Local IRB # 1905-001 **IRBNet #** 1421955

BUTLER HOSPITAL
INSTITUTIONAL REVIEW BOARD
PROTOCOL

1.) Project

Title of Project: Mobile After-Care Support Intervention for Patients with Schizophrenia following Hospitalization: Pilot RCT [Study A Consent Form Title: "Mobile After-Care Intervention to Support Post-Hospital Transition: Pilot RCT"; Study B Consent Form Title: "Mobile After-Care Intervention to Support Post-Hospital Transition: Stakeholder Interviews]

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2.) Description of Study

A. Specific Aims

Psychotic-spectrum disorders, including schizophrenia and schizoaffective disorder, are associated with disproportionately high societal costs related to treatment, disability, and morbidity/mortality. Patients' nonadherence to medications and missed appointments undermine the long-term management of these illnesses, making it difficult to achieve improved quality of life and ultimate recovery. The transition from inpatient to outpatient care confers the highest risk of nonadherence and premature drop out in this population. Despite post-discharge being a time of elevated risk, routine clinical settings often lack feasible and effective services to support patients' return to the community and reengagement with outpatient providers due to the current system of fragmented care. In the absence of such solutions, up to 50% of patients with psychosis will remain medication nonadherent, the healthcare system will continue to waste over $100 million annually on potentially preventable hospitalizations, and a substantial number of patients with psychotic disorders will continue to be at high risk for relapse and rehospitalization within the first month post-discharge.

The current project proposes to examine the feasibility, acceptability, and potential effectiveness of our novel response-adaptive app intervention, Mobile After-Care Support (MACS), to improve treatment adherence and self-coping in psychosis following hospitalization, in preparation for a future full-scale clinical trial. We propose to enroll hospitalized patients with schizophrenia spectrum disorders prior to discharge and provide them with the MACS app to use during the first 4 months post-discharge to improve adherence to oral psychotropic medications, appointment attendance, and active self-coping with illness. We will conduct a pilot randomized controlled trial (RCT) of MACS to assess its impact on outcomes of interest relative to an attention-matched control condition. We also will conduct qualitative interviews with clinician stakeholders.

Aim 1: Conduct a pilot RCT (n = 80) of MACS vs mobile app attention control. We will assess: a) acceptability/satisfaction with the mobile app; b) feasibility of the RCT design (e.g., recruitment, randomization, assessments); c) whether the mobile app improves our proposed target mechanisms of increased illness self-coping and treatment adherence; d) whether our mobile app improves primary (symptom severity) and secondary (functioning, rehospitalization) outcomes; and e) whether changes in our adherence and coping target mechanisms predict changes in clinical outcomes.

Aim 2: Conduct 30-minute, individual qualitative interviews with 20 clinical stakeholders (including support staff, clinicians, and administrators) at mental health hospital and outpatient treatment centers in the

RI area. Stakeholder interview agendas will assess: a) perceived barriers to patients' medication/appointment adherence, b) use of mobile devices to support aftercare, c) potential self-management strategies to improve patients' coping, d) challenges patients face upon return to the community post-discharge, e) challenges faced by clinicians/organizations treating this population, and f) preferences regarding the flow of information collected via EMA and what data would be most useful.

B. Background

Recent hospitalization predicts treatment nonadherence[1-3], and the transition from inpatient to outpatient services confers the highest risk of nonadherence and premature drop out[4,5]. Despite post-discharge being a time of elevated risk, routine clinical settings often lack feasible and effective services to support patients' return to the community and re-engagement with outpatient providers due to the current system of fragmented care. Cost, time, and other barriers limit the ability of clinicians to monitor transition problems when moving from inpatient to outpatient care. To our knowledge, there are no existing evidence-based interventions that are routinely used as a "warm hand-off" of patients from inpatient to outpatient care.

To date, adherence interventions for psychosis have produced promising, albeit mixed results[6-8]. The most fruitful approaches have drawn on cognitive-behavioral therapy for psychosis (CBTp), sometimes also integrating motivational interviewing and family therapy[7,8]. These efficacious interventions have been delivered in group formats, individually, and sometimes with patients' families. Most CBTp-based adherence interventions have been delivered as part of routine outpatient services and intervention length has ranged from 1 session to weekly sessions for up to 2 years. A recent review[9] concluded that the most useful ways of improving adherence include strengthening communication with providers, increasing motivation to take medications/attend appointments, and addressing common adherence barriers. Schizophrenia guidelines[10] state that interventions "behaviorally tailored" to address adherence have shown the most benefit, but that there was insufficient evidence to recommend any one specific adherence intervention for schizophrenia. A recent review[11] of 182 adherence RCTs concluded that many CBT interventions are efficacious, but more feasible formats are needed that can be implemented in real-world settings.

Given the need for simple, low-cost service delivery methods, the field is turning to an mHealth approach as a means of supporting active self-coping with illness and medication/appointment adherence. Mobile devices, such as smartphones, have become the ideal technological platform for in vivo assessment and personalized interventions delivered via apps. These ecological momentary assessment (EMA) or ecological momentary intervention (EMI)[12] methods reduce risk of retrospective biases in self-reports and can provide insights into patients' daily lives that could not be captured at clinic appointments alone. Also, ecological data collection can be used to trigger in-the-moment, tailored interventions, delivered electronically, thus reducing provider burden.

Clinical characteristics associated with schizophrenia, such as low motivation and cognitive impairments[13], may lead to pessimism about the feasibility of EMA in this population. Yet, accumulating research supports the short-term feasibility/acceptability of EMA in psychosis using mobile devices[14,15]. Various studies show that people with schizophrenia accept and can be trained to use EMA with compliance rates comparable to those of nonclinical populations[15-20]. Notably, EMA has demonstrated incremental validity over traditional retrospective reports in assessing symptoms associated with schizophrenia[19,21].

Most patients, even those acutely ill, have increasing familiarity with this technology[22]. For example, 81.4% of patients with severe mental illness (SMI) surveyed over the past 2 years reported mobile phone ownership[23]. Recent surveys have reported smartphone ownership in psychiatric populations of 62.5% in 2014[24], which is comparable to rates found in the general public. Further, national data indicate that smartphone use is particularly prevalent among ethnic minorities and lower-income individuals as this is the most feasible method for them to access the internet[25].

There is a growing body of research showing that various mobile approaches can support coping and improve treatment adherence in outpatients with psychosis; although none of these interventions has been designed to support patients' return to the community immediately following hospitalization. For instance,

Granholm et al.[17] conducted a study of 42 individuals with psychosis engaged in EMI for 12-weeks. In response to 12 daily prompts, participants answered questions on mobile devices and based on their responses received an immediate intervention that drew on CBT principles, including self-management of hallucinations, medication adherence, and socialization. Results were encouraging and showed positive changes in these targeted domains. However, it should be noted that participants were recruited from stable outpatient residential and treatment settings. Further, results from a study by Depp et al.[16] showed that EMI was feasible for patients with psychosis in 3 pilot clinical trials, but again, samples were limited to patients who were fairly stable and engaged in outpatient treatment in the community. Ben-Zeev et al.[26] also piloted 1-month EMI in a sample (n=33) of patients with schizophrenia/schizoaffective disorder already engaged in outpatient treatment groups. Patients used the mobile device 86.5% of days (average 5.2 times per day) and showed improvements in psychotic symptoms and depression. More recently, Ben-Zeev et al.[27] examined use of an EMI in 342 individuals with psychotic disorders recruited within 60 days of a hospitalization (but not directly at inpatient through discharge) and followed them for up to 6-months. This naturalistic study found that 44% of the sample used the intervention an average of 4.3 days per week.

We conducted a previous assessment only mobile study to assess the feasibility and acceptability of EMA in 65 patients with psychotic-spectrum disorders who were recently discharged from the hospital were assessed[28,29]. EMA was administered for four weeks via study-provided mobile devices. Feasibility was measured by study recruitment/retention rates, patients' connectivity, and completion rates. Quantitative and qualitative acceptability data were collected. Participants completed 28-31% of offered EMA assessments. The only significant predictor of reduced EMA completion was recent cannabis use. EMA completion was maintained from weeks 1 to 3 but significantly dropped at the fourth week. Patient acceptability feedback was generally positive; negative comments related primarily to technological problems. This was the first study to use EMA in recently discharged patients with psychotic-spectrum disorders. EMA is feasible and acceptable in this population, but completion rates were lower than in more stable samples. Future research should consider limiting the assessment period, screening for substance use, and integrating assessment with intervention elements to increase EMA engagement.

Despite the proliferation of smartphone-based EMA, to our knowledge, scant research has examined how best to share these data with providers. Clinicians and administrators work with a high volume of patients and more information about how to share EMA data in a way that will be efficient and meaningful is needed. Indeed, to ensure these data are helpful to providers and their provision of care, the field must have a clearer understanding of the content and process by which EMA-collected data can be shared with outpatient providers. At the "ground level," this includes administrative support staff, who are likely to be responsible for the flow of information into patients' charts. Administrators, such as clinic directors, might have unique perspectives regarding facilitators and barriers to conveying EMA data to providers. Lastly, clinicians will have first-hand knowledge and perspectives on what clinical information will be most useful and how this information should be formatted.

To maintain stability in patients with schizophrenia requires effective self-management of symptoms and consistent treatment adherence. Perhaps the most notable period in the continuum of care when coping and medication/appointment adherence are jeopardized is during the first months following discharge from acute hospitalization. Various factors associated with adherence have been described in our pilot work, and we have used these data to inform the development of a theoretically- and empirically-grounded, mobile intervention app following hospitalization, which we are currently in the process of developing. We will test the feasibility, acceptability, and potential effectiveness of our mobile app, that we call Mobile After-Care Support (MACS), to improve the target mechanisms of active illness self-coping and medication/appointment adherence post-hospital discharge. We plan to compare the MACS app to an attention-matched app that will assess variables of interest and provide non-adaptive information (i.e., education) in the context of a RCT design for patients recently hospitalized for psychosis. To aid in app development and planning, we will also conduct qualitative interviews of clinical stakeholders regarding their perspectives on the app.

C. Experimental Method

C1. Brief Description of Subjects

Study A. Participants in this study will consist of 80 patients diagnosed with schizophrenia-spectrum disorders who have been hospitalized for acute psychiatric reasons at Butler Hospital. See detailed inclusion/exclusion criteria below.
Study B. We also will select 20 clinical stakeholders for participation. These participants will be selected from clinicians, administrators, and support staff working at Butler Hospital, The Providence Center, and other mental health programs in the area. We do not propose recruiting a specific number of each group at this point. As is typical of qualitative methods, we will interview stakeholders until we have reached saturation on relevant themes. Therefore, the numbers for each type of stakeholder recruited will vary; although we will attempt to interview several for each category. See detailed inclusion/exclusion criteria below.

C2. Study Design

Study A. We will use the pilot RCT (n = 80) to assess MACS acceptability/ feasibility and its preliminary effectiveness relative to a control condition. Randomization will be used to help ensure balance among treatment conditions. We will stratify by diagnosis (schizophrenia/schizophreniform vs schizoaffective) and by gender (male vs female). We will conduct randomization using a computer generated list via REDCap held by a staff person no otherwise affiliated with the study. We will review patient acceptability/ satisfaction ratings and ease of use of mobile devices as measured by the CSQ-8 and patient qualitative interviews. These data will inform further refinements of the MACS app that will be used in future research.

Study B. We also will conduct 30-minute individual interviews of clinical stakeholders (n = 20). Interviews will be led by members of the investigator team and a study research assistant (RA) listening to the conversation and taking notes. Interview agendas will be developed so that participants will receive similar types of questions, as well as those that may be specific to their job responsibilities (e.g., clinician vs administrator).

C3. Specific Procedures or Treatments

MACS Protocol. We will use an established mobile software service (ilumivu.com) which provides a secure platform (Android or Apple IOS compatible) that can be programmed to administer the MACS app. It does not require a high degree of IT support and allows for tailoring of content without the need for trained programmers. Further, we chose a mobile app that works with most smartphones, is easy to download/install, and runs largely autonomously. Because we are using a flexible software platform to deliver our mobile intervention and not a static app specifically designed for this project, we have flexibility to make changes to the content of the app during the project in an iterative fashion based on what we learn from the data being collected. In addition, future implementation of the app can take advantages of ongoing improvements and updates to the platform that will be used in future iterations of our app-based interventions that would be proposed for a next step full-scale RCT if this project is successful.

The MACS app assesses and intervenes by fostering increased treatment adherence (medication/appointments) and self-coping with illness (active, planned, problem-solving focused) to reduce symptoms and improve functioning. Additionally, MACS will encourage participants who are already reporting adherence and healthy coping by using positive reinforcement strategies to maintain efforts and promote additional goal setting. MACS app strategies are linked to patients' specific assessment responses, allowing for a highly personalized self-management intervention experience. Primarily, MACS is constructed from common components we adapted from CBTp studies, including those testing mobile interventions[16,17] to improve self-coping and adherence behaviors. The MACS app provides interactive exercises delivered by the device designed to teach patients coping skills that they can use now and in the future. Exercises incorporate

graphics, feedback, and interactive menus to increase engagement. For instance, participants are instructed on how to use common CBT exercises for coping with psychotic symptoms (e.g., "Is there another explanation for what is going on right now? Let's explore some examples." or "Try doing what you want despite what the voices say. Let's practice how to do this now."). Another example targeting improved socialization teaches patients the benefits of socializing and encourages them to identify and record the names and numbers of support persons in the device that they plan to contact. MACS responses to medication nonadherence and missed treatment appointments come partly from Dr. Gaudiano's previous traditional and mobile intervention work improving treatment adherence in those with SMI[30]. There are a variety of possible reasons for nonadherence. If the reported reason is primarily logistical (i.e., no transportation, ran out of pills, forgot to take them), participants will be instructed to set phone/calendar reminders or contact their provider at the community clinic to address the problem. This information will also be conveyed to providers (through periodic reports generated by the study team that will summarize app data) so that the community clinic can reach out to participants to address adherence issues. If nonadherence is attributed to medication concerns (e.g., does not believe medications help, experiencing side effects), we will use previously tested techniques that encourage participants to communicate concerns to providers, remind them of costs vs benefits of medication in terms of symptom management, and teach them to engage in other brief problem-solving strategies delivered through the app[30]. If appointment nonattendance is reported, similar problem-solving strategies will be suggested. In response to negative affect and stressful life events, MACS provides various CBTp strategies[31], such ameliorating or circumventing the stressor when possible, or exploring alternative approaches to coping with distress that might be more adaptive, including app-based emotion regulation exercises[32]. To address low life satisfaction, MACS will use CBTp techniques derived from positive psychology research focused on building strength and resiliency[33]. For example, app interventions will encourage patients to savor experiences, cultivate gratitude, and rehearse mental imagery related to previous positive experiences. In addition, if the patient reports positive coping and treatment adherence, the app will deliver exercises that reinforce positive behaviors (e.g., "You seem to doing well. Let's identify a way to reward yourself for your hard work") and encourage additional goal setting to foster continued improvement (e.g., "You seem to be making good progress toward your goals. Now let's identify future goals that can build upon what you've accomplished so far.") In response to reported substance abuse, MACS will deliver brief interventions drawn from motivational interviewing[34,35], another approach in the CBT family, that probes for motivation for change based on an individual's self-reflection, consideration of pros and cons, and suggests stimulus control and reduced use goals[36,37]. Finally, safety risk will be assessed using one item from the Patient Health Questionnaire-9 ("Since the last survey, have you had thoughts that you would be better off dead or of hurting yourself in some way?"). Because patients' mobile device data will be uploaded remotely to secure servers, the safety risk item will be reviewed on a weekly basis by research staff. This type of "asynchronous communication" (i.e., a gap between patient and provider communication) is typical in mHealth applications because it is not feasible in real world practice to review patient data in real time by busy clinicians. Patients will be informed that their responses will not be reviewed in real time; instead, they will be given immediate instructions on the device for addressing safety (e.g., contacting crisis hotline). Patients will be contacted and assessed further by a clinician after the data are periodically reviewed by research staff per study safety procedures.

Mobile App Attention Control Protocol. As we plan to do with MACS, we will use an established mobile software service (ilumivu.com) which provides a secure platform (Android or Apple IOS compatible) that can be programmed to administer the attention control app. The control condition assessments will include the same frequency of prompts and types of questions as MACS, but will then diverge from MACS by providing participants with general didactic information about illness and treatment that is text-based, non-interactive, and not tied to assessment responses. Informational text will be adapted from a review of the literature about illness prevalence, associated clinical features, expected course and prognosis, various etiological explanations, and treatment options. Text will be brief and written in language and at a reading level appropriate for the participants.

Mobile Device Use. The MACS and attention control protocols will consist of daily prompted sessions. Each session will take ≤ 5-10 minutes and frequency of sessions will taper after the first month from three daily prompts to once daily for months 2-4. Every morning (9:00am default), afternoon (12:00pm default), and evening (9:00pm default) based on the person's typical schedule, participants will begin by responding to survey questions about symptoms, functioning, and adherence. Those using MACS will receive brief self-management CBTp interventions that will be adaptively tailored to correspond to responses provided by the participant (e.g., if nonadherence is reported, strategies addressing this problem will be presented by the device). The MACS morning survey will also remind participants about being adherent to medications and treatment appointments and offer suggestions for staying on track (if adherence is reported) or improving any nonadherence behaviors for the upcoming day. We will include a feature that will allow participants to delay (e.g., 15 min) the administration of a mobile session, if the participant is too busy or otherwise unable to use the device. The prompted app sessions are to ensure use of the program on a regular schedule. In addition, patients will be permitted "free use" of the mobile apps whenever they desire to increase the use of the devices based on their personal needs and schedule.

Mobile Software Service. We will use an established mobile software service (ilumivu.com) which provides a secure, HIPAA-compliant application (Android or Apple IOS compatible) that can be programmed to administer the MACS app and the attention control app. Responses will be uploaded when internet/cellular access is available to a web portal for remote access/downloading from a convenient web portal interface. Otherwise, responses are stored on the native app in an encrypted format until uploading can occur. App updates and fixes can also be sent remotely to the app when needed. Raw app data will not be automatically sent to providers. Instead, staff will review mobile data weekly to monitor safety and contact patients if safety risk is detected. Patients will be informed that mobile data will not be reviewed in real time and that they should contact providers/seek immediate help if needed. These risk data will also be included in the periodic reports that are sent to providers. Patients will be prompted by the device to contact a crisis hotline, their providers (numbers pre-programmed into the device), or 911/local hospital if they report an immediate safety risk.

Mobile Device Training/Support. For individuals in both conditions, after obtaining consent at hospitalization (baseline), a research assistant will help patients install the app on their own smartphone when possible for convenience. If a patient is unwilling to install the app or does not own a compatible smartphone, we will supply a dedicated mobile device to the participant for this purpose post-discharge and they will return the device at the end of the study. Patients will practice responding to app sessions to familiarize themselves with the program and troubleshoot technical problems. Patients will be instructed to contact the study if questions arise post-discharge about using the device. For individuals in the MACS condition only, we also will employ a master's level clinician to meet with participants to review their discharge plan prior to leaving the hospital and discuss how to use the app to support their aftercare. For both conditions, app training/support meetings will be held prior to discharge when possible. If a patient is unexpectedly discharged, participants will be asked to return to our clinic, and this meeting with be held as shortly after discharge as possible, or it will be conducted over the phone if the participant is unable to return to the clinic.

MACS communication with outpatient providers. For participants assigned to MACS only, at baseline, an initial discharge report will be sent by the study clinician to patients' outpatient providers (after obtained releases of information from the patient) based on assessment results. Additionally, to improve quality of care and timely communication between providers, periodic reports (e.g., bi-weekly the first month and monthly thereafter containing information on symptoms, safety, and adherence) will be sent to patients' outpatient clinicians throughout the study to improve care coordination. These reports will be generated using data collected via the app.

Assessments (see Table 1)

Participants will complete baseline measures, as well as diagnostic interviews at intake prior to hospital discharge (~1.5 hrs). Patients will return to our research office to complete traditional assessments at 1, 2, and 4 months to assess longer-term effects (~1 hr each).

MACS and attention control app assessments. Mobile app assessment items will be the same in both conditions. They are adapted from traditional measures and those used in other mobile studies in psychosis: a) affect[38], b) psychosis[15], c) social support[102], d) life satisfaction[39], e) functioning[40], f) treatment adherence[41], g) substance use[42], h) safety[44].

Target Mechanisms**.** Our target mechanisms are increases in: a) medication adherence, b) appointment adherence, and c) active self-coping with illness. a) We will employ MEMS[45] to objectively measure medication adherence during the post-hospital period for the primary oral psychotropic medication prescribed for participants in both conditions based on the following hierarchy/order: 1) antipsychotic, 2) mood stabilizer, 3) antidepressant, or 4) anxiolytic/hypnotic. MEMS uses an electronic pill cap that records bottle openings/closings and the corresponding time/date[46,47]. Patients will be trained by research staff to use MEMS at the start of the study. MEMS data will be downloaded at our research office at follow-up assessments and when patients receive medication refills. MEMS data will not be integrated into the MACS intervention and will be used instead for research data collection only. Similarly, pill counts also will be conducted at this time for back-up purposes. Electronic monitoring is recommended for objective adherence assessment[48]; MEMS has been used in studies of schizophrenia[49], including in our R21 pilot study. b) For appointment adherence, we will use the THI-4[50], which is a treatment utilization interview, to assess mental health appointments missed/scheduled. Medication/appointment adherence will be cross validated by obtaining releases for patients' outpatient medical records, and any discrepancies will be re-reviewed with the patient to obtain an accurate count. c) Coping with illness in schizophrenia will be assessed via the standardized and well-validated MACS-II[51,52]. MACS-II is an interview-based measure that assesses coping to 13 core symptoms of schizophrenia, including positive and negative psychotic symptoms, depression, cognition, hostility, and euphoria. Coping responses are then categorized based on 5 coping styles described by Carr[53], including passive illness behavior (e.g., lying in bed and doing nothing), active problem-solving (e.g., professional help seeking), passive problem-avoiding (e.g., isolation), active problem-avoiding (e.g., indulgence), and symptomatic behavior (e.g., obeying voices). Research has shown the MACS-II to be reliable and valid when used in samples with schizophrenia[54]. We also will administer the following: the BARS[59] which is a interview assessing the patient-reported percentage of missed doses over the past month for the primary oral psychotropic medication; the SUS[60] which is a 10 item self-report of app usability; the USE[61] which is a 30 item self-report of app satisfaction; the Brief COPE[62] which is a 28 item self-report measure of coping skills; and the PUQ which is a self-report measure we created for this study to collect data on participants' use of mobile phones and related technology.

Table 1. Traditional Assessments	**Construct assessed**	**Method**	**Time**
Structured Clinical Interview for DSM-5 (SCID-5; Psychotic, Mood, Substance Use Modules)[55]	Axis I diagnosis	Interview	Baseline (BL)
Mini-Mental State Exam (MMSE)[63]	Cognitive functioning	Interview	BL
Phone Usage Questionnaire (PUQ)	Phone use	Self-Report	BL
Medication Event Monitoring System (MEMS)[45]	Medication adherence	Objective	1,2,4
Antipsychotic Medication Beliefs and Attitudes Scale (AMBAS)[65]	Medication beliefs	Self-report	BL,1,2,4
Brief Adherence Rating Scale (BARS)[59]	Medication adherence	Interview	BL,1,2,4
Treatment History Interview-4 (THI-4)[50]	Appointment adherence	Interview	BL,1,2,4
Outpatient chart/medical records review	Treatment utilization	Objective	BL,1,2,4
Maastricht Assessment of Coping Strategies (MACS-II)[51,52]	Coping skills	Interview	BL,1,2,4
Brief Coping Orientation to Problems Experienced (COPE)[62]	Coping skills	Self-Report	BL,1,2,4
Brief Psychiatric Rating Scale (BPRS)[56]	Psychiatric symptoms	Interview	BL,1,2,4
WHO Disability Assessment Sched. 2.0 (WHODAS-2)[40]	Functioning	Self-Report	BL,1,2,4
Alcohol Use Disorders Identification Test (AUDIT)[42]	Alcohol use	Self-Report	BL,1,2,4
Drug Use Disorder Identification Test (DUDIT)[64]	Drug use	Interview	BL,1,2,4
Usefulness, Satisfaction, and Ease of Use Questionnaire (USE)[61]	Acceptability	Self-Report	1,4
System Usability Scale (SUS)[60]	Acceptability	Self-Report	1,4
Client Satisfaction Quest.-8 (CSQ-8)[57]	Acceptability	Self-report	1,4

End of Treatment Interview	Feedback	Interview	1,4

Clinical Outcomes and Other Measures. In addition to target mechanisms, we will assess clinical outcomes including: a) symptom severity (primary outcome), b) functioning, and c) re-hospitalization rates. a) We will use the BPRS,[56] a well-established interview measure of overall psychiatric symptom severity, including positive/negative psychotic symptoms, as well as mood symptoms and suicidality; b) the WHODAS-2[39,40], which is a brief self-report measure of functional impairment; and c) rehospitalizations obtained from the THI-4[50] as described above (and cross-checked with patients' medical records). In addition, the THI-4 will also be used to quantify overall treatment utilization, including the type and amount of mental health treatment received over follow-up (medications, psychosocial, hospitalizations, pharmacotherapy visits, ER visits, crisis calls, support groups). We also will administer the AUDIT/DUDIT, which measure alcohol/drug use and severity[42,58,64]. The MMSE[63] will be used to assess cognitive functioning at baseline in order to describe patients' baseline characteristics and to examine this variable as a potential predictor of treatment response in our analyses. The AMBAS[65] is a brief self-report measure of medication beliefs. Acceptability/satisfaction with the mobile apps will be assessed using an adapted version of the CSQ-8[57] at the end of the study. Finally, participants will complete an end-of-treatment interview in which they will be asked what they liked and did not like about the app and study participation.

Clinical stakeholder interviews. Basic demographic information will be collected from all participants using a short self-report measure. These data will include age, gender, ethno-racial background, education level, duration of employment in current position, and duration of employment in the field. Participants will complete a 30 minute individual interview by telephone or in-person, depending on their location. Prior to the interview, we will send participants a brief description of the mobile app we are developing and sample content. This interview will be scheduled at the participant's convenience and will be audio-recorded. Stakeholder interview agendas will assess: a) perceived barriers to patients' medication/appointment adherence, b) use of mobile devices to support aftercare, c) potential self-management strategies to improve patients' coping , d) challenges patients face upon return to the community post-discharge, e) challenges faced by clinicians/organizations treating this population, f) preferences regarding the flow of information collected via EMA and what data would be most useful from the app. Questions will be delivered in an open-ended format to allow participants to share their opinions.

C**4. Data Analysis**

We will use effect size changes to describe differences between groups over the time points on target mechanisms (adherence and coping), primary outcomes (overall symptom severity), and secondary outcomes (functioning, rehospitalization rates). We will calculate 95% confidence intervals (CIs) and clinical significance statistics (e.g., NNT). Because CIs will likely be large, these analyses may not permit definitive conclusions. Given the limitations and goals of pilot studies, we hope to build our case for future research by focusing primarily on the feasibility/acceptability of MACS and of the randomized design and the clinical significance of effects compared to our mobile attention control. Some parameters estimated in the pilot study (e.g., stability of outcome measures across time) may be helpful for informing estimates for a large scale, adequately powered RCT. Secondarily and consistent with analyses we would conduct in a future full-scale RCT, we will generate multilevel models to examine whether treatment condition, time, and the treatment condition X time interaction predicts change in outcomes (symptoms, functioning, re-hospitalization) and proposed mechanisms. Generalized estimating equations will be constructed to examine differences in rehospitalization rates over time. We will assess whether the groups differ on covariates at baseline (e.g., demographics) and, if so, include them in the statistical models. Given the smaller sample size, we will examine changes in mediators over time across conditions and correlations between mediators and outcomes, which are pre-requisites for formal mediation. We also will examine outcome predictors (e.g., baseline adherence) to identify possible moderators to test in future studies

Qualitative interviews will be recorded and the interviewer will keep notes of the conversation. The MPIs will develop an initial codebook with deductive codes. Then inductive codes capturing emergent themes will arise from team-level review of interviews. Once codes are developed, the research team will independently code remaining transcripts; 20% of transcripts will be double coded and reviewed to ensure inter-rater reliability. The MPIs will perform thematic analysis in which the passages assigned to codes will be read in aggregate to identify key themes.

C**5. Videoconferencing**

Due to COVID-19 restrictions and recent developments in the use and popularity of telehealth, we also will offer participants the ability to complete study assessment sessions by secure videoconferencing per current CNE policy (e.g., HIPAA-compliant Zoom). Participants will be informed of the potential risks and limitations of videoconferencing related to confidentiality issues in the consent form. Participants who do not have or want to use videoconferencing will still be able to complete study assessments over the phone.

D. Material Inducements

For Study A, we will compensate patient participants for completion of in-person assessments $30 each at the baseline, 1, 2, and 4 month follow-ups, with an additional $10 increase for each consecutive follow-up completed (i.e. if all appointments are completed, patient participants will be compensated $30, $40, $50, and $60 at each timepoint, for a possible total of $180). Patient participants who are found to be ineligible for the study following administration of the SCID (used to determine/confirm diagnosis) will be compensated $15 for their time (half of the full baseline compensation amount). Patient participants will be compensated an additional $20 for returning the electronic pill caps or a borrowed study phone, if applicable, for up to $200 total. For completion of mobile surveys during the first month post-discharge, patient participants will be compensated $0.25 per completed app session up to three per day (for a possible total of $22.50). In total, patient participants can be compensated up to $222.50 for their participation. For Study B, we will compensate stakeholder participants $50 for completion of the interviews.

E. Training of Research Personnel

The research assistants (RAs) will be directly supervised by Drs. Gaudiano and Moitra. All RAs in the psychosocial treatment program undergo extensive training in screening medical records (including the appropriate permissions to access electronic medical records), approaching patients on the units, obtaining consent to participate, collecting and entering data, and maintaining confidentiality. All RAs have received training in the informed consent process and their ethical responsibilities when conducting research. Additionally, all RAs will receive specific training in the assessment instruments to be administered. Drs. Gaudiano and Moitra also will train and supervise the master's level clinician who will meet with patients for the initial app session before discharge and send brief reports during the study to patients' community clinicians based on assessment data collected.

3) Human Subjects

A. Subject Population

Study A. Participants in this study will consist of 80 patients diagnosed with schizophrenia-spectrum disorders who have been hospitalized for acute psychiatric reasons at Butler Hospital.

Inclusion criteria are: (1) currently hospitalized in inpatient or partial hospitalization; (2) DSM-5 criteria for schizophrenia, schizoaffective, schizophrenia unspecified/other, or mood disorder with psychotic features (bipolar or major depressive disorder) specified based on the Structured Clinical Interview for DSM-5[55] (SCID-5); (3) 18 years or older; (4) prescribed oral psychotropic medication upon discharge; and (5) ability to speak and read English (materials written at a 5th grade reading level). Exclusion criteria are: (1) planned discharge to

supervised living setting or participation in formal outpatient adherence programs (e.g., medication packaging) or (2) pregnancy or other medical condition (e.g., dementia as indicated by patients' medical charts) contraindicating use of antipsychotic medications.

Including patients who have stepped down to partial hospitalization following a recent inpatient hospitalization allows us to recruit patients who would have been eligible during their inpatient stay, but were missed for recruitment due to short lengths of stay or related issues. Additionally, recruiting partial hospital patients will increase our ability to meet recruitment goals by reaching other individuals who might benefit from this project. Research staff will obtain permission to approach from the patients' partial hospital attending physician before approaching and recruiting patients who meet study criteria. Study related consent process and assessments will be conducted during times that do not interfere with partial staff schedules or patient treatment sessions.

Study B. We also will select 20 clinical stakeholders for participation (clinicians, administrators, and support staff). Inclusion criteria are: (1) age 18 or older, and (2) works as a clinician, administrator, or support staff person in a mental health program or facility providing services to patients with psychosis.

B. Recruitment and Consent Procedures

Study A. If the patient appears appropriate based on the routine electronic chart review of hospital admissions (including inpatient and partial hospital admissions), the study will be explained to the patient's treating physician. If the physician agrees it is clinically appropriate, a member of the research team will then approach the patient. All participants will be asked to provide releases of information for their community treatment providers so that the investigators can obtain records to corroborate patient self-report of treatment utilization and for those randomized to MACS, send brief reports to clinicians at follow-up. We also will collect the names and numbers of additional contact persons and collect permission to contact them in the event that we are not able to reach the patient during the study. After obtaining permission for this purpose, we will contact participants via text and/or email to schedule follow-up contacts and check in with them periodically to prompt their use of the app.

Remote Recruitment Procedures. Due to COVID-19, we will conduct consent and baseline procedures remotely for staff and patient safety. We have worked with hospital staff to develop the following procedures, which will prevent the need to have direct contact with participants for health reasons. We propose that research assistants will continue to review AVATAR records of inpatients and partial patients remotely (via secure VMware remote portal) to identify those who might meet criteria for the study. Once a potential participant is identified, the RA will email (Butler to Butler account) or call the hospital staff social worker or therapist who will collect a contact permission form (attached) from the patient. The form is worded more broadly at this point because we plan to obtain permission also to use it for other ongoing studies. The social worker already meets with the patient for other clinical purposes on the unit (e.g., psychosocial assessment, discharge planning). If the person is quarantined because of COVID-19, the social worker will not approach to collect contact permission. The form will document whether or not they are interested in being contacted about the study (and their preferred method of contact) following discharge. For those who agree to be contacted, they will also indicate if they agree to research staff leaving voice messages during telephone outreach and mailing them study information at their current address. The social worker or unit clerk will email (Butler to Butler account) or call the research assistant and confirm when a patient agrees to be contacted and the contact form will be retained for our records. We will periodically provide food to the unit as a thank you to them for collecting these forms.

The research assistant will then call the participant after discharge, and if they are interested, conduct the consent process over the phone to obtain verbal consent (see attached remote consent form). The consent

process will be audio recorded and stored on a secure server as verification of consent. Afterward, the patient will be mailed (or emailed if they prefer) a copy of the consent form to keep for their records. The RA will attempt to contact the participant during the first 2 weeks post-discharge to obtain consent. Once the consent is completed, the RA will collect the necessary information needed to complete releases of information for the participant's outpatient providers over the phone. The research assistant will then enter the information into designated forms on REDCap and email these releases using a secure link via REDCap to the participant for them to provide their electronic signature. The participant will then be able to sign the releases electronically through REDCap. This remote procedure for collecting releases may also be conducted at later time points during the study should a treatment provider change.

The research assistants will also review the medical records of partial hospital patients and procedures will be similar to those described above for inpatients. Once a potential participant has been identified, the research assistant will contact the patient's treating physician in the partial program, and the research study will be explained to them. If the physician agrees it is clinically appropriate, a member of the research team will approach the patient while they are attending partial to consent them and begin baseline assessments when they are not in treatment sessions. If attending partial remotely, the research assistant will contact the patient via telephone using the contact information listed in their record. If the participant is interested, the research assistant will conduct the consent process over the phone to obtain verbal consent. The consent process will be audio recorded and stored on a secure server as verification of consent. Afterward, the patient will be mailed (or emailed if they prefer) a copy of the consent form to keep for their records. After obtaining consent, the RA will collect information for the participant's outpatient providers, and email them to the participant using a secure link through REDCap. The participant will sign the releases electronically through REDCap.

After obtaining consent, the RA then will proceed to conduct the baseline assessment over the phone to confirm eligibility. We will follow all study safety procedures as previously outlined in the protocol. If entered into the study, all subsequent study procedures will be conducted remotely, including initial orientation of the study app (i.e., the participant will be given training and instructions for how to download and use the app on their smartphone) and follow-up assessments.

Study B. We will consult with our investigator team to identify appropriate clinical stakeholders to approach about study participation. Once identified, Drs. Gaudiano or Moitra or another member of the research team will contact the stakeholder directly to introduce the study. If interested and the interview is done in person, the participant will review and sign the consent form. They will be given a copy for their records. If the interview is done over the phone, the participant will be sent a copy of the consent form prior to the interview. Then the person will be consented over the phone. The consent process will be audiorecorded as documentation of consent. The participant will also be asked to return a signed copy of the consent form and to keep a copy for their records.

C. Potential Risks

Potential risks of study participation include: coercion, clinical deterioration/suicidality, loss of confidentiality/privacy, and adverse events (see details below).

D. Protection of the Subject

D1. Measures to Minimize Potential Risks

Coercion

Risks. The risk of potential coercion is judged to be minimal.

Minimization. The risk of coercion will be minimized by following standard procedures for obtaining informed consent. We will fully explain the study procedures, risks, benefits, and alternatives to all patients. Also, patients who do not consent or who withdraw at any time will receive usual clinical treatment with no prejudice. Additionally, participant remuneration will be set at modest monetary levels as used in similar studies, including our pilot work. We will obtain permission form the patient's treating physician to ensure that approaching the patient for research participation is clinically appropriate. We will stress that the decision by stakeholders about whether to participant in the study will not be affect their employment status.

Risk of clinical deterioration/suicidality

Risks. In this type of population, the risk of clinical deterioration is present.

Minimization. Clinical deterioration, including suicidality will be monitored in multiple ways. 1) During in person interviews, study staff will assess for suicide risk, symptoms, and clinical deterioration and take appropriate action if needed. 2) The mobile app will contain questions regarding suicide risk and psychotic symptoms in every session, and will prompt participants to contact a crisis hotline, 911, and/or their local treatment provider/hospital if such risk is reported for immediate assistance. 3) Mobile device data will be uploaded onto secure servers remotely. As real-time data review is not feasible or sustainable in typical clinical settings, mobile data will be reviewed weekly by the study clinician as part of his/her routine monitoring and report-writing duties. This type of strategy is known as asynchronous communication (where there is a gap between communications compared with synchronous or "live" communication) and is often adopted in mobile health research. Patients will be informed that their responses will be reviewed periodically (not in real time), and that they may be contacted by study staff if safety risk is detected for the purposes of providing further assessment and assistance as necessary.

If any patient manifests clinical deterioration or psychotic relapse during study assessments or other study contacts (based on ratings in the severe range of > 5 for the items assessing psychotic symptoms from the Brief Psychiatric Rating Scale), we will either: (1) inform the patient's clinician, or (2) if the patient is not currently in treatment (at follow-up), we will provide the patient with a referral to a qualified clinician. This also applies if a participant manifests significant suicidal or homicidal ideation or risk, and we will take whatever steps necessary to ensure the patient's and/or other's safety. At the time that suicidality and/or clinical deterioration is identified, a study clinician will immediately evaluate the participant. In such cases, research staff will immediately contact one of the principal investigators, Drs. Moitra or Gaudiano, both of whom are licensed clinical psychologists and whom will be on-call at all times. Depending upon the specific situation, steps taken to ensure a participant's safety may involve: (1) escorting the patient to the hospital's ER for evaluation by an independent clinician and possible hospitalization, (2) alerting inpatient staff to the patient's level of risk, (3) notifying the patient's clinician, primary care physician, and/or family member for whom we have releases of information, or (4) calling the appropriate police departments. See adverse events reporting procedures below.

Confidentiality and loss of privacy

Risks. It is possible that confidential information provided by participants could be inappropriately disclosed to those outside the study. This includes through the uploading of data to the National Institute of Mental Health Database (NDA). Also, a text message or email could be intercepted or sent to an incorrect email address or phone number. Lastly, someone other than the participant may see or hear study related contacts done using videoconferencing. However, the risk of loss of privacy is judged to be minimal.

Minimization. Confidentiality will be maintained by numerically coding all data, by disguising identifying information, by keeping all data in locked file drawers, and by keeping electronic data on password-protected and secure servers. We will follow NDA guidelines to ensure that deidentified data are confidentially and securely updated. To further minimize risk, all electronic communications will be monitored by limiting access to authorized team members only, removing all PHI from messages, and transmitting all communications through a secure server. Text messages will be sent from a phone that is dedicated for use in this research

study that only research staff have access to. Participant information will be accessible only to research staff. Identifying information will not be reported. Study provided phones will be password-protected and encrypted. If participants choose to use their own smartphones, they will be encouraged to password protect their devices. The app will not be password protected but data is stored in such a way that information cannot be accessed after entered. All data (apps, documents, pictures, etc.) will be wiped clean from the phone before reuse. Only research staff will have access to any email communications and the dedicated study phone. All text and email communications will be limited to scheduling research-related appointments or study-related reminders, and will not send any messages containing urgent information or protected health information. We will keep interviews from stakeholders confidential and will not disclose this to their co-workers or supervisors. We will remove personally identifying information when reporting on stakeholder feedback so that individuals cannot be identified based on their specific comments. Participants will be informed of the potential risks to privacy when using videoconferencing. However, videoconferencing is optional, participants are informed about these risks in the consent, and they are instructed how to minimize this risk when using the technology. We also will use videoconferencing technology approved through current CNE policy that encrypts the communication (e.g., HIPAA compliant Zoom).

Risk of adverse events

Risks. In this type of population, the risk of adverse events occurring is present.

Minimization. Although this population may be at high risk for adverse events, it is unlikely that an adverse event will be caused by the research study. Our proposed mobile intervention was developed for people with psychosis and therefore, does not pose the same risks that a pharmacology trial might hold. In the case an Adverse Effect (AE) or a Serious Adverse Effect (SAE) related to the intervention were to occur, a written report of the AE or SAE will be prepared for submission to Dr. Linda Carpenter, the Chair of the Butler Hospital IRB. Any such AEs or SAEs will be presented to the full committee of the Butler Hospital IRB as soon as it is feasible. The report of such intervention-related AEs or SAEs will include whether they were expected or unexpected, a rating of severity of the event, a brief narrative summary of the event, whether the informed consent should be changed as a result of the event and whether all enrolled participants should be notified of the event. Finally, as part of the annual progress report (noncompeting continuation application) to NIH, we would provide summary information on all AEs and SAEs that have occurred during that year.

D2. Measures to Ensure Confidentiality

Breach of confidentiality is unlikely because all staff with access to participant data and identifying information have been trained in the management of sensitive clinical information. All data will be treated as confidential, and will only be available to research and clinical staff. Study data will be identified by participant code only, and no identifying information will ever be stored in association with participant data. Data will only be available to government or regulatory agencies as required by law. Prior to any assessment, participants will be informed of the limits of confidentiality regarding suicidal or homicidal intent, child or elder abuse, or inability to care for the self. All data will be stored on encrypted drives or a secure server within the Butler Hospital information technology system. Electronic data will be stored on password-protected computers. All electronic communications will be transmitted via secure, encrypted servers. No PHI will be included in any electronic communications. All paper records will be stored in a locked file cabinet within a locked office on Butler Hospital grounds. Butler Hospital has clear HIPAA regulations in place to ensure research compliance for both psychiatric and medical records. Additionally our mobile software service (ilumivu.com) is a HIPAA-compliant platform for the collection of EMA data and secure transmission of those data to an encrypted, cloud-based central server with dedicated data backup operated by the company. Study phones will be encrypted and password-protected and wiped clean of data before reuse. Text messages will only be sent from a phone dedicated for use in this research study, and will only be accessible to research staff. All text and email communications will be limited to scheduling research-related appointments or study-related reminders, and will not send any messages containing urgent information or protected health information.

D3. Data Safety Monitoring Plan

1. **Data management and protection.**

Drs. Gaudiano and Moitra will have responsibility for day-to-day monitoring of the quality of operations in all data collection. There are several sources of data. Research participants will complete questionnaires. Research assistants also code all data from research interviews. Only the participants' study identification number will appear on any of the final paper data collection instruments. Finally, the audio recordings will be recorded onto a dedicated device. The recordings will be downloaded after the interviews onto secure servers and the files will be deleted from the devices. The recordings will be transcribed and the audio files will be destroyed after study completion. A study ID will be used to identify the recordings. Otherwise, they are not connected with the primary study database in any way.

This study will use Care New England's instance of REDCap for the collection and storage of data. The study will not collect or store any actual data within REDCap until the project has been moved into REDCap's production environment. REDCap is a secure, web-based application developed by Vanderbilt University for building and managing surveys and databases. It is primarily designed to support online or offline data capture for research studies, quality improvement, and operations. REDCap provides easy data manipulation (with audit trails for reporting, monitoring and querying patient records), real-time data entry validation, and an automated export mechanism to common statistical packages. Care New England's instance of REDCap is hosted within the Care New England data center in Warwick, RI. This REDCap instance is role-based and is fully integrated with CNE's Active Directory structure. It enjoys 24/7/365 enterprise-level support and security inherit to CNE's HIPAA-compliant data center. Network transmissions (data entry, survey submission, and web browsing) to and from REDCap are protected via TLS 1.2 encryption. REDCap's data is stored on encrypted servers within CNE's data center. The REDCap Consortium is composed of thousands of active institutional partners in over one hundred countries who utilize and support REDCap. REDCap was developed specifically around HIPAA-Security guidelines, and more information about the consortium and system security can be found at http://www.projectredcap.org/.

All data collected by the research team are considered part of the subject's confidential record. Paper data forms collected from research participants will be kept in a locked file cabinet. All data will remain confidential. All data is stored on a secure research server, and backed up daily. Patient identifying information will be stored in a separate database and will be password protected in addition to being on a secure server.

Consistent with requirements by this study's funding source, NIMH, deidentified data will be uploaded to NIMH's NDA twice yearly (January and July) for the duration of the study. Research staff will follow procedures outlined in the NDA, including creating global unique identifiers for each participant to further ensure their confidentiality.

2. **Safety Plan and Adverse Event Identification and reporting**

Drs. Gaudiano and Moitra will be responsible for overseeing the daily safety of all participants. There are several ways in which they will become aware of adverse events. First, research staff will ask patients about serious adverse events (as defined by Office of Human Research Protections (OHRP); e.g., inpatient hospitalization). Second, all study staff will be trained in the OHRP definitions of adverse events that are also unanticipated problems; serious adverse events; or unanticipated problems that are not adverse events. All study staff are required to report any event that might meet one of these criteria to one of the PIs immediately both verbally and in writing. Any report of a serious adverse event will result in one of the PIs contacting the participant to further assess the event.

Adverse Events Definitions

Adverse Event – any unfavorable and unintended sign, symptom or disease temporally associated with the use of a medical or behavioral treatment or intervention regardless of whether it is considered related to the treatment or intervention.

Expected Adverse Event – an event that may be reasonably anticipated to occur as a result of the study procedure and is described in the consent form.

Unexpected Adverse Event – any adverse event which is not described in the consent form and is unanticipated. An event that might have been anticipated but is more serious than expected or occurs more frequently than expected, would be considered an unexpected adverse event.

Serious Adverse Event- (21 CFR 312) include any untoward medical occurrence that at any dose results in death or the immediate risk of death, hospitalization or prolonging of an existing hospitalization, persistent or significant disability/incapacity or a congenital anomaly/birth defect (NIH guide-6/11/99).

Study Definitions

Specifically, we will consider the following events Serious Adverse Events (SAE):

a. Death for any reason;
b. A suicide attempt, defined as any action taken with intent to die, as stated by the patient or noted in the medical record;
c. Inpatient psychiatric hospitalization

Additionally, we will consider the following events non-serious unanticipated problems:

a. Evidence of coercion to participate;
b. Participant distress resulting in stopping of the assessment or intervention;
c. Access of confidential information by a non-authorized person.

Severity

Each adverse event will be graded in terms of severity:

a. Non-severe adverse event
b. Severe adverse event resulting in hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity.
c. Life-threatening adverse event
d. Fatal adverse event

Attribution

For each adverse event, one of the following attributions is assigned:

Definite: Adverse event is clearly related to intervention
Probably: Adverse event is likely related to intervention
Possible: Adverse event may be related to intervention
Unlikely: Adverse event is doubtfully related to intervention
Unrelated: Adverse event is clearly not related to intervention

Suicidality. Because we will be recruiting individuals with psychiatric disorders, we may have some participants who disclose having suicide ideation or behavior. At the time that suicidality is identified by any study staff member for in-person assessments, they will contact a study clinician who will immediately evaluate that person. All study staff (e.g., research assistants) are trained in the Psychosocial Research protocol for managing suicidality. All clinical faculty in our research group, including Drs. Gaudiano and Moitra are experienced in management of suicidality and other clinical emergencies. Drs. Gaudiano and Moitra, both licensed psychologists, will be available during regular business hours. After hours there is always a licensed

mental health clinician (psychologist or psychiatrist) available on call by cell phone or pager in the Psychosocial Research Program.

When a clinician is asked to conduct an immediate evaluation, he or she will use our standard guidelines for conducting a suicide risk assessment. The clinician will determine whether it is necessary to take immediate action to prevent the participant from causing harm to him/herself. If needed, the study clinician may have a family member bring the person to Butler Hospital, send an ambulance, or transfer the participant to a local hospital emergency department. If the participant is not in immediate danger of hurting him or herself, we will take the following actions. First, we will inform the patient about procedures for contacting emergency services should they find themselves at risk for self-harm. Second, with the patient's permission, we will contact their mental health clinician to inform them of the suicidality. We will urge the patient to make an appointment with that provider to discuss treatment options. Third, if the patient consents, we will speak with one of their family members to ensure that he/ she is aware of the seriousness of the patient's symptoms and the agreed-upon treatment plan. We will provide treatment referrals if the patient wishes. Regardless of outcome, suicide assessments are always documented in writing.

Mobile device data will be uploaded onto secure servers remotely. As real-time data review is not feasible or sustainable in typical clinical settings, mobile data will be reviewed weekly by research staff. This type of strategy is known as asynchronous communication (where there is a gap between communications compared with synchronous or "live" communication) and is often adopted in mobile health research. Patients will be informed that their responses will be reviewed periodically (not in real time), and that they may be contacted by study staff if safety risk is detected for the purposes of providing further assessment and assistance as necessary.

Adverse Event Reporting. Based on the sources of information detailed above as well as direct patient contact and/or consultation with the scientific team, Drs. Gaudiano and Moitra will determine if the event is: a) an adverse event that is also an unanticipated problem related to study procedures or intervention; b) a serious adverse event; or c) an unanticipated problem that is not an adverse event. Considering the nature of the study and sample, we expect serious adverse events to occur, including suicide attempts and rehospitalizations (e.g., due to relapse). However, given the nature of the study, it is unlikely that SAEs will be related to the study procedures. The other adverse events that are possible include: inadvertent disclosure of protected health information and coercion. If any of these adverse events occur, or any other unanticipated events that are identified, the following procedure will be activated:

The research staff member who observes or is notified of an adverse event will contact the MPIs or their designee immediately. The MPIs or their designee will complete a Butler Hospital IRB Adverse Event Form for each event that will include a level of severity and determine attribution (intervention-related or not). Reporting timeframes will vary by SAE type;

1) **expected (i.e., psychiatric rehospitalization, suicide attempt) and unrelated SAEs**: reviewed by the MPIs ; provided to the DSMB in bi-annual data reports;
2) **unexpected or related SAEs**: to Butler IRB and DSMB within 10 days of ascertainment;
3) **all deaths**: to Butler IRB and DSMB within 5 days of ascertainment.

3. Data and Safety Monitoring Board (DSMB)

The DSMB will be constituted and will be responsible for monitoring the safety of participants and the quality of the data, as well as deciding on the appropriate termination of the study either when significant benefits or risks have been uncovered or when it appears that the clinical trial cannot be concluded successfully. Members of the DSMB include Kim Mueser, Ph.D. (Chair; Professor, Boston University), Louisa Sylvia, Ph.D. (Associate Professor, Massachusetts General Hospital), and Roger Vilardaga, Ph.D. (Assistant Professor, Duke University). These DSMB members have experience serving on other DSMBs and conducting research on severe mental illness and mobile technologies.

Both MPIs and the DSMB Chair will develop the Data Safety Monitoring Plan. It will then be circulated to the rest of the DSMB for feedback and approval. The board members will review the initial DSMB protocol to ensure that it captures the information necessary to evaluate the safety and efficacy of the study. The DSMB will then receive DSM reports bi-annually. A DSM report will include concerns about significant safety and data monitoring issues such as recruitment, retention, and quality of data collected.

Operating procedures of the DSMB include monitoring the protocol to evaluate the safety of the participants as pre-specified in the DSMP of the protocol, monitoring efficacy of the intervention being tested, and evaluating performance of the trial, as well as study admission data and protocol compliance. The specific content of the reports to the DSM include information about AEs and/or SAEs, treatment retention, recruitment, reasons for dropout, and interim efficacy data.

Only reports that meet the criteria of being a death (within 5 calendar days) or SAEs that are unexpected/related to study procedures (within 10 calendar days) will be reported to the DSMB within the specified timeframe after learning of the event. Summary reports of all adverse events will be provided to DSMB in bi-annual reports. Finally, as part of the annual progress report (noncompeting continuation application) to NIH, we would provide summary information on all adverse events that have occurred during that year.

As they deem necessary, the members of the DSMB will evaluate whether the presence of early unanticipated therapeutic results, side effects or adverse consequences are significant enough to warrant amendment, suspension, or early termination of the study and will independently make recommendations to the PIs to continue, to amend or to terminate the trial. Recommendations related to the study will be made in a written DSMB Report by the Board's Chairperson to the Principal Investigator and this DSMB Report, along with the DSMB meeting minutes, will be sent to the NIH Project Officer for the study.

E. Potential Benefits

The anticipated benefits of the study are threefold: the results will be used to advance understanding of the factors related to aiding patients' transition from inpatient or partial hospitalization to outpatient services, and to gather significant knowledge about the potentially beneficial role of a mobile device-based aftercare support tool. By participating in the clinical research project, participants may benefit from the additional intervention that they will receive. The study data provided to NDA may help researchers around the world learn more about mental health and how to help others who have problems with mental health. The risks associated with participation are minimal.

F. Risk-Benefit Ratio

Given the minimal level of risk(s) to the patients as outlined above for participating in the study, and the likelihood that some will benefit from the additional treatment, and the even greater possibility of benefits to the larger population of adults with psychosis transitioning out of the hospital, the risk/benefit ratio seems favorable.

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5) CRITERIA FOR WAIVER OF AUTHORIZATION FOR USE OF PROTECTED HEALTH INFORMATION (PHI)

5A. Does the requested use of PHI involve more than minimal risk to privacy?

☐ **YES [if " YES," project is not eligible for PHI Waiver]**

☒ **NO [if "NO," address 1-3 below]**

1. Plan to Protect Patient Identifiers from Improper Use and Disclosure:

Potential risks due to loss of confidentiality will be minimized by having all information collected and handled by research staff trained to deal appropriately with sensitive clinical issues. All research personnel will receive training in research ethics and be approved by the institution to conduct research. All information will be kept in locked files. Electronic data will be stored on encrypted drives/servers and password protected. Data will be available only to authorized personnel and subject codes will be used to store information in databases. No subject will be identified in any report of this project.

2. Plan to Destroy Identifiers or Justification for Retaining Identifiers:

PHI will be destroyed upon study completion plus 1 year.

3. Assurances that the PHI will not be Re-used or Disclosed:

Information collected will only be used for the purposes described below and will be treated as confidential material as described above.

5B. Could the research be practicably conducted without a waiver?

☐ **YES** ☒ **NO**

5C. Could the research be practicably conducted without access to and use of the PHI?

☐ **YES** ☒ **NO**

5D. PHI is only needed for activities preparatory to research

☒ **YES** ☐ **NO**

6) DESCRIPTION OF PHI TO BE COLLECTED UNDER WAIVER

Chart reviews of new patients will be routinely conducted by study staff to determine if they are likely to meet inclusion/exclusions criteria for the study as described above. PHI to be obtained: patient demographic and contact information (name, address, telephone numbers, gender, age, race, marital status, occupation status) and patient psychiatric/treatment history (diagnoses and suicide history, past and current psychological and/or pharmacological treatments, current mental health provider contact information, lab results).

7) ADVERTISEMENTS

Study brochure; see attached.

8) INFORMED CONSENT FORM (ICF), ASSENT OF MINOR & PARENTAL PERMISSION FORM

See attached.