative methods to assess the aims of our study to ensure that participants views are adequately captured. In developing our concept/study design, we have combined information from research with service users (e.g. information gathered from ClinTouch and Actissist proof-of-concept study participants), expert academics, clinical academics and NHS senior Trust management (Professor Damien Longson, Dr Remy McEnvoy). The study will be conducted in three distinct but related phases. Phase 1 will involve study set up (including establishing an Expert Reference Group and joint Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC) to consult into the study throughout the life of the project) and refinements to the app software based on feedback gathered in Actissist 1. Phase 2 will be enhancing the look-and-feel of the app and evaluating the app in a randomised controlled trial (RCT) to test efficacy in a fully powered trial. At the end of the final follow-up assessment time point these participants will be invited to take part in an exit interview to assess usability and acceptability of the app. People who refuse to participate in the trial of the software and who drop out of the study will also be invited to take part in an exit interview. The final phase will involve data analysis, dissemination, and discussion with UMIP regarding potential downstream and commercialization opportunities of the software. The entire study will run for 36 months including preliminary phases and write up.

The starting point is the Actissist software developed and validated in the DPFS project (Actissist 1). We will improve the look-and-feel of the software and refine the protocols in response to user-feedback; conduct a fully-powered, single-blind RCT with allocation to either Actissist + TAU or ClinTouch + TAU to evaluate the benefit of Actissist over routine symptom-monitoring. We have chosen an efficacy trial as we have established proof-of-concept and will follow MRC guidelines for developing complex interventions. In refining the software and clinical protocol, we have engaged service users, gathered detailed qualitative feedback from Actissist 1 study participants, and engaged the NHS by convening groups of staff/Trust management. The project will run over three phases that build sequentially with

clear stopping milestones, with an in-built interim recruitment milestone during the RCT to ensure recruitment is on track as planned.

Phase 1. App refinements (Months 1-5). Protocol and software refinement; user engagement; database development; Expert Reference Group (ERG) established and one meeting held. The objectives of this phase are to: 1. refine content and protocol following stakeholder feedback gathered in Actissist 1; 2. beta-test acceptability and usability in 5 NHS/University staff members over 1-week; 3. build the study database; 4. establish an ERG ready to meet quarterly over the life of the study and to have met once before the milestone end; 5. establish a joint Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC).

Design/participants: Based on qualitative feedback in Actissist 1 and from ongoing stakeholder consultation, we will refine the Actissist app to meet the needs and expectations of users in the longer-term targeted at usability and personalisation. We will beta-test the updated software with 5 stakeholders who will be interviewed at the beginning and end of the test period. For example, beta-testers will be followed up at a time and location mutually convenient for both the researcher and participants and will be asked about the benefits and problems of using the app, views about the user interface, any omissions in the intervention, positive/negative impact of the app in managing mental health and areas for improvement. The software will be developed for the Android operating system initially. System prototypes will be produced in development iterations, reviewed by the ERG and research team who will provide feedback on the user interface, software performance and usability, which will be incorporated into each iteration of the system. Emphasis will be placed on data security. There will be no web pages (or any other server based resource) associated with Actissist or ClinTouch (control condition) accessible to patients.

Phase 2. Randomised Controlled Trial (RCT). (Months 6-33)-with an in-built interim milestone at the request of the MRC (Months 6-12) and a service user and staff survey. The aims of this phase are to 1. Deploy Actissist and ClinTouch apps and evaluate efficacy on symptom scores and other clinical/functional outcomes and user acceptability 2. ongoing software refinement and enhance the look-and-feel of the app following user feedback; 3. data entry management and completion.

Design: Randomised, single-blind, controlled, efficacy trial. Qualitative exit interviews with study participants, analysed using thematic analysis.

Method: Patients will be recruited across secondary services in North West England and will be randomised (using SealedEnvelope.com) to Actissist + TAU (n=85) or ClinTouch + TAU (n=85) who will use the software 6 days/week for 12-weeks alongside TAU. Participants will receive training in using the software, which will be pre-loaded on a loaned Smartphone or downloaded on a participant's own Smartphone. A researcher will also help participants set treatment goals at the software training session so that participants can work towards a pre-specified goal throughout the intervention period. At end of treatment, 12-weeks post-randomisation and 24-weeks post-randomisation, a researcher blind to group allocation will collect outcome data (e.g. symptoms, functioning, quality of life, empowerment), which will be managed on a statistical database. Clinical participants will be reimbursed (£20) at each assessment point and for any qualitative interviews they take part in. The project officer or another member of the research team will phone, text or email (depending on participant preference) participants at weeks 1, 2, 4, and 8 to check the app is working smoothly and remind participants to charge the device, alert the participant to the receipt of the mARM survey (in weeks 4 and 8), and in week 11 to establish a date for the researcher conducting the follow up assessments. Safety concerns will be managed in close consultation with care co-ordinators. Qualitative interviews will be conducted with purposefully selected participants (n >20) after the 12 week post-randomisation assessment, and with around 15 Trust staff whose client's participated in the trial to explore acceptability and usability of Actissist 2.0. Over a 19-month recruitment period, 170 consenting early intervention psychosis patients recruited from NHS Trusts across the North West of England who express an interest and are able to give informed consent will be randomised to TAU plus Actissist (N=85) or TAU plus ClinTouch (N=85). Randomisation will be conducted using an independent online randomisation tool (www.sealedenvelope.com), according to a standard operating procedure developed by Emsley, the project statistician.

Clinicians will identify and approach patients to invite them to participate in the study. Potential participants will be given the participant information sheet and the opportunity to ask any questions they might have before being offered 24 hours to consider participation. The participant information sheet will explain the difference between Actissist and ClinTouch. Participants will be reminded to seek advice from someone they trust before making a decision about whether they would like to participate in the study. The study will also be supported by the local Clinical Research Network (CRN), so clinical studies officers (CSOs) will also approach patients about the study.

An additional route for recruitment will be referral of individuals exiting other studies operating within the same Trusts as Actissist whose clinical characteristics reflect the inclusion criteria for Actissist, specifically having experienced a first episode of psychosis within the past 5 years. Specifically – the Cognitive Approaches to Combatting Suicidality (CARMS); this is a study also sponsored by the University of Manchester that has received Ethics approval (ref: 17/NW/0089).

These potential participants will have already signed an item on the consent form for CARMS to state that they are happy to be approached about taking part in other research studies they may be eligible for. Potential participants referred to the Actissist study via CARMS will have fully completed their trial period on CARMS before joining Actissist to ensure that they are not receiving two experimental psychological interventions simultaneously.

Referrals from CARMS to Actissist: To ensure that potential participants do not feel coerced into taking part in Actissist, the researcher arranging the final follow up assessment for CARMS will introduce the Actissist study and ask if it might be something they would be interested in taking part in. If it is, the researcher will outline over the phone the information in appendix 2 of the CARMS Participant Information Sheet (PIS) 1, which explains that their data (which will be identifiable) will be shared with the Actissist team. This document will be discussed alongside the Actissist Participant Information Sheet (PIS) and its Appendix 1. The researcher will ensure that participants understand that if they provide informed consent for their data from CARMS to be used in the Actissist study, then they would only complete the assessment measures unique to the Actissist baseline assessment. The researcher will then arrange for the potential participant would like to be sent the Actissist PIS and the Actissist PIS appendix by post.

CARMS participants joining Actissist will sign the CARMS Consent form Appendix 2 to say that they agree for their data (which will be identifiable) to be used by Actissist. In order for Actissist to receive this data, the participant will need to also sign the corresponding item on the CARMS Consent Form Appendix 1.

Referrals from Actissist to CARMS: The process of referral would mirror the steps set out in the previous paragraph. The researcher arranging the final follow up assessment for Actissist will introduce the CARMS study and ask if it might be something they would be interested in taking part in. If it is, the researcher will discuss over the phone the CARMS Participant Information Sheet (PIS), Appendix 1 of the CARMS PIS and Appendix 2 of the Actissist PIS. The researcher will ensure that participants understand that if they provide informed consent

for their data from Actissist to be used in the CARMS study, then they would only complete the assessment measures unique to the CARMS baseline assessment. The researcher will arrange for the potential participant would like to be sent the CARMS PIS and the CARMS PIS appendix by post.

Actissist participants joining CARMS will sign the Actissist Consent form Appendix 2 to say that they agree for their data (which will be identifiable) to be used by CARMS. In order for CARMS to receive this data, the participant will need to also sign the corresponding item on the CARMS Consent Form Appendix 1.

Service user and staff surveys. There is limited evidence regarding UK smartphone ownership rates in individuals with early psychosis and mental health care staff and even less regarding what staff and service users actually think about receiving a smartphone app for psychosis. In qualitative studies during the proof-of-concept trial, we identified specific facilitators and barriers to use and components staff and service users would want to see in an app. However, due to the limited number of participants recruited in qualitative research, it was not possible to generalise this information to staff and service users as a whole. Therefore, two surveys have been developed in order to explore whether the findings obtained in the qualitative studies exist on a larger scale. This survey (EMIS) will be distributed to both service users in the Actissist 2.0 trial and individuals who are not participating. Therefore, a separate participant information sheet and consent form has been created for individuals not taking part in the trial. Additionally, the staff survey (EMIS-CV) will be administered to the relevant stakeholders in both primary and secondary health care service settings. Like recruitment for the full Actissist 2.0 trial, recruitment for the survey components will be facilitated through attendance at NHS team meetings and via Clinical Studies Officers. We anticipate a minimum number of 300 responses to the EMIS (including 170 trial participants) and 300 responses to the EMIS-CV.

To facilitate achieving the minimum number of responses we aim for with these two surveys we will also make the EMIS and EMIS-CV available online via the University of Manchester's approved survey hosting platform. Potential survey respondents will be directed to the web surveys' online information explaining what the survey is about. If the participant wishes to complete the survey they will first be asked to answer of screening questions to confirm eligibility; for service users the questions will establish that they are 16 years or older and have experienced an episode of psychosis, for staff the screen will confirm that they have experience of working in a professional capacity with clients who have experienced

psychosis. On fulfilling these criteria the individual will proceed to the relevant survey. For service users, on completion and exit from the survey they will be offered the opportunity to send their email address to the study Project Officer to be entered into a prize draw; this will not be offered to mental health professionals. Both service users and mental health professionals will be offered the opportunity to send their email address to the Project Officer if they should wish to receive a summary of the findings at the end of the study. Email addresses for the prize draw and for receipt of study findings will be held in separate secure databases to the survey responses so that responses may not be linked to individuals.

Additionally, for the service user online survey we will broaden the eligibility for respondents: they will not have to be within 5 years of a first episode of psychosis or currently under the care of services. Experience of psychosis, having received a diagnosis of psychosis or had treatment in the past for psychosis will be acceptable.

Posters about the study and inviting service users and NHS staff to respond to the survey have been developed. Paper versions will be posted in the University of Manchester notice boards in departments where service users and staff may see them. Electronic versions of the posters will be uploaded to the Actissist 2.0 website, relevant research websites (e.g., MQ Mental Health), and linked to in project social media posts as well as other social media sites (e.g., Reddit).

Phase 3 (Months 33-36) Data analysis; dissemination; strategy and business planning.

Objectives: complete data analysis; dissemination will occur as detailed in the communications plan (attached); develop a strategic plan encompassing an analysis of the regulatory requirements for CE Mark and IP position, and review of potential partners/licensees to market. Commercial opportunities for Actissist will include a comprehensive analysis and monitoring of the prior art throughout the project's duration, development of an appropriate IP strategy and, if necessary, a preliminary assessment of freedom to operate. Market research identifying market needs for this technology and possible business models for commercial exploitation will be conducted.

Sample size calculation.

Phase 1: Involves approx. 5 staff members of either a local NHS Trust or University of Manchester to beta-test the Actissist app for 7 days and provide feedback on the usability and functionality of the app.

Phase 2: 170 participants recruited over 19 months. 63 per group will have 80% power to detect an effect size of 0.4 (6 points on the PANSS with an SD of 15), based on a two-group t-test with a 0.05 two-sided significance level, assuming a baseline-endpoint correlation of 0.6. Allowing 20% loss to follow-up, in order to maintain 80% power we will recruit 85 patients per group (N=170). The SD, correlation and attrition rate are based on figures from Actissist 1.0. Randomisation will be 1:1, and stratified by service (early intervention vs community mental health).

Service user ehealth and mHealth Interest Survey (EMIS). We anticipate recruiting upwards of 300 participants (including 170 full trial participants) to complete the EMIS in order to obtain a representative sample.

eHealth and mHealth Interest Survey (EMIS-CV). We anticipate recruiting upwards of 300 participants to complete the EMIS-CV in order to obtain a representative sample.

Qualitative interviews with non-participants/early withdrawers. Individuals who decide not to participate, or who withdraw early from the intervention, will be invited for a one-off interview to explore their reasons for not participating. It is not possible to accurately predict the number of service users who decide to participate in this phase; however, we expect a minimum number of 5 participants.

Phase 3: N/A

Therefore, in total, we expect the sample size of the overall project to be N=605 (170 trial plus EMIS; 130 EMIS-only); 300 EMIS-CV; 5 non-participant/early withdrawal interviews).

Inclusion criteria.

- (a) Phase 1: Staff from secondary care mental health services in local NHS Trusts and University of Manchester staff who provide informed consent. We shall include a range of professions with different levels of experience/expertise to ensure a range of views about the usability and functionality of the app are gathered.
- (b) Phase 2:
Full trial: i. meet ICD-10 criteria for a schizophrenia-spectrum diagnosis (ICD codes F20, F22, F23, F25, F28, F29) as confirmed by the treating clinician or Early Intervention for Psychosis Service entry criteria, operationally defined using the Positive and Negative Syndrome Scale (PANSS) and/or the psychosis transition criteria of the Comprehensive Assessment of At-Risk Mental States; ii. in contact with mental health services; iii. within 5 years from onset of first psychotic episode,

deemed by the treating clinician; iv. meet a criterion level of positive symptoms severity, indicated by a score of >3 (symptom present) on any PANSS positive item and a score of >3 (symptom present) on any PANSS negative or PANSS general items; v.. English speaking; vi. aged 16 years or older; vii. capacity and willingness to provide informed consent; viii. not currently participating in another trial.

Service user eHealth and mHealth Interest Survey (EMIS): i. experience of psychosis (within 5 years of initial episode); ii. in current contact with either an early intervention service or a secondary care mental health service; iii. English speaking; iv. aged 16 years or older; v. capacity to provide informed consent.

eHealth and mHealth Interest Survey - Clinician Version (EMIS-CV): i. experience of working with individuals experiencing early psychosis; ii. current employment in primary or secondary mental health services or the third sector (e.g. charity).

Qualitative interviews with non-participants/participants who have withdrawn: i. early psychosis (within 5 years of initial episode); ii. in current contact with either an early intervention service or a secondary care mental health service; iii. English speaking; iv. aged 16 years or older; v. capacity to provide informed consent.

Exclusion criteria.

- i) Anyone with psychosis not in contact with a NHS mental health service.
- ii. Anyone less than 16 years old at the point of recruitment.
- iii) Anyone not capable of giving informed consent.
- iv) Non-English proficient.
- v) Score <3 on all PANSS positive, negative and general items.

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.

Changes to participants' care team.

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

Research procedures.

Staff involvement.

Staff members will be recruited through secondary care mental health services in local NHS Trusts and/or through the University of Manchester. Staff will be identified through managers and via presentations at staff team meetings. Where staff are invited to take part in beta-testing and feedback following beta testing they will be given an information sheet. They will be advised that they do not have to take part and if they choose not to take part this will not affect any other professional duties that they carry out. They will sign a consent form before being interviewed.

Service user involvement.

Participants across all phases will be recruited within 5 years of an initial episode of psychosis primarily through early intervention services or community mental health teams across the North West of England. The key worker will identify and approach patients to invite them to participate in the study. If a patient expresses an interest in participating their preferred contact details will be passed on to the researcher by the referring clinician. An additional route for potential recruits will be referral to Actissist from studies operating within the same Trusts whose participants have completed their involvement with that research study and who may meet the key eligibility criteria for Actissist of experiencing a first episode of psychosis within the previous 5 years. These individuals will be identified by the study research team and offered an opportunity to find out more about participating in Actissist.

A trained researcher will then meet with the potential participant at a time or place convenient for them to briefly ask about their experiences to identify whether the person is likely to meet the eligibility criteria. If the service user is suitable, they will be asked to consent to the study and complete the baseline assessment. After the participant has consented and completed the baseline assessment, a trained researcher will arrange to meet with the participant to take them through the app functions and to invite them to set some goals to work towards throughout the intervention period.

The Actissist software will emit a pseudo-random alert 3 times a day, 6 days a week over 12 weeks with branching items targeting key relapse factors in FEP (medication non-adherence, symptoms, socialisation, perceived criticism and substance misuse). Participants will choose either to use a loaned smartphone which is pre-loaded with the app or the researcher may download the application onto their own handset. For those participants randomised to the ClinTouch (control) condition, for parity with the demands of the Actissist condition participant's will submit one and a half data points daily with 10 branching items covering

positive psychotic symptoms, anxiety and mood as validated in a previously validated MRC study (PI: Lewis). As each full data point is collected over two separate alerts, this equates to receiving three alerts every day. As with ACTISSIST, participants will choose either to use a loaned smartphone which is pre-loaded with the app or the researcher may download the application onto their own handset. Both the active and control condition apps will be used 6 days a week over 12 weeks.

In the unlikely event that a participant loses a smartphone, the participant will be provided with a replacement; if the participant loses the replacement smartphone, they will be offered one further replacement. If participants lose both replacements, they will not receive a further replacement smartphone; however, in this situation, participants would still be given the opportunity to take part in the follow-up assessments.

At the participant's final assessment for the trial, 24 week follow up, the researcher will issue him/her a debrief document. This document is intended to explain the purpose of the study, act as a signpost to health apps available online approved by the NHS and also includes links to other online resources, e.g., TED talks and blogs that were included within the Actissist app for participants to explore. The document also explains how participants can find out about other research projects that they might be interested in taking part in in the future.

For participants that have opted to receive information in the future about Actissist 2.0 on the Future Contact form they will receive a quarterly newsletter.

Participant payment.

Some participants in the Actissist and ClinTouch conditions will choose to borrow a smartphone, which will be loaded with £30 of phone credit to support data connectivity to last the duration of the study. All participants will be reimbursed £20 for completing assessments (total of £60 per participant x 3 assessment occasions). This is to compensate for their time and contributions. In order to ensure that we are covering the data usage costs associated with a participant using their own handset we will remunerate participants with £10 every month (total of £30), if such costs are incurred. We will also pay for their travel costs, if such costs are incurred.

We will pay members of the Expert Reference Group (ERG) £20 per ERG meeting to attend quarterly ERG meetings for the duration of the project. This is to compensate for their time and contributions. We will also pay for their travel costs, if such costs are incurred.

Staff payment.

NHS health staff will not be paid directly to participate in the study. As is usual practice, time spent will be reimbursed to their employing NHS Trust via service support costs agreed by the local Clinical Research Network (CRN). University staff will not be paid directly to participants but study involvement will be agreed with the employees line manager.

3.0 OUTCOMES AND MEASURES

Primary outcome: psychotic symptoms measured by PANSS total score.

Secondary outcomes: symptom distress, mood, functioning/social functioning; drug use frequency; perceived criticism; medication adherence; user-empowerment; well-being; quality of life; recovery; service and health economic measures. Treatment domains will also be measured via daily ambulatory-monitoring outcome assessment questions in the Actissist group. We will also collect demographic information and mobile and app usage rates.

A trained research assistant will undertake the following participant assessments in both Actissist and ClinTouch groups at baseline, 12 weeks and 24 weeks post-randomisation. Measures have been selected which map directly onto hypothesised mechanisms of change as well as known predictors of relapse.

Primary Outcome Measure

1. Mental Health Status: The Positive and Negative Syndrome Scale, PANSS, (Kay et al, 1987) is a valid and reliable 30-item rating scale subdivided into three symptom categories: positive symptoms (e.g. Delusions, hallucinatory behaviour), negative symptoms (e.g. blunted affect, emotional withdrawal), and general symptoms (e.g. anxiety, tension).

Note: Participants that may join Actissist having recently completed involvement in a research study that included the PANSS assessment at final follow up, plus additional questionnaire measures in common with the baseline for Actissist, will be advised that **with their written consent**, the Actissist team will request these data from their final follow up on previous study. If the participant agrees, then only the additional secondary outcome measures in the following section will be completed.

Secondary Outcome Measures

We will also assess changes in symptoms, substance use, emotional distress, recovery, quality of life and well-being, service / app engagement and health economic indices.

- (i) *Mental Health Status:* The Psychotic Symptoms Rating Scales (PSYRATS; Haddock et al., 1999) is a well-validated assessment of the frequency and intensity of hallucinations and delusion in people with psychosis. The PSYRATS is typically administered as a semi-structured interview. It is typical to administer the PSYRATS items within the PANSS semi-structured interview to aid in the scoring of the PANSS items P1 Delusions and P3 Hallucinatory behaviour, consequently the (formal) administration of this measure will not necessitate additional participant time. The Calgary Depression Scale for Schizophrenia (CDSS; Addington, Addington, & Schissel, 1990) is a well validated assessment of depressive symptoms in people with psychosis. The CDSS is typically administered as a semi-structured interview. It is typical to administer the CDSS items within the PANSS semi-structured interview to aid in the scoring of the PANSS item G6 Depression, consequently the (formal) administration of this measure will not necessitate additional participant time. The Personal and Social Performance Scale (Morosini, Magliano, Brambilla, Ugolini & Pioli, 2000) is a brief interview measure of social functioning thought to be easier to administer than other traditionally used measures. Excellent psychometric properties were reported in the original validation article. Perceived criticism scale (Hooley & Teasdale, 1989) is a measure of perceived criticism by a significant other. This scale was adapted by Schlosser and colleagues (2012) to create the perceived criticism and perceived warmth scale. Seven items are rated using a 1 (not at all critical) to 10 (very critical) scale. Previous research suggests that the PCPW scale has good predicative validity and is not correlated with current symptoms of depression or anxiety. It takes approx. 3 minutes to complete. Recovery will be measured using The Questionnaire about the Process of Recovery QPR (Law, Neil, Dunnn & Morrison, 2014) is a validated measures of recovery in psychosis. The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS; Tennant, et al., 2006) is a measure of well-being and has been validated with users of mental health services.
- (ii) *Substance use measures:* Time Line Follow Back for drugs and alcohol (TLFB; Sobell & Sobell, 1992) is an assessment method that obtains estimates of daily alcohol and other drug use and has been evaluated with clinical and nonclinical populations. Participants provide retrospective estimates of their daily cannabis use over a specified time period (3 months). The TLFB will be administered at baseline, 12 weeks and 24 weeks post-randomisation. Additionally, participants will be asked to complete the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST; World Health Organisation Working Group, 2002) at baseline, 12 weeks and 24 weeks post-randomisation to identify changes in general drug after the

intervention period. To characterise the sample, participants will be asked to complete the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) at baseline. The AUDIT contains 10 self-report items about alcohol-related experiences and has been well validated for use in clinical research. The original AUDIT records alcohol consumption over the past 12 months; however, this is regularly amended in trials to 3 months for the purposes of follow-up assessments. Therefore, the AUDIT will be administered to measure alcohol consumption over the past 3 months at baseline, 12 weeks and 24 weeks post-randomisation to identify any changes in alcohol consumption. The Cannabis Use Disorders Identification Test-Revised (CUDIT-R; Adamson et al., 2010) will be used to measure cannabis use over the past 3 months at baseline, post-treatment and follow-up. The Drug Use Disorders Identification Test-Extended (DUDIT-E; Berman et al., 2007) will also be administered at baseline, 12 weeks and 24 weeks post-randomisation for cannabis use only to explore perceptions of drug use and treatment readiness.

- (iii) *App Engagement*: A quantitative feedback questionnaire will be given to service users at the end of the study to collate their opinions on the usefulness of the technology. The user version of the Mobile Application Rating Scale (uMARS; Stoyanov, Hides, Kavanagh & Wilson, 2016) is a reliable method to assess the quality of mobile health (mHealth) apps and will measure the quality of both the Actissist and ClinTouch apps. The Quantitative Feedback Questionnaire (QFQ; Ainsworth et al., 2013) was developed to assess the acceptability and feasibility of utilising the ClinTouch app within a service user sample. The QFQ consists of 22 items pertaining to the integration of the technology into the daily routine and methodological reactivity and a further 10 questions enabling the participant to give their views on using the app they were allocated to. The mobile Agnew Relationship Measure (m-ARM; Berry et al. in press) will measure therapeutic alliance with the apps. Whilst all other measures will be paper-based, the m-ARM will be delivered at two points during the intervention period (month 1 and month 2) via a text message link. This will allow participants to complete two assessments of therapeutic alliance on a secure University of Manchester-managed survey site without the burden of a researcher visiting them to complete the assessment at two different timepoints. Only participants' unique study ID will be entered into the m-ARM survey database. At the end of the intervention period these data will be analysed by a PhD student member of the research team using factor analysis to shorten and refine the measure. This analysis will help to establish 'user acceptability' of the app and inform its further development, e.g., improving personalization.

- (iv) *Health Economics*: Euro-QoL Five Dimension (EQ-5D-5L; EuroQol group, 1990) is a measure of health status and preference for different health status. It is a self-rated descriptive system with five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Patients respond by describing they have no problems, slight problems, some problems, severe problems, extreme problems or that they are unable to do the activity. While the EQ-5D-5L is very commonly used in the UK context, its sensitivity and appropriateness in people with schizophrenia has been questioned (Brazier et al., 2014). The Client Service Receipt Inventory (CSRI; Beecham & Knapp, 2001) measures service utilisation, income, accommodation and other cost-related variables.
- (v) The Empowerment Rating Scale, ERS, (Rogers et al, 1997) is a 28-item scale designed to measure empowerment in users of mental health services. It takes around 15 minutes to self-administer. It shows good internal reliability (Cronbach's Alpha = 0.86). Item examples include, 'I am often able to overcome barriers,' and, 'I have a positive attitude about myself'.
- (vi) The Internalised Stigma of Mental Illness Inventory (ISMI; Ritsher, 2003) is a 29-item scale designed to measure internalised stigma in individuals with mental health problems. The scale has been validated in a wide range of clinical samples, including psychosis, and has demonstrated high internal consistency, test-retest reliability and construct validity.
- (vii) The eHealth and mHealth Interest Survey (EMIS) has been developed by the research team and is based on the findings obtained from the qualitative studies administered in the proof-of-concept trial. Service users in the Actissist 2.0 trial will be asked to complete the survey during the app set-up visit to minimise burden. Service users who are not in the Actissist trial will be asked to complete the surveys and then return them to the research team via their care coordinator or the CSO. Alternatively, a link to the survey will also be made available for participants to complete the survey online using the secure RedCap website. The survey contains 55 questions relating to technology ownership, use and interest and takes approximately 20 minutes to administer.
- (viii) The eHealth and mHealth Interest Survey - Clinician Version (EMIS-CV) has been developed by the research team based on findings obtained in focus groups with staff working in early intervention services in the proof-of-concept trial. Staff working in both primary and secondary health care services will be asked to complete either an online or paper-based version of the EMIS-CV. The survey contains 26 questions to elicit staff perceptions of service user technology ownership and engagement and

views towards the use of digital tools for early psychosis and takes approximately 8 minutes to administer.

(Total administration time - approx. 90 minutes).

Qualitative measures.

Individual qualitative interviews will comprise semi-structured in-depth interviews following an interview schedule. Staff will be asked to provide qualitative information following beta testing in Phase 1 about the usability of the app and a further sample of around 15 Trust staff whose client's participated in the trial will be interviewed to explore acceptability and usability of Actissist 2.0. Following the 12 week post randomization follow up assessment, >20 exit interviews (across both groups) with trial participants will be performed. A purposive sample will be sought to ensure maximum variation of sample and to elicit a broad range of views. This will include a balance of participants who have had a good outcome, those who have dropped out of the intervention or who refused participation, and control participants (specific interview guides have been developed for each group). The invitation to participate in a qualitative interview will be offered to the participants sampled for this stage of the study by a blind member of the research team; a mutually convenient date/ time will be agreed with the participant for the researcher to conduct the exit interview. Interviews will explore participants' experiences and expectations of the app, participants' views on the content, duration and intensity of the app (particularly focusing on perceptions of usefulness, engagement with the technology and facilitators/barriers to implementation), the role of mHealth apps within psychiatric management and self-management, perceived benefits of the app, disappointments/concerns and ongoing support needs. Participants who decline the trial will be invited to have a single time-point interview to explore views and experiences of current care and potential use of technologies such as mobile phones in mental health care. Interviews with participants who decline to participate in the trial, but would still be willing to take part in an interview, and with participants who withdraw early from the trial will be conducted at a time and place convenient for the participant or via the telephone, depending on participant preference.

3.1 Software systems, interface and compliance with NHS security standards.

The three general principles of information security (confidentiality, integrity and availability) will be followed in the implementation of Actissist and ClinTouch. All data transmitted to and from the app 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 is downloaded from the Actissist or ClinTouch sites, these data will be securely encrypted with a pass phrase of appropriate length and complexity. Data transfers are secured by using standard web security protocols (TLS). 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 be lost or stolen and removes the need for personal data storage on the device. The purpose of the server in this case is secure data storage.

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 (AES-256). We will also recommend that participants set a passcode to access their smartphone. All smartphones provided by the research team will require a passcode for access. By using the ClinTouch real-time data capture capability, we will be minimising the storage of confidential data on the smartphone as data will be wirelessly uploaded to a secure server (keeping identifiable data stored on the phone to a minimum). All participants recruited in the study will give their informed consent, and this will include the risks of data security. These measures should be sufficient to prevent unauthorized data access, should the phone be lost or stolen.

4.0 Intervention

Actissist Intervention. The Actissist intervention is grounded in the cognitive maintenance model of psychosis, which proposes that cognitive appraisals contribute to the emergence of unhelpful beliefs and influence the interpretation of psychotic experiences. Specific functions of the app are informed by cognitive behaviour therapy (CBT) content described in various published academic works and by the views and insights from research with service users and EIS clinicians, expert clinical academics and software engineers during the Actissist proof-of-concept study. The Actissist app targets five domains: perceived criticism; socialisation; cannabis use; paranoia; and distressing voice-hearing. Medication adherence is monitored on a weekly basis. The Actissist app works as follows: the app emits an alarm prompting participants to access the app at 3 pseudo-randomised time points per day, 6 days a week between the hours 10 am to 10 pm (or at the patient's preferred time) for 12-weeks alongside usual treatment. The prompts serve as a reminder to use the app and requests that the participant accesses one/more of the target treatment domains (if applicable). Participants can either snooze (for up to 30 minutes) or decline interacting with the app at any given alarm alert. Participants can also self-initiate use, providing them with the flexibility to engage with the app as and when required. Participants complete a series of self-assessment questions that are structured as question-answer exchanges, which are

then followed by normalising messages and cognitive and behavioural strategies for managing distressing experiences. There are multiple messages associated with each branched response to minimise boredom and repetition within the app. In addition to the self-assessment questions, participants can access multi-media material, including audio relaxation and mindfulness exercises, patient recovery stories, an open diary, mental health fact sheets, external links to web-related content (e.g. Technology, Entertainment and Design (TED) talks, useful websites), and a graphical summary of data points entered for each domain accessed. The multi-media material is contained within the app. At its simplest, the multi-media repository can contain a list of URLs to content on the web, and so the management of this section of the app is akin to managing a list of favourites or bookmarks in a web browser. Managing this type of content requires a similar level of expertise to managing a Facebook page, for example. Users can also customise the aesthetics of the app. During the initial consultation with the researcher at the app set-up session, patients will be trained on using the app and how to navigate through the app. Akin with CBT principles, the researcher will invite each participant at the app set-up session to choose a goal to work towards over the intervention period. Progress towards the goal will be monitored and reviewed fortnightly within the app.

The multi-media material (MMM) is contained within the app, and the app will provide an interface for adding, modifying and deleting RPMM content. At its simplest, the MMM can contain a list of URLs to content on the web, and so the managements of the RPMM are akin to managing a list of favourites or bookmarks in a web browser. The MMM will also allow multi-media content from the smartphone's local storage to be added such as photos or music. We envisage that managing this type of content will require a similar level of expertise to managing a Facebook page.

ClinTouch (control) condition: ClinTouch triggers, collects and wirelessly uploads symptom and mood data to a server 6-days/week for 12-weeks. Participants indicate the degree to which they agree/disagree with 14 symptom-statements since the last entry. As per the Actissist condition, mobile handsets will emit an alarm at 3 pseudo-random times of the day, with a 'snooze' option available if participants are occupied.

A research assistant will train participants in how to use the software. Software will be pre-loaded on a loaned smartphone or downloaded on the participant's own smartphone. Safety concerns will be managed in close consultation with participants' care co-ordinators and emergency contacts are clearly available on both apps.

For both conditions, a trained research assistant will train participants in how to use the software. For both Actissist and ClinTouch, participants will view written 'in-app' instructions and a printed hard copy of instructions on how to use the app. Software will be pre-loaded on a loaned smartphone or downloaded on participant's own smartphone. The project officer will phone, text or email (depending on participant preference) all participants at weeks 1, 2 4, and 8 to check the app is working smoothly and remind participants to charge the device, alert the participant to the receipt of the mARM survey (in weeks 4 and 8), and in week 11 to book a date for follow-up assessments. Concerns will be managed in close consultation with participants' care co-ordinators and emergency contacts will be clearly available in the menu options on both apps.

5.0 Data collection, management and analysis

Data Collection Methods

All outcome measures will be administered at baseline and subsequently at 12 weeks and 24 weeks post-randomisation 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. Accuracy in administering and scoring the PANSS at baseline and at the 12 and 24 week follow up stage is critical in order to detect any change that might be attributable to the app the participant used. To ensure that important details aren't missed, the PANSS assessments will be digitally recorded using an encrypted device to enable our research team to review participants' responses when scoring the assessment. Recordings will be downloaded to a secure server on return to the office and deleted at the end of the study once reliability of rating has been assured. Regular training sessions including the use of 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. The option to conduct the PANSS assessment over the telephone at 12 and 24 weeks post-randomisation will be offered to participants whose circumstances may have changed since baseline assessment, e.g., they are now working. 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 (Appendix 1).

Note: for participants recruited to Actissist, who give written consent for their most recent PANSS, and other questionnaire data collected at final follow up in their previous study that is common to the Actissist baseline to be shared by their previous study team, the time taken for the completion of the baseline measures will be substantially reduced.

Protection Against Bias

Our assessment of the primary outcome will be blinded. Blindness of raters is ensured using a variety of procedures, including briefing participants prior to assessment not to disclose their allocation and data protection of randomisation information. RAs will remain blind to group allocation. An RA who did not conduct the phone set up session will conduct the follow up assessment to maintain the blind. The project officer, or a member of the research team independent to the follow up procedure, will book follow up appointments to further ensure blinding is maintained. Unblindings will be regularly monitored and recorded. Deliberate unblinding would only occur in the case of a serious adverse incident such as risk towards self/others by a participant. The statistician will be blinded during the analysis by withholding the identity of the randomised groups and only once the analysis is completed and interpreted will these be revealed. Due to the nature of the intervention, all participants will be unblinded and fully aware of their allocation to the intervention or control groups.

Randomisation Process

The randomisation process will be conducted by a remote internet based randomisation service (www.sealedenvelope.com). The allocation sequence will be developed using a computer random number generator to allocate participants on a 1:1 ratio, stratified by service (early intervention vs community mental health).

Once the eligibility of a patient has been confirmed and informed consent has been obtained, the researcher will assign a unique identification number to the patient and send this to the project manager. Having accessed the randomisation website, the project officer will enter only the identification number into the randomisation service, submit this information, and the next treatment allocation will be revealed on screen. Participants will then be informed of their allocation status. An email confirmation of the identification number, the allocated treatment and the date and time of randomisation is sent to the project officer. We have previous experience of using web-based randomisation in this setting, and do not anticipate any practical issues arising in this study. The randomisation list will be kept by the remote randomisation service (www.sealedenvelope.com), and kept separate to the collection of outcomes on the study database. The randomisation list will only be revealed to the researchers once all the recruitment is completed.

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.

6.0 Statistical Analysis

Quantitative Data.

The quantitative data analysis will be carried out under the supervision of Professor Richard Emsley at Kings College London. The study database is hosted on the University of Manchester's Health eResearch Centre secure server; authorised login from another university site for co-investigators is possible to remove the need for electronic transfer of data via email in password protected files. Our primary analysis will be by an intention-to-treat approach using all randomised participants and report data in line with the CONSORT 2010 Statement (Schultz et al., 2010) showing referral and attrition rates (i.e. participant flow). The primary outcome measure will be psychotic symptoms (PANSS Total Score) based on the fact that the Actissist app targets key psychosis domains and we observed a signal on PANSS total score post-treatment in our feasibility trial. Treatment effects on the primary and secondary outcomes will be estimated using standard linear regression models. No interim analysis is planned. Every effort will be made to follow up all participants in both arms for assessments, and the analysis will use, where appropriate, statistical techniques for handling missing data.

Data obtained from the EMIS and EMIS-CV will be analysed descriptively (i.e. mean scores and percentage rates of ownership and interest) by a clinical doctorate student. Additionally, the student will link trial participants' responses to the EMIS survey questionnaire to their app usage data during the intervention period and the change in their clinical outcome scores. Linking will be achieved using pseudonymised information, i.e., participants' unique study ID on the EMIS survey response form and ID on the Baseline/ 12 and 24 week time point follow up CRFs (and/or study databases for these time points) only. There will be no requirement to access files with participant identifiable information. The EMIS responses from non-trial participants and EMIS-CV responses from mental health care staff are obtained via online survey and are anonymous.

Trial participants' EMIS responses, app usage and change in clinical outcomes will be examined to understand service user smartphone and technology ownership and health app use and how this effects clinical outcomes in digital health interventions .Mental health professionals' use and confidence in using technology and smartphones and their engagement with apps for health management is explored in the clinician survey.

Qualitative data.

Qualitative data will be digitally recorded, transcribed by the research team, checked for accuracy and analysed using thematic analysis (Braun & Clarke, 2006) by the PI, research assistants and qualitative methodologist (Edge). We shall ask participants, as well as the ERG, to review and verify themes, usually referred to as 'member checking' or 'participant verification'. Additionally, clinical members of our research team (Haddock and Berry) will rigorously review the research process. This 'peer verification' process (together with member checking) is a recognised method of ensuring 'trustworthiness' of the data and subsequent findings (Gibson & Brown, 2009). Records of field notes will be maintained and reflections providing adjunctive data will be used to illuminate and justify interpretative decisions. NVivo (2012) qualitative software package will be used to support data management and analysis.

7.0 Research Governance

Project Management Group (PMG)

Operational management and governance of the study and transitions between phases will be through the Actissist Project Management Committee (PMG) comprising who will ensure that the project is delivered according to the protocol and ethical guidelines. The PMG will meet monthly and consists of the following individuals:

- Professor Sandra Bucci (Principal Investigator)
- Dr Natalie Berry (Research Assistant)
- Ms Rose Dicken (Research Assistant)
- Ms Rosa Pitts (Research Assistant)
- Dr Alyson Williams (Project Officer)
- Professor Gillian Haddock (Co-Investigator)
- Professor Katherine Berry (Co-Investigator)
- Professor Richard Emsley (Study Statistician)
- Mr Matthew Machin (Technical Lead)

The PMG will report to the wider Investigator team on a three-monthly basis. A member from the University of Manchester Intellectual Property (UMIP) division will also be invited to

project meeting on a quarterly basis. A member from the Medical Research Council (MRC) will also be invited to attend PMG meetings as required in the funding guidelines and more regularly if necessary.

Combined Trial Steering Committee (TSC) and Data and Ethics Monitoring Committee (DMEC)

Although it is not a requirement, a joint TSC/DMEC will be established in the interest of best practice. The TSC/DMEC will have access to unblinded comparative data as it accrues and monitor these data, the quality of these data, monitor adverse events and make recommendations to the PMG on whether there are any ethical or safety issues on whether the study should continue. The TSC/DMEC will meet at the outset and then annually; although, additional meetings may be arranged if required. The TSC/DMEC will consist of the following individuals:

- Independent Chair (Prof Max Birchwood)
- Clinical representative (Dr Amy Hardy)
- Service user representative (Miss Stephanie Allan)
- Independent statistician (Ms B Cundill)

Measuring Adverse Events

At each study visit, or as otherwise specified in the protocol, the PI (or delegate) is responsible for eliciting details of any adverse events (AEs) that may have occurred since the previous study visit and ensuring that these are evaluated appropriately. The Actissist research team will assess the 'relatedness' of an event in the first instance. Conclusions will be included in the event report, and this will be sent to the relevant recruiting R&I Departments (Greater Manchester Mental Health NHS Foundation Trust and Pennine Care NHS Foundation Trust) and to Prof. Max Birchwood (Independent TSC/DMEC Chair), who will also assess the 'relatedness' of an event and communicate their conclusions to the Actissist PMG. The PI will periodically (for example quarterly) perform and document a review of all adverse events occurring on the study, in order to identify any trends such as an increase in numbers or severity of events.

8.0 Ethics and Dissemination

Research Ethics Approval

Research ethics approval has been granted by the West of Scotland Research Ethics Committee (REF: 17/WS/0221).

Protocol Amendments

The views from members of the PMG will be sought on any proposed amendments to the Actissist 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 Actissist Protocol and to the ISRCTN Registry.

Consent

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

For individuals joining Actissist that have been referred from CARMS, signing Appendix 2 of the CARMS Consent form gives permission for CARMS to share their final assessment data with the Actissist research team. Additionally, Appendix 1 of the Actissist Consent form permits the Actissist team to request the final CARMS follow up assessment data. The reciprocal documents for Actissist participants choosing to join the CARMS study have also been developed. See Method, page 8.

A separate consent form will be provided for individuals who only wish to take part in the EMIS or qualitative interviews about technology use.

Confidentiality

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

- **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 Actissist. All data transmitted to and from Actissist 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 Actissist 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.

- **Software systems, interface and security compliance standards:** a range of measures is in place to help ensure the security of the Actissist and ClinTouch apps and the data generated by its users. The apps are hosted on a University of Manchester web server and has standard measures in place to prevent unauthorised access. 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 Actissist and ClinTouch currently comply.
- **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.
- **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 PI and the study RAs and Project Officer. 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 Manchester.
- **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.

Dissemination Plan

We will produce an Actissist 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 and possible book chapters. Participants will be informed of the results by being offered written and/ or face-to-face feedback.

Appendix 1

PROTOCOL FOR MANAGING DISCLOSURE OF RISK **Randomised controlled trial participants** **Qualitative study participants**

Rationale

During a session or other contact with Actissist research staff a participant may indicate an intention to harm themselves or others. Participants may also provide information to the effect that a child or other vulnerable person may be in danger. Any information of this nature **must** be acted upon.

At the beginning of each research interview/assessment the participant will be informed that what is discussed is private and confidential except if they indicate any current intention to harm themselves or others, or if they provide information to the effect that a child or other vulnerable person may be in danger. In such situations the staff member has a legal duty to report this information.

Procedure

In the case that the participant indicates current intention to harm themselves or others, the researcher must remind the participant of their duty of care to break confidentiality (as already outlined at the commencement of the interview), unless there are circumstances that would contraindicate telling the participant of the need to break confidentiality (e.g. risk to safety of staff). The researcher must then pass this information on to a member of the participants clinical care team. The immediacy of this action will be dependent on individual circumstances.

If an imminent risk is identified, immediate action should be taken and the session should change focus to the imminent threat. However, if the participant reports that they intend to place themselves or others at risk of harm at some point in the distant future, action by the researcher may involve continuing with the session in light of the information discussed, reviewing how they are feeling at the end of the session and calling a member of the care-team following this. A similar course of action should be taken if a participant reports a historic risk event, which has not already been reported to their care team (e.g. a previous suicide attempt), this will include following flowchart 3.

If the participant indicates that a child / other vulnerable person may be in danger, in addition to contacting the participants care team, the respective Child or Adult Safeguarding Team should also be contacted (see contact details below). In either case the participant should be informed that confidentiality needs to be broken and, if at all possible, will be encouraged to work in collaboration with the relevant staff member to this end.

If the identification of risk (on-going or unreported historic) occurs during a face to face contact the individual may be given the option of phoning the care co-ordinator themselves in the presence of the staff member or staying in the room whilst a call is made. Alternatively, the individual may choose to wait in a safe place such as an adjoining room (if this is possible). Based upon the telephone discussion, the researcher will follow any reasonable request made by a member of the care team.

If a risk is identified and the care co-ordinator, psychologist and / or psychiatrist are not contactable (and such a course of action is recommended by clinical members of the research team), a call should be made within the hours of 9am – 5pm Monday to Friday to the duty worker for the appropriate Community Mental Health Team. Outside of the duty

workers working hours a call should be made to the Crisis Team or if necessary accompanying the participant to A&E. Contact details are listed in Appendix 2. Once again, the researcher will act in accordance with any action plan agreed and any reasonable request made by the clinical care team. This may involve faxing information over to A&E, accompanying the individual to A&E, etc.

If risk is disclosed during telephone contact, the individual will be informed that confidentiality will need to be breached. The same plan as above will be implemented and the individual should be called back to feedback the planned actions.

In the event that the individual discloses that a child / vulnerable adult may be in danger, the Child / Adult Safeguarding Team should be contacted. In all cases where a child or vulnerable adult is thought to be at risk researchers must adhere to the trusts safeguarding policy. If it is outside of 9am – 5pm and there is considered to be imminent risk to a child / vulnerable adult the police should be informed. However, the appropriate safeguarding team should also be informed. Details of out of hours Child / vulnerable Adult Safeguarding Team services are listed in Appendix 2.

If the researcher is uncertain as to the appropriate course of action to take they should initially contact the project lead (Professor Sandra Bucci). If the project lead is unavailable, flow diagram 3 should be followed. In the unlikely event that all avenues are exhausted the worker should follow the previously outlined plan (commencing with contacting the Care Co-ordinator).

If the participant or someone else has committed a crime then it may be necessary to phone the police as soon as possible. If the client is currently harming him or herself or has done so recently, and there is a need for medical attention, it would be important to negotiate with the client that they attend hospital or that they allow an ambulance to be called. If the client refuses to seek medical attention and there is a serious (e.g. life-threatening) and immediate risk to the participant's health an ambulance should be called. If the injury is not deemed to pose a serious and immediate risk to health, the participants care team should be contacted. The mental health team or duty psychiatrist would ensure that anyone refusing medical attention was assessed under the Mental Health Act. A decision regarding the need for a compulsory admission to hospital will then be made by an approved social worker in accordance with the Mental Health Act 1983.

Ensure that you record all information and actions taken, including telephone calls and discussions with your project lead/clinical supervisor, in the participant's file.

FACTORS TO CONSIDER IF A PARTICIPANT EXPRESSES HARM TO SELF OR OTHERS

If a participant you are working with expresses ideas of harm to self or others these are important factors to consider and pass on:

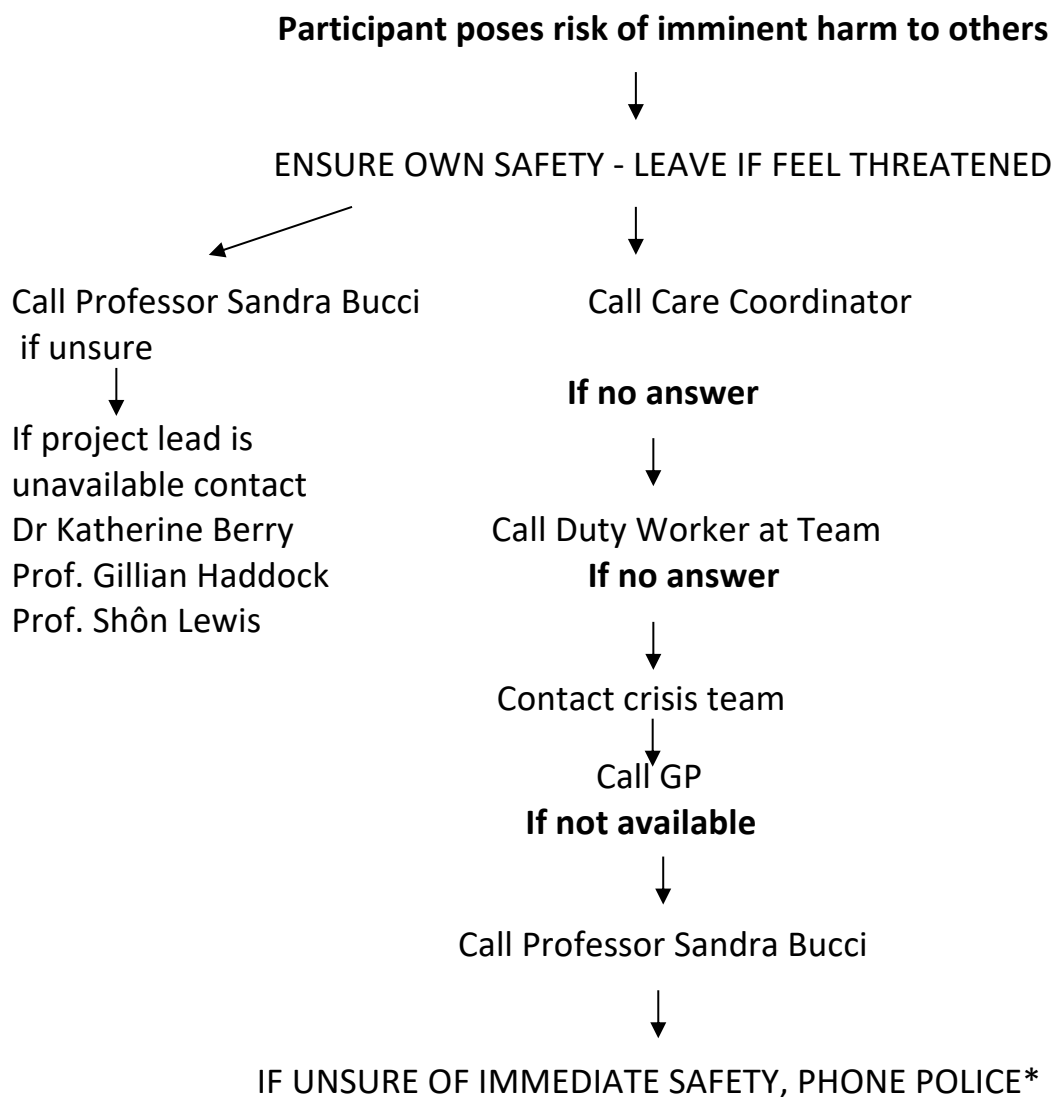
- Ideation (frequency, intensity, duration, triggers)
- Plans/intent
- Access to means to carry out plans
- Timeframe
- Protective factors

- Access to support/isolation
- Hopelessness
- Drug or alcohol use
- Command hallucinations and perceived power or control over voices

Any concerns you have should be discussed with the project lead as soon as possible. If your project lead is unavailable contact another clinical member of the research team (Prof. Gillian Haddock, Dr Katherine Berry, or Prof. Shôn Lewis).

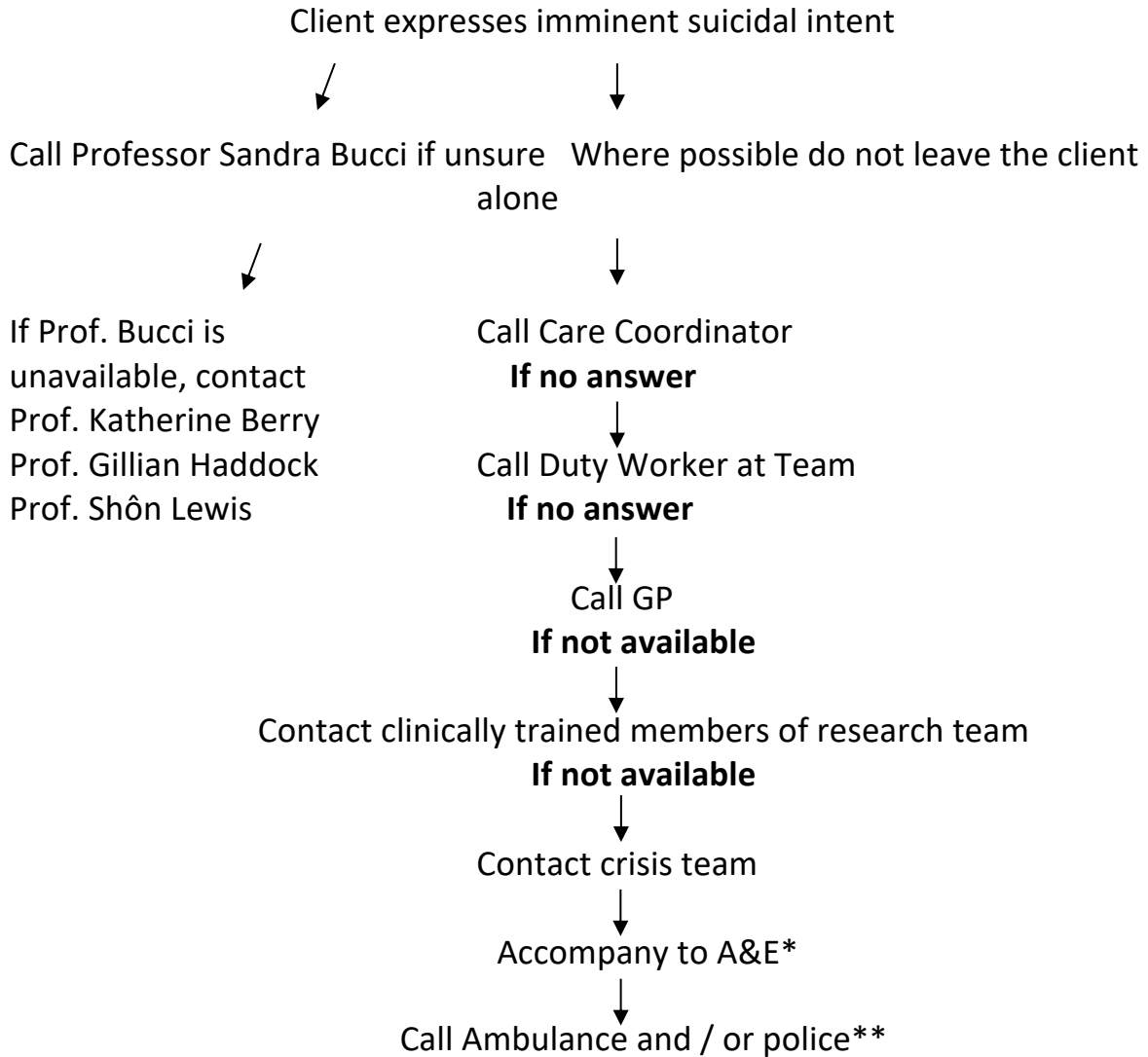
**FLOWCHART 1: CONTACTS FOR PARTICIPANTS
WITH IDENTIFIED INTENT TO HARM OTHERS**

**In situations where a Child / vulnerable Adult is at risk the appropriate
Safeguarding Team should be contacted.**



*Contacting emergency services (e.g. police) is the last resort and this option should only be exercised if all other options have been tried (or this course of action has been advised by clinically trained researchers) and there is a clear indication of an imminent risk to others.

**FLOWCHART 2: CONTACTS FOR PARTICIPANTS
WITH IDENTIFIED IMMINENT SUICIDAL INTENT**

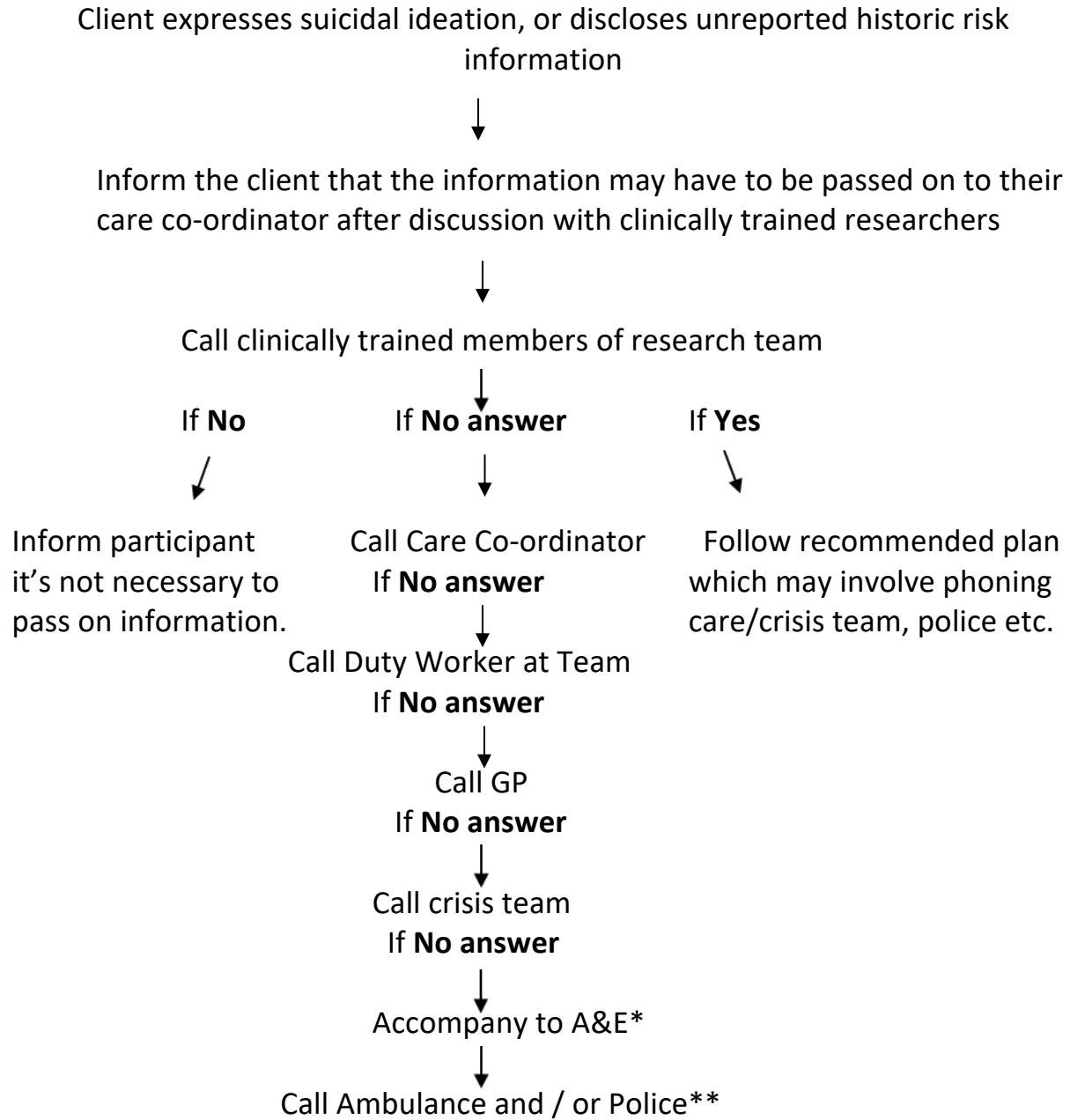


**Accompany the participant to A & E if they are willing to attend. Insurance purposes do not permit the transporting of patients in researcher's vehicles. Consequently in this circumstance it may be necessary to call a taxi, walk, or phone an ambulance.*

****Contacting emergency services (e.g. police) is the last resort and this option should only be exercised if all other options have been tried (or if this course of action has been advised by clinically trained researchers) and there is a clear indication of an imminent risk to self.**

FLOWCHART 3: CONTACTS FOR PARTICIPANTS

WHO EXPRESS SUICIDAL IDEATION OR UNREPORTED HISTORIC RISK INFORMATION



**Accompany the participant to A & E if they are willing to attend. Insurance purposes do not permit the transporting of patients in researcher's vehicles. Consequently in this circumstance it may be necessary to call a taxi, walk, or phone an ambulance.*

****Contacting emergency services (e.g. police) is the last resort and this option should only be exercised if all other options have been tried (or if this course of action has been advised by clinically trained researchers) and there is a clear indication of an imminent risk to self.**

APPENDIX 1: DISCLOSURE OF RISK DURING AN INTERVIEW

PROCEDURE: DISCLOSURE OF RISK DURING AN INTERVIEW

Researchers are to follow these guidelines in the event that, when conducting an interview, they identify that a participant might be at risk, or could pose a risk either to themselves or to others. The examples presented herein are not prescriptive and should be modified according to the situation.

- **Prior to commencing an interview** with a participant, the researcher will carefully explain that, although the interview is going to be confidential, if any risk is identified or disclosed during the interview, then the researcher will have to communicate these concerns to other professionals:

"Before we begin the interview, I just want to explain again that what we will talk about will be confidential. However, if I feel that from what you say there might be a risk to either yourself or other people I will need to pass this on to other staff members. But if I do this, I will tell you".

- If during the interview a participant's account indicates that they might be distressed or they disclose some type of suicidality or risk factors for suicidality, the researcher will reflect the distress they appear to be in and will ask if they want to continue the interview, and/or offer a brief break:

"You seem to be going through a hard time at the moment – do you want to continue with the interview? You know we can take a break at any time or we can stop if you want to".

"It sounds like there have been a few things upsetting you recently – are you okay to continue with the interview or would you prefer to take a bit of a break for a few minutes?"

- If during the interview the participant has disclosed a clear risk of suicidality (for instance, a description of plans for self-harming, or explaining that they are in possession of medication to take an overdose), at the end of the interview the researcher will explain the need to communicate this to staff:

"You've spoken about wanting to take an overdose with some medication you have, and it sounds like you are quite upset about some of the things we've been talking about. What I'm going to do, like we'd talked about at the beginning, is to speak

with your care co-ordinator and tell them how you are feeling so that they know what's going on for you and so that they can help you"

- If during the interview the participant's account indicates or suggests a possible risk of suicidality (for example, talking about occasional fleeting feelings of wanting to die, or sometimes wishing they could just be gone to end their problems), the research assistant will try to ascertain some further information:

"You've said that you sometimes wish you could just be gone and end your problems, have you recently had this kind of thought? Do you mean that you have a plan for this or are they just thoughts?"

"You said that you sometimes have felt like you want to die – if you were to feel like this again, do you think you would communicate this to staff?"

At the end of the interview, the research assistant will talk about this with the participant:

"You said that sometimes you have felt like you want to die, although not in the last week – do you mind if I just mention this to your care co-ordinator, so that they are aware too?"

If the participant accepts, this information can be given to staff.

If the participant declines, the researcher will contact Professor Sandra Bucci in the first instance (and then Prof Gillian Haddock, Professor Katherine Berry, or Prof Shôn Lewis if Professor Bucci is unavailable), to consult with them, on a case-by-case basis, the need to report this to staff.

- If any risk of suicidality has been disclosed by a participant during an interview and this risk needs to be reported to the care team, the researcher will do so verbally to a member of the care team:

"During a research interview, [participant's name and surname] has described plans and intent to take an overdose if access to medication was available. This was communicated to [staff name and role]. [Participant] is aware that I have passed this information on to their care team."

APPENDIX 2: LIST OF USEFUL CONTACTS

ACTISSIST Staff Contact Details:

| | |
|-----------------------------|------|
| Study Landline | XXXX |
| Prof Sandra Bucci | XXXX |
| Prof Gillian Haddock | XXXX |
| Prof Katherine Berry | XXXX |
| Prof Shôn Lewis | XXXX |

Community Support Resources For Participants:

| | |
|--|---|
| Manchester and Salford Samaritans | 72-74 Oxford St, Manchester M1 5NH 0161 236 8000 |
| Manchester Mind | Zion Community Centre, 339 Stretford Road, Hulme, Manchester, M15 4ZY 0161 226 9907 |
| Manchester Assertive Outreach | PO Box 201 Manchester M21 8WR 0161 881 4799 |

Child Protection Service Contact Details:

If a child is at immediate risk, contact the police on 999

Manchester

0161 234 5001 (24 hour service) or email mcsreply@manchester.gov.uk

Salford (inc. Prestwich) (8.30 – 4.30) 0161 603 4500

Duty (out of hours) 0161 794 8888

Trafford (8.30 – 4.30) 0161 912 5125

Duty (out of hours) 0161 912 2020

Bolton (9 - 5) 01204 337729

Duty (out of hours) 01204 337777

Other

- NSPCC Child Protection helpline on 0808 800 5000 (free 24 hour service)
- Childline 08001111 (a free 24 hour helpline for children)

ACCIDENT AND EMERGENCY NUMBERS

| | |
|----------------------------|---|
| Manchester Royal Infirmary | Oxford Road, Oxford Road, Manchester, M13 9WL 0161 276 4147 |
| North Manchester General | Delaunays Road, Crumpsall, Manchester, M8 5RB 0161 624 0420 |
| Wythenshawe Hospital | A Block, Wythenshawe Hospital, Southmoor Road, Manchester M23 9LT 0161 291 6041 |
| Salford Royal Infirmary | Hope Building, Salford Royal, Stott Lane, Salford, M6 8HD 0161 789 7373 |
| Trafford General Hospital | 0161 748 4022 |
| Royal Bolton Hospital | 01204 390390 |

CRISIS TEAM CONTACT NUMBERS:

GMMH

Crisis Line: 0161 922 3801

This line is in operation from Mon-Thurs 5pm - 9am and from 5pm on a Friday until 9am Monday. (The Crisis line is also open on Bank Holidays).

Pennine Care Area

Pennine Care Support Line 07500 785 870

9.0 References

Adamson SJ, Kay-Lambkin FJ, Baker AL, Lewin TJ, Thornton L, Kelly BJ, Sellman JD. An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R). *Drug Alcohol Depend.* 2010; 110(1-2), 137-143.

Addington D, Addington J, Schissel B. A depression rating scale for schizophrenics. *Schizophr Res.* 1990;3(4):247–51.

Ainsworth J, Palmier-Claus JE, Machin M, Barrowclough C, Dunn G, Rogers A, et al. A comparison of two delivery modalities of a mobile phone-based assessment for serious mental illness: native smartphone application vs text- messaging only implementations. *J Med Internet Res.* 2013;15(4):e60.

Alvarez-Jimenez, M., Priede, A., Hetrick, S.E., Bendall, S., Killackey, E., Parker, A.G., McGorry, P.D. & Gleeson, J.F. (2012). Risk factors for relapse following treatment for first episode psychosis: A systematic review and meta-analysis of longitudinal studies. *Schizophrenia Research*, 139(1-3), 116-128.

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders: Global assessment of Functioning Scale* (4th ed). Washington, DC.

Babor, T. F., Higgins-Biddle, J. C., Saunders, J. B., & Monterio, M. G. (2001). *AUDIT. The Alcohol Use Disorders Identification Test* (2nd ed). Geneva: World Health Organisation.

Beecham, J., & Knapp. M. (2001). *Costing psychiatric interventions*, in G. Thornicroft (ed.) *Measuring Mental Health Needs*, Gaskell.

Berman, A. H., Palmstierna, T., Källmen, H., & Bergman, H. (2007). The self-report Drug Use Disorders Identification Test: Extended (DUDIT-E): reliability, validity and motivational index. *Journal of Substance Abuse Treatment*, 32(4), 357-369.

Berry, K., Salter, A., Morris, R., James, S. G., & Bucci. S. (In Press). Assessing therapeutic alliance in the context of m-health interventions for mental health problems. *Journal of Medical Internet Research*.

EuroQol Group, (1990). EuroQol - a new facility for the measurement of health-related quality of life. *Health Policy*, 16, 119-208.

Gibson, W. J. & Brown, A. (2009). Working with qualitative data. *London: Sage Publications Ltd.*

Haddock G, McCarron J, Tarrier N, Faragher E. Scales to measure dimensions of hallucinations and delusions: the psychotic symptom rating scales (PSYRATS). *Psychol Med.* 1999;29(04):879–89.

Hooley, J.M. & Teasdale, J.D. (1989) Predictors of relapse in unipolar depressives: expressed emotion, marital distress, and perceived criticism. *Journal of Abnormal Psychology*, 98, 229–235.

Kay, S. R., Fliszbein, A., & Opfer, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, 13(2), 261.

Lancaster, G. A., Dodd, S. & Williamson, P. R. (2004). Design and analysis of pilot studies: recommendations for good practice. *Journal of Evaluative Clinical Practice*, 10(2), 307-312.

Law, H., Neil, S.T., Dunn, G. and Morrison, A.P., 2014. Psychometric properties of the Questionnaire about the Process of Recovery (QPR). *Schizophrenia research*, 156(2), pp.184-189.

Morosini, P. L., Magliano, L., Brambilla, L., Ugolini, S. & Pioli, R. (2000). Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatrica Scandinavica*, 101(4), 323-329.

National Institute for Health and Clinical Excellence (NICE) (2009). Schizophrenia: Core intervention in the treatment and management of schizophrenia in adults in primary and secondary care. *Public Health Guidance 82.*

NHS (2012). Approved Cryptographic Algorithms Good Practice Guideline, Crown Copyright. Available online at: <http://systems.hscic.gov.uk/infogov/security/infrasec/gpg/acs.pdf>

NVivo qualitative data analysis software; QSR International Pty Ltd. Version 10, 2012.

Palmier-Claus, J.E., Ainsworth, J., Machin, M., Barrowclough, C., Dunn, G., Barkus, E. & Lewis, S.W. (2012). The feasibility and validity of ambulatory self-report of psychotic symptoms using a smartphone software application. *BMC Psychiatry*, 12, 172.

Penn, D.L., Waldheter, E.J., Perkins, D.O., Mueser, K.T. & Lieberman, J.A. (2005). Psychosocial treatment for first-episode psychosis: a research update. *American Journal of Psychiatry*, 162 (12), 2220-2232.

Ritchie, J. & Lewis, J. (Eds). (2003). *Qualitative research practice: A guide for social science students and researchers*. London: Academic Press.

Ritsher, J. B., Otilingam, P. G., & Grajales, M. (2003). Internalised stigma of mental illness: psychometric properties of a new measure. *Psychiatry Research*, 121(1), 31-49.

Rogers, S., Chamberlin, J., Ellison, M., Crean, T., (1997). A consumer-constructed scale to measure empowerment among users of mental health services. *Psychiatric services*, 48, 1042-9.

Schlosser, D. A., Muklowitz, D. J., O'Brien, M. P., De Silva, S. D., Zinberg, J. L., & Cannon, T. D. (2012). A randomised trial of family focused treatment for adolescents and young adults at risk for psychosis: study rationale, design and methods. *Early Intervention on Psychiatry*, 6(3), 283-291.

Schulz, K. F., Altman, D. G. & Moher, D. (2010). CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ*, 340, c332.

Skinner, H. A. (1982). The drug abuse screening test. *Addictive Behaviours*, 7(4), 363-371.

Sobell, L.C. & Sobell, M.B. (1992). Timeline followback: a technique for assessing self-reported alcohol consumption. In: Litten R., Allen, J. eds. *Measuring Alcohol Consumption: Psychological and Biochemical Methods*. Totowa, N.J.: Humana Press, 41-72.

Španiel, F., Vohlídka, P., Kožený, J. Novák, T., Hrdlička, J., Motlová, L. & Höschl, C. (2008). The information technology aided relapse prevention programme in schizophrenia: an

extension of a mirror-design follow-up. *International Journal of Clinical Practice*, 62, 1943-1946.

Stoyanov, S. R., Hides, L., Kavanagh, D. J., & Wilson, H. (2016). Development and validation of the user version of the Mobile Application Rating Scale (uMARS). *JMIR mHealth and uHealth*, 4(2), e72.

The Schizophrenia Commission (2012). *The abandoned illness: a report from the Schizophrenia Commission*. London: *Rethink Mental Illness*.

Tennant, R., Hiller, L., Fishwick, R., Platt, S., Joseph, S., Weich, S., ... & Stewart-Brown, S. (2007a). The Warwick-Edinburgh mental well-being scale (WEMWBS): development and UK validation. *Health and Quality of Life Outcomes*, 5(1), 63.

Thompson, K., Kulkarni, J. & Sergejew, A. (2000). Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophrenia Research*, 42, 241-247.

World Health Organisation (WHO) ASSIST Working Group. (2002). The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability and feasibility. *Addiction*, 97(9), 1183-1194.