BMJ Open

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042751
Article Type:	Protocol
Date Submitted by the Author:	15-Jul-2020
Complete List of Authors:	Polillo, Alexia; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Foussias, George; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Wong, Albert; Centre for Addiction and Mental Health, Campbell Family Mental Health Research Institute; University of Toronto, Psychiatry Ampofo, Augustina; Centre for Addiction and Mental Health Stergiopoulos, Vicky; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Anderson, Kelly; Western University, Epidemiology & Biostatistics Bromley, Sarah; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition D'Arcey, Jessica; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Institute of Medical Science de Oliveira, Claire; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Institute of Health Policy, Management and Evaluation Duda, Lillian; Centre for Addiction and Mental Health Henderson, Joanna; Centre for Addiction and Mental Health, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health; University of Toronto Faculty of Medicine, Psychiatry Kidd, Sean; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Kurdyak, Paul; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Wang, Wei; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Zaheer, Juveria; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Voineskos, Aristotle; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Kozloff, Nicole; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry
Keywords:	Schizophrenia & psychotic disorders < PSYCHIATRY, Clinical trials < THERAPEUTICS, Child & adolescent psychiatry < PSYCHIATRY, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Public

	health < INFECTIOUS DISEASES

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Authors

Alexia Polillo, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

George Foussias, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Albert H.C. Wong, MD, PhD, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Augustina Ampofo, BA, Centre for Addiction and Mental Health, Toronto, Canada

Vicky Stergiopoulos, MD, MHSc, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Kelly K. Anderson, PhD, Department of Epidemiology and Biostatistics, Western University, London, Canada

Sarah Bromley, OT, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health, Toronto, Canada

Jessica D'Arcey, MSc (candidate), Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Institute of Medical Science, University of Toronto, Toronto, Canada

Claire de Oliveira, MA, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Lillian Duda, MPA, Centre for Addiction and Mental Health, Toronto, Canada

Joanna Henderson, PhD, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Sean A. Kidd, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Paul Kurdyak, MD, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Wei Wang, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Juveria Zaheer, MD, MSc, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Aristotle N. Voineskos, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Nicole Kozloff, MD, SM, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Corresponding author
Nicole Kozloff, Centre for Addiction and Mental Health
250 College Street, 7th floor
Toronto, ON M5T 1R8
n.kozloff@mail.utoronto.ca
416-535-8501

Word count
3980/4000 words

Keywords
Schizophrenia and psychotic disorders
Early psychosis intervention
Mobile health interventions
Patient and family engagement
Pragmatic clinical trials

ABSTRACT

Introduction

Psychosis is a disabling condition that typically has its onset in adolescence and early adulthood. Many young people with psychosis have difficulty navigating services or are reluctant to engage in treatment until their illness becomes an emergency. Consequently, nearly half of all new psychotic disorders are diagnosed in the emergency department (ED). Most young people who present to the ED with psychosis do not receive timely follow-up with a psychiatrist, and even fewer with early psychosis intervention (EPI) services. We aim to use short message service (SMS), a low-cost, low-complexity, youth-friendly approach, to improve transitions from the ED to EPI services.

Methods and analysis

This is a protocol for a pragmatic randomized, single blind, controlled trial with accompanying economic and qualitative evaluations conducted at the Centre for Addiction and Mental Health (CAMH) in Toronto, Canada. A consecutive series of 186 participants aged 16 to 29 referred by the CAMH ED to CAMH's EPI program will be recruited for a trial of a 2-way SMS intervention involving reminders, psychoeducation, and check-ins. The primary outcome will be attendance at the first consultation appointment assessed through chart reviews. Secondary outcomes will include indicators of longer-term service engagement as well as symptoms and functioning 6 months following study enrollment, and health service utilization for up to 2 years using administrative data. A cost-effectiveness analysis and qualitative analysis exploring user perspectives of the intervention will also be performed. Patients and families with lived experience will be engaged in all aspects of the project.

Ethics and dissemination
Research ethics board approval has been obtained from CAMH. Findings will be reported in scientific journal articles and shared with key stakeholders including youth, family members, knowledge users, and decision makers.

Trial registration number clinicaltrials.gov #NCT04298450

ARTICLE SUMMARY

Strengths and limitations of this study

- Pragmatic randomized controlled trial leveraging mobile health technology, chart reviews, routinely collected administrative data, and economic and qualitative evaluations.
- Intervention well-positioned for local adoption as well as scale and spread to other EPI programs and youth mental health services more broadly.
- Collaboration with health system decision-makers, knowledge users, team members with clinical and research expertise, people with lived experience of psychosis, and key relationships with organizations well-positioned to support widespread implementation.
- Conducting the trial at a single site will support streamlined recruitment but may limit generalizability of our findings.

INTRODUCTION

Psychosis, characterized by delusions and/or hallucinations, typically manifests during adolescence or early adulthood. It is the characteristic presentation of schizophrenia and schizoaffective disorder, and often occurs in bipolar disorder.[1] These disorders can cause significant dysfunction: in disability weighting surveys used to establish global disease burden, participants rated schizophrenia as the disorder most disabling for individuals.[2] Young people experience greater mortality by up to 24-fold in the year following a first psychotic disorder diagnosis compared to peers in the general population.[3] In the long term, psychotic disorders are associated with ongoing increased mortality particularly by suicide,[4] substance use disorders, homelessness, victimization, acts of violence,[5] and high economic costs due to healthcare use as well as lost productivity.[6 7] Early psychosis intervention (EPI) is a model developed to provide treatment early in the course of illness to improve patients' long-term trajectories and reduce the burden on individuals and their families. The rationale for EPI has been strengthened by consistent findings that long duration of untreated psychosis is associated with greater symptom burden, lower likelihood of remission and poor social functioning and global outcomes.[8] Members of our team have shown that EPI service use is associated with a four-fold reduction in all-cause mortality for young people with psychosis compared to those who do not access EPI services.[9] EPI services have also been associated with improved access to psychiatric care, reduced risk of relapse, fewer hospital readmissions, and increased employment rates.[9-13] EPI can be a lifechanging and lifesaving intervention for young people with psychosis.

EPI programs are well-established in Ontario and provide services to young people with early psychosis across the province.[14] Despite this, and the clear mandate for EPI programs to promote their services and minimize barriers to care, many youth with psychosis in Ontario either never access these services, or enter them far later than indicated.[15] In Canada, nearly half of all new psychotic disorders are diagnosed in the ED.[16] We recently found that among young people across Ontario presenting with psychotic disorders to the ED for the first time, 40% received no outpatient mental health follow-up within 30 days and only 45% saw a psychiatrist.[17] The reasons young people with psychosis discharged from the ED did not receive follow-up were unclear in this study: both issues of access (availability and awareness of services) and engagement (youth following through on referrals) are potential explanations. Our experience at the Centre for Addiction and Mental Health (CAMH) in Toronto, where our EPI program sees referred patients for consultation within 2 weeks on average, suggests a problem of engagement: according to clinic data, 50% of the youth referred from the ED do not attend their first EPI consultation appointment (compared with approximately 30% from all other referral sources). It is clear that new approaches are required to engage this population in accessing evidence-based care that is life-saving and improves illness outcomes. In surveys of patients and families in EPI services, appointment reminders are cited as a top factor that would improve service engagement, with a preference for email and text communication.[18-20]

Mobile health technologies are increasingly being tested to improve outcomes among young people with mental illness. Short message service (SMS) or text message is a commonly used mode of communication by adolescents and young adults: in a survey of users of community mental health services, access to mobile phones approached 100%.[21] SMS is associated with low user and financial burden. SMS does not require people to own a smartphone, have data plans, or have access to wireless internet. In a study of people with psychosis, participants were found to be highly engaged with an SMS intervention.[22] SMS reminders have been associated with improved service engagement in psychosis across studies,[23] including twice the attendance rates for initial appointments in an EPI program.[24] An ongoing pilot study at CAMH investigating the effect of a weekly 2-way SMS intervention on

service engagement during the first year of EPI treatment found this approach to be feasible and valued by participants.[25] We are unaware of any studies examining interventions specifically to improve the transition in care from the ED to EPI for young people with psychosis, using mobile health technologies or otherwise.

Objectives

"ED to EPI," a pragmatic randomized, single blind, controlled trial[26] with accompanying economic and qualitative evaluations, aims to improve the transition from the ED to EPI services for youth with psychosis using an SMS text messaging intervention. It is pragmatic in its participant eligibility criteria (broad and inclusive), comparison intervention (usual care), follow-up intensity (low), primary trial outcome (objective, meaningful and assessed under usual conditions), measurement of participant compliance and practitioner adherence to study protocol (unobtrusive), and analysis of primary outcome (inclusive, i.e. intention-to-treat).[27] Our study team, in addition to clinicians and researchers, includes a patient and family member with lived experience of using EPI services and key decision-makers to increase the relevance and uptake of the intervention. We will assess the effectiveness of an SMS intervention in improving attendance at the first EPI appointment, as well as longer-term service engagement, and system-level outcomes, enabled through data linkage with ICES (previously known as the Institute for Clinical Evaluative Sciences), which holds data on all hospital and physician visits for the province. We will also evaluate the cost effectiveness of the intervention and explore young people's perspectives on its various components. Specifically, our primary objectives are to:

1. Evaluate the effect of an SMS intervention on attendance at the first consultation appointment within 30 days of study enrolment;
2. Assess indicators of longer-term service engagement 6 months following study enrolment;
3. Determine system-level outcomes, including ED visits and psychiatric hospitalizations, as a function of receiving the SMS intervention, and its cost effectiveness, factoring costs of the intervention and cost offsets of health service utilization;
4. Explore young people's experiences of the intervention and their perspectives on its various components.

METHODS AND ANALYSIS

Study setting

The study setting will be the Gerald Sheff and Shanitha Kachan Emergency Department at CAMH, Ontario's only 24-hour stand-alone psychiatric emergency service. The ED also houses a drop-in "Bridging Clinic" which provides care to less acute patients who are diverted after ED triage, and rapid follow-up care for patients discharged from the ED and CAMH inpatient units. Together, they serve approximately 1,200 patients each month. The EPI program at CAMH receives over 600 referrals for suspected psychosis annually, approximately 25% of which are from the ED and Bridging Clinic. Reflecting the Ontario EPI Program Standards, CAMH EPI services are delivered by multidisciplinary teams, employ strategies to promote early entry and ongoing engagement, and provide pharmacotherapy and psychosocial therapies for an average of 3 years.[14] Patients are assigned to the next available and/or most appropriate psychiatrist and case manager (nurse, social worker, or occupational therapist) for a joint consultation appointment, typically within 2 weeks, and are contacted by phone by the EPI program administrator to book and confirm their appointment. After the initial appointment is confirmed, patients receive a phone call reminder the day before their scheduled appointment. As part of routine care, patients who do not attend their scheduled first appointment receive follow-up calls to reschedule an appointment for up to 30 days from the initial referral.

Eligibility criteria

Study inclusion criteria mirror the intake criteria for the CAMH EPI program. Participants will be eligible for the study if they: 1) are between 16 and 29 years old and 2) have been referred by the CAMH ED to CAMH EPI services for suspected psychosis. Our only exclusion criterion is inability to communicate in basic written English. In our pilot SMS study at CAMH, fewer than 5% of potential participants were excluded for lacking a phone; we have budgeted to offer 5% of participants access to a prepaid cellphone for the duration of the study.[25]

Intervention procedures

Study participants will be recruited at the time of EPI referral for a trial of an SMS intervention designed to engage them during the waiting period for their consultation appointment. They will be randomized to receive either sham or active SMS intervention. Sham SMS will consist of 1 message sent just after enrolment indicating that they will be contacted for an appointment. Active SMS intervention will include the initial message sent to the control group, plus a series of subsequent messages. These will include the following content: 1) appointment reminders and instructions, 2) psychoeducational material, and 3) 2-way communication check-ins to rate distress (Figure 1). Messages sent back by participants will be monitored by the research team, and the case manager assigned to their consultation appointment will be notified and will respond accordingly if there are indicators of elevated distress. The intervention will continue until the patient attends the first consultation appointment, or for up to 30 days if the patient does not attend, which reflects the program's practice of closing referrals for non-attending patients.

Messages will be sent through CAMH's in-house Research Electronic Data Capture (REDCap) platform via a third-party plug-in, Twilio, which supports routing of SMS messages to participant devices.[28-30] All data is stored securely on CAMH's REDCap servers or in a locked office and password-protected database on CAMH's secure network. The purpose of the sham intervention is to separate out the content of the intervention (i.e. reminders, psychoeducation, 2-way check-ins) from the effect of simply receiving SMS messages, decreasing participant bias.

Assignment of intervention

Immediately after informed consent, participants will be randomized by REDCap to the active or sham intervention. Generation of the randomization sequence will be managed by the study biostatistician who is not involved in enrolling participants or assigning intervention arms. Randomization will be stratified by sex (male or female) and referral source (ED or Bridging Clinic), using a computer algorithm to determine a randomized, blocked allocation of participants into intervention groups within strata. The predetermined computer algorithm is housed in REDCap, and is locked, allowing for concealed assignment before individual randomization. Once randomized, treatment assignment will be known only by the study personnel involved in managing the SMS intervention and the case manager monitoring text message responses; the principal investigator and study personnel involved in the chart review and the ICES analysis will remain blind to treatment assignment. Study personnel involved in the qualitative interviews and analysis will also be aware of treatment assignment since only individuals receiving the active intervention will participate in this component of the project.

Sample size

Our sample size calculations are based on the primary outcome of rate of attendance at the EPI program consultation appointment. The current rate of attendance at the first consultation appointment for patients referred from the ED and Bridging Clinic is 50%; we have powered our study to increase the rate of attendance to 70%, which is the average for all

referral sources other than the ED and Bridging Clinic. A total of 186 participants (93 per group) will provide >80% power to detect a change in attendance from 50% to 70% at alpha <0.05. Non-compliance and loss to follow-up are not a concern for our primary outcome since these are counted in the outcome as nonattendance at the consultation. Adjusting analyses for covariates expected to affect attendance (e.g., age, sex) is expected to further increase power. The sample sizes for secondary and exploratory outcomes will be smaller, as only some participants who attend the first appointment will be deemed eligible for, offered, and enrolled in EPI services.

Study procedures

We will recruit 186 patients consecutively referred from the CAMH ED and Bridging Clinic to the CAMH EPI program at the time of discharge. During business hours and into the evening, research staff will be on call to the ED to recruit patients as soon as they are identified for the study. Eligible participants who present after hours may be identified by ED staff and referred to the research team who will send them an e-consent form via SMS or email. Additionally, potential participants who are missed in the ED/Bridging clinic may be identified by the EPI clinic administrator who will approach them over the phone and send them an e-consent form via SMS or email. We have used the approach of having clinical and administrative staff obtain verbal consent to send e-consent forms in other studies with this population.[19]

As part of informed consent, participants will be asked to consent to a review of their chart, a follow-up web-based survey, and linkage of their information to data held at ICES. They will also be given the option to provide consent to be re-contacted for participation in a qualitative interview. There will be no additional in-person assessments for the quantitative component of this study. CAMH uses an electronic health record, which facilitates data abstraction from multiple clinical programs (i.e., both the ED and Bridging Clinic and EPI program). Research staff and students will be trained by the clinician principal investigators to abstract data into a structured database.

All study participants will receive a $10 e-giftcard once the baseline e-visit is complete. Participants in the active intervention group who complete a web-based survey will receive another $10 e-giftcard and those who complete an in-person qualitative interview will receive a $50 e-giftcard. It will be clarified through the consent process that honoraria are to compensate participants for their time and will not be tied to clinical appointment attendance.

Outcome measures

Chart review

Outcome measures are shown in Table 1. CAMH uses many standardized assessment forms which increases the completeness of patient data. Demographic variables, clinical diagnoses, substance use, duration of untreated psychosis (measured as the period of time from first onset of psychotic symptoms to initiation of EPI services and initiation of treatment with an antipsychotic or mood-stabilizing medication), characteristics of the ED visit from which they were referred (voluntary vs. involuntary status, timing), and family involvement in care will be abstracted from the chart at the time of consultation. Additional variables will likely be available but only for patients accepted into the EPI program, and this will be reflected in the data analysis. These include several assessments that are performed routinely in the EPI program. The Service Engagement Scale (SES)[31] is a brief validated tool designed to measure engagement with community mental health services. In 14 items, it assesses patients' availability for treatment, collaboration, help-seeking behaviours and treatment adherence on a four-point Likert scale with higher scores indicating difficulties in service engagement. The Brief Psychiatric Rating Scale (BPRS)[32] is an interviewer-rated measure of psychiatric symptoms

commonly used as an outcome measure for psychotic disorders. The Clinical Global Impression (CGI)[33] is a clinician-rated measure of the patient's global severity of illness prior to and after initiating a medication. It includes subscales for Severity and Improvement. Medication and appointment nonadherence will also be assessed over 6 months of treatment. Lastly, after 6 months, current EPI enrolment status will be assessed and categorized as: not offered or enrolled in treatment (e.g., because they did not ultimately have psychosis), enrolled but disengaged prematurely, accepted for treatment but transitioned to other services, or continued in treatment.

Administrative data

Primary data collected for the study will be linked deterministically to data sources held at ICES via participants' unique health card numbers. The information available for each participant will be de-identified, stored, and analyzed onsite at ICES following procedures approved by Ontario's Information and Privacy Commissioner. The following ICES data sources will be used: the Ontario Mental Health Reporting System (OMHRS), capturing hospitalizations on adult inpatient mental health units,[34] the Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), capturing all hospital admissions including hospitalizations on child and adolescent inpatient mental health units,[35 36] National Ambulatory Care Reporting System (NACRS) which captures all ED visits,[37] Ontario Health Insurance Plan (OHIP) claims database, which captures outpatient physician visits,[35] Registered Persons Database, which contains health card numbers, demographic information, and deaths, and Ontario Drug Benefits (ODB) claims database, which provides information on all covered prescriptions (based on financial need for those under age 65 and for young people up to age 25 who lack private insurance). These data will also be used for cost effectiveness analysis. Outcomes examined in the linked ICES data are listed in Table 1.

Table 1. Summary of outcome measures and covariates

Type	Variables	Data Source
Demographic characteristics	Age	Chart review (CAMH Health Equity form and notes)
	Sex and gender	
	Sexual orientation	
	Race/ethnicity	
	Born in Canada	
	Religious/spiritual affiliation	
	Highest level of education	
	Source of income and family income	
	Number of people supported by income	
	Employment status	
	Legal history	
	Housing status	
	Living situation	

	Experience of homelessness	
	Relationship status	
Clinical characteristics	Clinical diagnoses	Chart review
	Substance use	
	DUP	
	Family involvement in care	
	BPRS[32]	
	CGI[33]	
Service engagement	Attendance at consultation appointment	Chart review
	SES[31]	
	Medication and appointment nonadherence	
	EPI enrolment status	
System-level outcomes*	Number of ED visits	NACRS[37]
	Number of inpatient mental health hospitalizations	OMHRS,[34] CIHI-DAD[35 36]
	Number of days in inpatient mental health hospitalizations	OMHRS,[34] CIHI-DAD[35 36]
	Number of outpatient mental health visits	OHIP[35]
	Prescription drugs – psychiatric medications, continuously vs. noncontinuously prescribed	ODB
	Mortality	Registered Persons Database

*Administrative data held at ICES
CAMH, Centre for Addiction and Mental Health; DUP, duration of untreated psychosis; BPRS, Brief Psychiatric Rating Scale; CGI, Clinical Global Impression; SES, Service Engagement Scale; EPI, early psychosis intervention; ED, emergency department; OMHRS, Ontario Mental Health Reporting System; CIHI-DAD, Canadian Institute of Health Information Discharge Abstract Database; NACRS, National Ambulatory Care Reporting System; OHIP, Ontario Health Insurance Plan; ODB, Ontario Drug Benefits.

Statistical analysis

Primary analysis

Descriptive and graphical statistics will be used to summarize the data on all randomized participants and to confirm that there are no group differences in baseline demographics and clinical characteristics. Distributional assumptions will be inspected and appropriate transformations or non-parametric methods will be applied as necessary. In general, generalized linear models[38] will be used throughout. These models account for deviation from normal assumption of the outcome variables and control for covariates.

Our analysis of the primary outcome will be a logistic regression to examine the likelihood of attendance at the EPI consultation with treatment assignment using risk ratios.[39] We will carefully select demographic variables and factors known to influence treatment engagement (e.g., substance use, family involvement in care)[40] to be included in the model as covariates. A difference in attendance between groups will be declared at a significance level of 0.05. Similar models will be used to address the secondary hypotheses, with specific types of models appropriate to each outcome, including time-to-event analysis to examine premature disengagement from services. Administrative data outcomes will be examined using generalized linear models with proper distribution assumptions.

Additional analyses: moderation and generalizability

We plan to conduct two additional exploratory analyses. First, we will run moderation analyses on potential effect modifiers by adding an interaction term between the potential moderator and the treatment assignment indicator in the generalized linear models. We are specifically interested in the moderation effects of health equity factors including gender, race/ethnicity, and housing status. A significant interaction will provide evidence that the treatment effects may be different in the subgroups. A second exploratory analysis will be conducted to evaluate the impact of selection bias of the study sample and estimate the population average treatment effects by employing weighted analysis using propensity scores.[41]

Missing data

The risk of missing data is mitigated through the use of chart review and analysis of administrative data. While the primary outcome will not suffer from attrition, other outcomes will, as some follow-up data will only be available for participants who attended their consultation appointment and those who are enrolled in CAMH EPI services. For these additional outcomes, we plan to use multiple imputation methods developed by Schafer to correct potential bias that could be introduced by missing data.[42]

Economic evaluation

We will undertake a cost-effectiveness analysis examining attendance at the consultation appointment as the outcome, adopting the perspective of the public third-party payer (i.e., the Ontario Ministry of Health). We will collect data on the costs of delivering both arms of the intervention. In addition, using a costing algorithm available at ICES,[43] we will estimate all direct patient-level healthcare costs incurred by the public third-party payer for the intervention and control groups, which will include costs of hospitalizations, ED visits, physician services (i.e., primary care, psychiatry and other) and diagnostic tests, outpatient prescription drugs for individuals covered under the provincial public drug insurance plan, and other hospital-based care. Assuming that all subjects will incur (non-zero) healthcare costs, we will use a generalized linear model with a gamma distribution and log link to model healthcare costs. We will use a net benefit regression approach to model probabilities of cost effectiveness for each additional patient referred who attends their consultation appointment in the intervention compared with control group.

Understanding patient experiences: Survey and qualitative analysis

Participants in the active intervention group will receive a one-time survey sent as a web-link to their phone or email address. Survey topics include user experience, attitudes toward the SMS intervention, its perceived benefits and challenges, acceptability, and suggestions for improvements. Those who consent to participate in the qualitative research component will be re-contacted by phone or email to participate in semi-structured interviews to gain a more in-depth

understanding of survey topics. A subsample of 10-15 participants in the active intervention group will be purposively selected to maximize diversity of age, gender, and service attendance. We will use critical realist theory as an underlying framework to guide our interviews, surveys, and analysis.[44] Interviews will be completed until thematic saturation is achieved, estimated at 12 participants. Interviews will be digitally audio-recorded and transcribed verbatim. Surveys will be completed and stored in REDCap. Transcriptions and survey responses will be analyzed using thematic content analysis in NVivo-11. Research participants will be invited to assist with member checking to confirm that themes reflect their experiences. The analysis can inform future improvements to the intervention and considerations for broader implementation, privileging the experiences of the patients attending these programs.

PATIENT AND PUBLIC INVOLVEMENT

A youth and family member who previously received EPI services have been engaged in helping shape the intervention and study design from project inception. They are active members of the project's Steering Committee that meets monthly to inform study design, implementation, evaluation, and dissemination of results. They will have key roles in the plan to spread the intervention, if successful, to other EPI programs by working with patients and families to adapt the intervention to local contexts. Additional youth with lived experience of receiving EPI services have been consulted on an ad hoc basis through the CAMH Youth Engagement Initiative to provide detailed feedback on the SMS intervention. Patient and family representatives on the research team are compensated for their time.

ETHICS AND DISSEMINATION

The study was approved by the Research Ethics Board (REB) at the Centre for Addiction and Mental Health. The study protocol was prepared according to SPIRIT guidelines (Supplemental File)[45] and registered with clinicaltrials.gov on March 6, 2020 (NCT04298450; https://clinicaltrials.gov/ct2/show/NCT04298450?term=ed+to+epi&draw=2&rank=1). REB-approved protocol amendments will be posted on the site. The principal investigators and study team will meet regularly to review accrued data, data confidentiality, any adverse events, adherence to protocol design, recruitment and implementation. This intervention has been designed to have high likelihood of adoption and readiness for spread and scale-up because it responds to a critical need, has a strong evidentiary basis, has advantages over existing practice and is both low complexity and low cost.[46] This trial focuses on a particularly vulnerable population—young people transitioning from adolescence to adulthood and from the ED to EPI services—but the basic intervention is widely applicable. The software platform utilized to coordinate this intervention is available at no charge, and the SMS functionality for sending and receiving messages carries a nominal fee, supporting broad uptake.

The results of the trial will be reported in scientific journal articles and shared with key stakeholders as they become available. Our study team includes the co-chair of the Early Psychosis Intervention Ontario Network, a network of over 50 EPI programs across Ontario, and several members of the Canadian Consortium for Early Intervention in Psychosis, providing a durable and established community of practice for immediate spread. De-identified participant data will be available upon reasonable request other than system-level data held at ICES. Requests can be made by contacting the principal investigator Dr. Nicole Kozloff at nicole.kozloff@camh.ca and will be managed by the Steering Committee.

CONCLUSIONS

This pragmatic randomized-controlled trial of a low-cost, low-complexity SMS intervention aims to improve the transition from the ED to EPI services for young people with psychosis. It targets a brief but critical period: if young people cannot even get in the door to EPI

services, there is no way for them to reap the many known benefits of EPI care. Improving the ED to EPI transition has the potential to result in more young people with psychosis getting appropriate treatment earlier. The proposed intervention is also likely to be easily adaptable to other referral pathways to EPI services and youth mental health services more broadly. At potentially lower cost to the health system, applying this SMS intervention to the ED to EPI transition has the potential to lead to improved short-term symptoms and functioning, long-term disease trajectories, decreased burden on patients and families, and fewer deaths among young people with psychosis.

Figures

Figure 1. Study intervention schedule*

*This figure represents a summary of the intervention schedule and is not exhaustive of text message content

SMS, short message service; Right arrow, incoming text messages received by participants; Left arrow, outgoing text messages sent by participants

Author contributions

NK is the principal investigator who conceived the original study design and obtained funding, with most of the current authors having contributed to the funding application, and all authors having participated in revisions to the study design for important intellectual content. AP and NK drafted the protocol. AA and LD consulted on patient and public involvement. WW consulted on the biostatistical analysis plan. All authors read, revised and approved the final version of the manuscript.

Funding statement

This work was supported by the Canadian Institutes of Health Research Transitions in Care Team Grant #165726 as well as by the CAMH Foundation. The funders were not involved in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities.

Competing interests statement

The authors declare no competing interests.

Patient and public involvement

Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research.

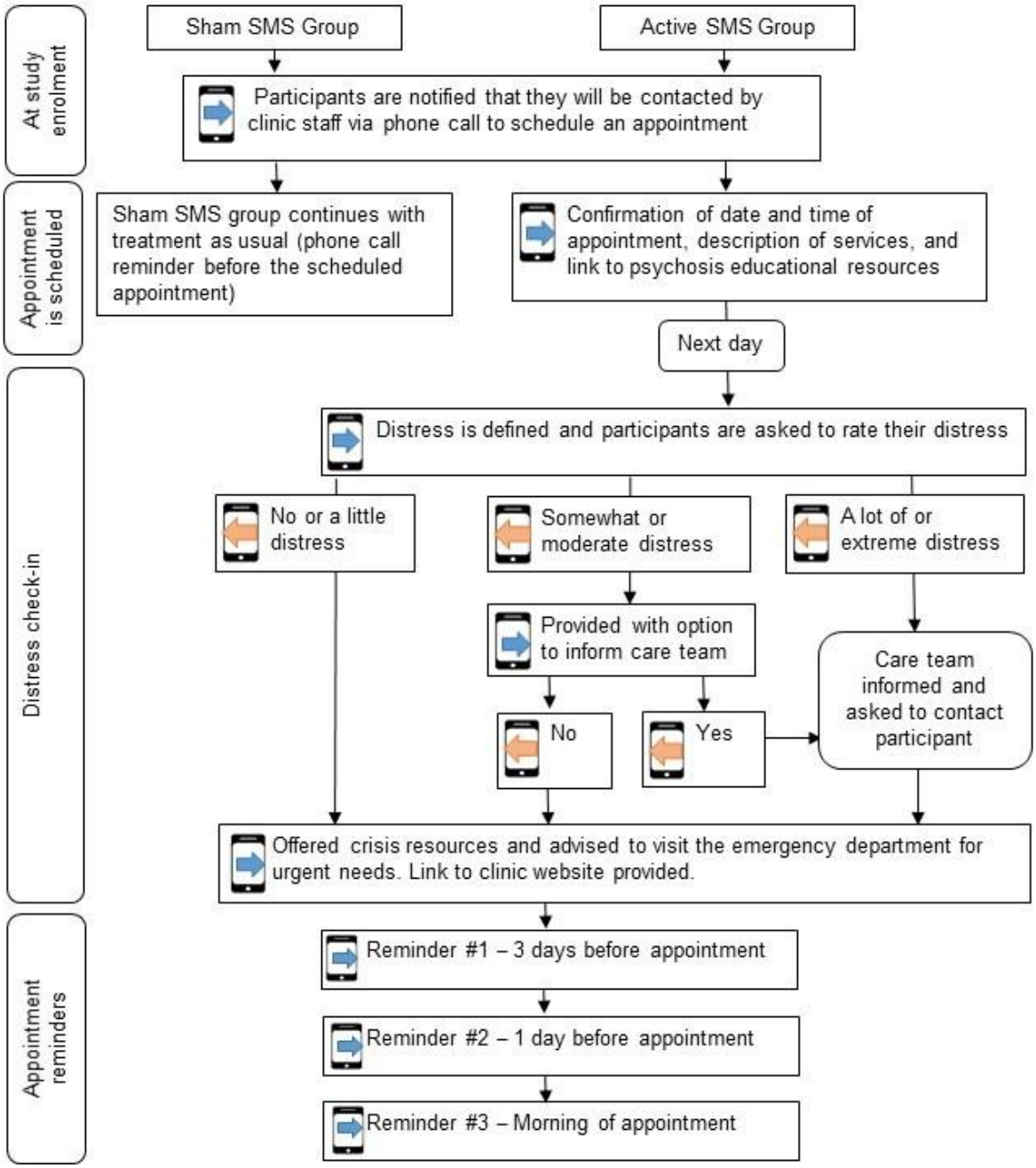
REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. - 5th ed. Arlington, VA: American Psychiatric Publishing 2013.
2. Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013;382(9904):1575-86. doi: 10.1016/s0140-6736(13)61611-6
3. Schoenbaum M, Sutherland JM, Chappel A, et al. Twelve-month health care use and mortality in commercially insured young people with incident psychosis in the United States. *Schizophr Bull* 2017;43(6):1262-72. doi: 10.1093/schbul/sbx009
4. Zaheer J, Olfson M, Mallia E, et al. Predictors of suicide at time of diagnosis in schizophrenia spectrum disorder: A 20-year total population study in Ontario, Canada. *Schizophr Res* 2020 doi: 10.1016/j.schres.2020.04.025 [published Online First: 2020/06/09]

5. Lieberman JA, First MB. Psychotic disorders. *N Engl J Med* 2018;379(3):270-80. doi: 10.1056/nejmra1801490
6. de Oliveira C, Cheng J, Rehm J, et al. The economic burden of chronic psychotic disorders in ontario. *J Ment Health Policy Econ* 2016;19(4):181-92. [published Online First: 2016/12/20]
7. Goeree R, Farahati F, Burke N, et al. The economic burden of schizophrenia in Canada in 2004. *Curr Med Res Opin* 2005;21(12):2017-28. doi: 10.1185/030079905x75087
8. Penttila M, Jaaskelainen E, Hirvonen N, et al. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2014;205(2):88-94. doi: 10.1192/bjp.bp.113.127753
9. Anderson KK, Norman R, Macdougall A, et al. Effectiveness of early psychosis intervention: comparison of service users and nonusers in population-based health administrative data. *Am J Psychiatry* 2018;175(5):443-52. doi: 10.1176/appi.ajp.2017.17050480
10. Craig TK, Garety P, Power P, et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ* 2004;329(7474):1067. doi: 10.1136/bmj.38246.594873.7C [published Online First: 2004/10/16]
11. Petersen L, Jeppesen P, Thorup A, et al. A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ* 2005;331(7517):602. doi: 10.1136/bmj.38565.415000.E01 [published Online First: 2005/09/06]
12. Malla A, Schmitz N, Norman R, et al. A multisite Canadian study of outcome of first-episode psychosis treated in publicly funded early intervention services. *Can J Psychiatry* 2007;52(9):563-71. doi: 10.1177/070674370705200904 [published Online First: 2007/10/24]
13. Bond GR, Drake RE, Luciano A. Employment and educational outcomes in early intervention programmes for early psychosis: a systematic review. *Epidemiol Psychiatr Sci* 2015;24(5):446-57. doi: 10.1017/S2045796014000419 [published Online First: 2014/07/16]
14. Ontario Ministry of Health and Long-Term Care. Early Psychosis Intervention Program Standards. Toronto, ON, 2011.
15. Anderson KK, Norman R, Macdougall AG, et al. Estimating the incidence of first-episode psychosis using population-based health administrative data to inform early psychosis intervention services. *Psychol Medicine* 2018:1-9. doi: 10.1017/s0033291718002933
16. Anderson KK, Fuhrer R, Wynant W, et al. Patterns of health services use prior to a first diagnosis of psychosis: the importance of primary care. *Soc Psychiatry Psychiatr Epidemiol* 2013;48(9):1389-98. doi: 10.1007/s00127-013-0665-3
17. Kozloff N, Jacob B, Voineskos AN, et al. Care of youth in their first emergency presentation for psychotic disorder: a population-based retrospective cohort study. *J Clin Psychiatry* 2018;79(6) doi: 10.4088/JCP.17m11947 [published Online First: 2018/11/13]
18. Lal S, Dell'Elce J, Tucci N, et al. Preferences of young adults with first-episode psychosis for receiving specialized mental health services using technology: a survey study. *JMIR Ment Health* 2015;2(2):e18. doi: 10.2196/mental.4400 [published Online First: 2015/11/07]
19. Patient and Family Perspectives on Improving Engagement in Early Psychosis Intervention. Congress of the Schizophrenia International Research Society; 2019; Orlando, Florida, USA.
20. Using REDCap to evaluate youth and family perspectives on engagement in early psychosis intervention. REDCap Con December 2019; Toronto, Ontario, Canada.

21. Ennis L, Rose D, Denis M, et al. Can't surf, won't surf: the digital divide in mental health. *J Ment Health* 2012;21(4):395-403. doi: 10.3109/09638237.2012.689437 [published Online First: 2012/06/21]
22. Kauppi K, Kannisto KA, Hatonen H, et al. Mobile phone text message reminders: measuring preferences of people with antipsychotic medication. *Psychol Med* 2015;168(1-2):514-22. doi: 10.1016/j.schres.2015.07.044
23. D'Arcey J, Collaton J, Kozloff N, et al. The use of text messaging to improve clinical engagement for individuals with psychosis: systematic review. *JMIR Ment Health* 2020;7(4):e16993. doi: 10.2196/16993
24. Thomas IF, Lawani AO, James BO. Effect of short message service reminders on clinic attendance among outpatients with psychosis at a psychiatric hospital in Nigeria. *Psychiatr Serv* 2017;68(1):75-80. doi: 10.1176/appi.ps.201500514
25. Using short message service as a means of engagement in early psychosis. IEPA 11th International Conference on Early Intervention in Mental Health - "Prevention and Early Intervention: Broadening the Scope"; October 7-10 2018; Boston, Massachusetts, USA. Early Interv Psychiatry.
26. Meinecke AK, Welsing P, Kafatos G, et al. Series: pragmatic trials and real world evidence: paper 8. data collection and management. *J Clin Epidemiol* 2017;91:13-22. doi: 10.1016/j.jclinepi.2017.07.003
27. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clinical Epidemiol* 2009;62(5):464-75. doi: 10.1016/j.jclinepi.2008.12.011
28. Vanderbilt University. REDCap (research electronic data capture) 2018 [Available from: https://www.project-redcap.org accessed April 2 2020.
29. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010 [published Online First: 2008/10/22]
30. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208 [published Online First: 2019/05/13]
31. Tait L, Birchwood M, Trower P. A new scale (SES) to measure engagement with community mental health services. *J Ment Health* 2002;11(2):191-8. doi: 10.1080/09638230020023570-2 [published Online First: 2002/01/01]
32. Flemenbaum A, Zimmermann RL. Inter- and intra-rater reliability of the Brief Psychiatric Rating Scale. *Psychol Rep* 1973;32(3):783-92. [published Online First: 1973/06/01]
33. Guy W. Clinical Global Impressions. ECDEU Assessment Manual for Psychopharmacology. Rockville, Maryland: National Institute for Mental Health 1976:218-22.
34. Canadian Institute for Health Information. Ontario Mental Health Reporting System, Data Quality Documentation, 2015-2016. Ottawa, ON: CIHI, 2017.
35. Williams JI, Young W. A Summary of Studies on the Quality of Health Care Administrative Databases in Canada. In: Goel V, Williams JI, Anderson GM, et al., eds. Patterns of Health Care in Ontario The ICES Practice Atlas. 2nd ed. ed. Ottawa, ON: Canadian Medical Association 1996.
36. Juurlink DN, Preyra C, Croxford R, et al. Canadian Institute for Health Information Discharge Abstract Database: A Validation Study. Toronto, ON: Institute for Clinical Evaluative Sciences, 2006.
37. Canadian Institute for Health Information. CIHI Data Quality Study of Ontario Emergency Department Visits for Fiscal Year 2004-2005--Executive Summary. Ottawa, ON: CIHI, 2008.

38. McCullagh P, Nelder JA. Generalized Linear Models, Second Edition;. London, UK: Chapman and Hall 1989.
39. McNutt LA, Wu C, Xue X, et al. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003;157(10):940-3. [published Online First: 2003/05/15]
40. Doyle R, Turner N, Fanning F, et al. First-episode psychosis and disengagement from treatment: a systematic review. *Psychiatr Serv* 2014;65(5):603-11. doi: 10.1176/appi.ps.201200570 [published Online First: 2014/02/19]
41. Wang W, Ma Y, Huang Y, et al. Generalizability analysis for clinical trials: a simulation study. *Stat Med* 2017;36(10):1523-31. doi: 10.1002/sim.7238 [published Online First: 2017/01/27]
42. Schafer JL. Analysis of incomplete multivariate data;. London, UK: Chapman & Hall 1997.
43. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *Cmaj* 2016;188(3):182-88. doi: 10.1503/cmaj.150064 [published Online First: 2016/01/13]
44. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa
45. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583 [published Online First: 2013/01/09]
46. Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009;4:50. doi: 10.1186/1748-5908-4-50 [published Online First: 2009/08/12]



Supplementary File 1: Protocol reporting checklist based on SPIRIT guidelines

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	11
Funding	#4	Sources and types of financial, material, and other support	12
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	12
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	12
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	12

Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	12
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6

Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	9-11
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7-9
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	6-7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document	6

		that is unavailable to those who enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	6
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	7, 9
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values).	6, 7-8, 11

		Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9-11
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	10
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	11
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	11
Ethics and dissemination			

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	7, 11
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	11
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11

Appendices

Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	7, 11
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	11

BMJ Open

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042751.R1
Article Type:	Protocol
Date Submitted by the Author:	21-Sep-2020
Complete List of Authors:	Polillo, Alexia; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Foussias, George; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Wong, Albert; Centre for Addiction and Mental Health, Campbell Family Mental Health Research Institute; University of Toronto, Psychiatry Ampofo, Augustina; Centre for Addiction and Mental Health Stergiopoulos, Vicky; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Anderson, Kelly; Western University, Epidemiology & Biostatistics Bromley, Sarah; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition D'Arcey, Jessica; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Institute of Medical Science de Oliveira, Claire; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Institute of Health Policy, Management and Evaluation Duda, Lillian; Centre for Addiction and Mental Health Henderson, Joanna; Centre for Addiction and Mental Health, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health; University of Toronto Faculty of Medicine, Psychiatry Kidd, Sean; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Kurdyak, Paul; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Wang, Wei; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Zaheer, Juveria; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Voineskos, Aristotle; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Kozloff, Nicole; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry
Primary Subject Heading:	Mental health

Secondary Subject Heading:	Health services research
Keywords:	Schizophrenia & psychotic disorders < PSYCHIATRY, Clinical trials < THERAPEUTICS, Child & adolescent psychiatry < PSYCHIATRY, Information technology < BIOTECHNOLOGY & BIOINFORMATICS

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Authors

Alexia Polillo, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

George Foussias, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Albert H.C. Wong, MD, PhD, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Augustina Ampofo, BA, Centre for Addiction and Mental Health, Toronto, Canada

Vicky Stergiopoulos, MD, MHSc, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Kelly K. Anderson, PhD, Department of Epidemiology and Biostatistics, Western University, London, Canada

Sarah Bromley, OT, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health, Toronto, Canada

Jessica D'Arcey, MSc (candidate), Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Institute of Medical Science, University of Toronto, Toronto, Canada

Claire de Oliveira, MA, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Lillian Duda, MPA, Centre for Addiction and Mental Health, Toronto, Canada

Joanna Henderson, PhD, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Sean A. Kidd, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Paul Kurdyak, MD, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Wei Wang, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Juveria Zaheer, MD, MSc, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Aristotle N. Voineskos, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Nicole Kozloff, MD, SM, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Corresponding author
Nicole Kozloff, Centre for Addiction and Mental Health
250 College Street, 7th floor
Toronto, ON M5T 1R8
n.kozloff@mail.utoronto.ca
416-535-8501

Word count
4295/4000 words

Keywords
Schizophrenia and psychotic disorders
Early psychosis intervention
Mobile health interventions
Patient and family engagement
Pragmatic clinical trials

ABSTRACT

Introduction

Despite the overwhelming evidence supporting early intervention for psychosis, many young people with psychosis experience long delays to treatment. While nearly half of all new psychotic disorders are diagnosed in the emergency department (ED), most young people who present to the ED with psychosis do not receive timely follow-up with a psychiatrist, and even fewer with early psychosis intervention (EPI) services. We aim to test an intervention delivered using short message service (SMS), a low-cost, low-complexity, youth-friendly approach, to improve transitions from the ED to EPI services.

Methods and analysis

This is a protocol for a pragmatic randomized, single blind, controlled trial with accompanying economic and qualitative evaluations conducted at the Centre for Addiction and Mental Health (CAMH) in Toronto, Canada. A consecutive series of 186 participants aged 16 to 29 referred by the CAMH ED to CAMH's EPI program will be recruited for a trial of a 2-way intervention involving reminders, psychoeducation, and check-ins delivered via SMS. The primary outcome will be attendance at the first consultation appointment within 30 days of study enrolment assessed through chart reviews of routinely-collected clinic data. We will also review participants' charts and link with provincial health administrative data to examine longer-term service engagement and system-level outcomes, including ED visits and psychiatric hospitalizations, 6 months and up to 2 years after baseline. A cost-effectiveness analysis of the intervention will be performed and web-based surveys and qualitative interviews will explore young people's perspectives on the intervention. Patients and families with lived experience will be engaged in all aspects of the project.

Ethics and dissemination
Research ethics board approval has been obtained. Findings will be reported in scientific journal articles and shared with key stakeholders including youth, family members, knowledge users, and decision makers.

Trial registration number clinicaltrials.gov #NCT04298450

ARTICLE SUMMARY

Strengths and limitations of this study

- Pragmatic randomized controlled trial leveraging mobile health technology, chart reviews, routinely collected administrative data, and economic and qualitative evaluations.
- Intervention well-positioned for local adoption as well as scale and spread to other EPI programs and youth mental health services more broadly.
- Collaboration with health system decision-makers, clinical stakeholders, knowledge users, team members with clinical and research expertise, people with lived experience of psychosis, and key relationships with organizations well-positioned to support widespread implementation.
- Conducting the trial at a single site will support streamlined recruitment but may limit generalizability of our findings.

INTRODUCTION

Psychosis, characterized by delusions and/or hallucinations, typically manifests during adolescence or early adulthood. It is the characteristic presentation of schizophrenia and schizoaffective disorder, and often occurs in bipolar disorder.[1] These disorders can cause significant dysfunction: in disability weighting surveys used to establish global disease burden, participants rated schizophrenia as the disorder most disabling for individuals.[2] Young people experience greater mortality by up to 24-fold in the year following a first psychotic disorder diagnosis compared to peers in the general population.[3] In the long term, psychotic disorders are associated with ongoing increased mortality particularly by suicide,[4] substance use disorders, homelessness, victimization, acts of violence,[5] and high economic costs due to healthcare use as well as lost productivity.[6 7] Early psychosis intervention (EPI) is a model developed to provide treatment early in the course of illness to improve patients' long-term trajectories and reduce the burden on individuals and their families. The rationale for EPI has been strengthened by consistent findings that long duration of untreated psychosis is associated with greater symptom burden, lower likelihood of remission and poor social functioning and global outcomes.[8] Members of our team have shown that EPI service use is associated with a four-fold reduction in all-cause mortality for young people with psychosis compared to those who do not access EPI services.[9] EPI services have also been associated with improved access to psychiatric care, reduced risk of relapse, fewer hospital readmissions, and increased employment rates.[9-13] EPI can be a lifechanging and lifesaving intervention for young people with psychosis.

EPI programs are well-established in Ontario and provide services to young people with early psychosis across the province.[14] Despite this, and the clear mandate for EPI programs to promote their services and minimize barriers to care, many youth with psychosis in Ontario either never access these services, or enter them far later than indicated.[15] In Canada, nearly half of all new psychotic disorders are diagnosed in the ED.[16] We recently found that among young people across Ontario presenting with psychotic disorders to the ED for the first time, 40% received no outpatient mental health follow-up within 30 days and only 45% saw a psychiatrist.[17] The reasons young people with psychosis discharged from the ED did not receive follow-up were unclear in this study: both issues of access (availability and awareness of services) and engagement (youth following through on referrals) are potential explanations. Our experience at the Centre for Addiction and Mental Health (CAMH) in Toronto, where our EPI program sees referred patients for consultation within 2 weeks on average, suggests a problem of engagement: according to clinic data, 50% of the youth referred from the ED do not attend their first EPI consultation appointment (compared with approximately 30% from all other referral sources). It is clear that new approaches are required to engage this population in accessing evidence-based care that is life-saving and improves illness outcomes. In surveys of patients and families in EPI services, appointment reminders are cited as a top factor that would improve service engagement, with a preference for email and text communication.[18-20]

Mobile health technologies are increasingly being tested to improve outcomes, including symptoms, appointment attendance, and medication adherence, among young people with mental illness, particularly psychosis.[21-23] Short message service (SMS) or text message is a commonly used mode of communication by adolescents and young adults: in a survey of users of community mental health services, access to mobile phones approached 100%.[24] SMS is associated with low user and financial burden. SMS does not require people to own a smartphone, have data plans, or have access to wireless internet. In a study of people with psychosis, participants were found to be highly engaged with an SMS intervention.[25] SMS reminders have been associated with improved service engagement in psychosis across studies,[22] including twice the attendance rates for initial appointments in an EPI program.[26] An

ongoing pilot study at CAMH investigating the effect of a weekly 2-way SMS intervention on service engagement during the first year of EPI treatment found this approach to be feasible and valued by participants.[27] We are unaware of any studies examining interventions specifically to improve the transition in care from the ED to EPI for young people with psychosis, using mobile health technologies or otherwise.

Objectives and Hypotheses

"ED to EPI," a pragmatic randomized, single blind, controlled trial[28] with accompanying economic and qualitative evaluations, aims to improve the transition from the ED to EPI services for youth with psychosis using an SMS text messaging intervention. It is pragmatic in its participant eligibility criteria (broad and inclusive), comparison intervention (usual care), follow-up intensity (low), primary trial outcome (objective, meaningful and assessed under usual conditions), measurement of participant compliance and practitioner adherence to study protocol (unobtrusive), and analysis of primary outcome (inclusive, i.e. intention-to-treat).[29] We also leverage linked routinely collected data through ICES (previously known as the Institute for Clinical Evaluative Sciences), which holds data on all hospital and physician visits for the province. We will also evaluate the cost effectiveness of the intervention and explore young people's perspectives on its various components. Our study team, in addition to clinicians and researchers, includes a patient and family member with lived experience of using EPI services and key decision-makers to increase the relevance and uptake of the intervention. Specifically, our primary objectives are to:

1. Evaluate the effect of an SMS intervention on attendance at the first consultation appointment within 30 days of study enrolment;
Hypothesis 1: The SMS intervention will increase rate of attendance at the consultation appointment.
2. Assess indicators of longer-term service engagement 6 months following study enrolment;
Hypothesis 2: The SMS intervention will lead to improved indicators of longer-term service engagement (Service Engagement Scale scores and dropout rates).
3. Determine system-level outcomes, including ED visits and psychiatric hospitalizations, as a function of receiving the SMS intervention, and its cost effectiveness, factoring costs of the intervention and cost offsets of health service utilization;
Hypothesis 3: The SMS intervention will lead to decreased use of acute care services (ED visits and psychiatric hospitalizations) and will be cost-effective relative to the control condition, based on improved rate of transition from the ED to EPI services and anticipated reductions in use of costly acute care services.
4. Explore young people's experiences of the intervention and their perspectives on its various components.
This is an exploratory research question that seeks to understand how young people experience the SMS intervention and how they perceive its various components impact their service engagement.

METHODS AND ANALYSIS

Study setting

The study setting will be the Gerald Sheff and Shanitha Kachan Emergency Department at CAMH, Ontario's only 24-hour stand-alone psychiatric emergency service. The ED also houses a drop-in "Bridging Clinic" which provides care to less acute patients who are diverted after ED triage, and rapid follow-up care for patients discharged from the ED and CAMH inpatient units. Together, they serve approximately 1,200 patients each month. The EPI program at CAMH receives over 600 referrals for suspected psychosis annually, approximately 25% of which are from the ED and Bridging Clinic. Reflecting the Ontario EPI Program

Standards, CAMH EPI services are delivered by multidisciplinary teams, employ strategies to promote early entry and ongoing engagement, and provide pharmacotherapy and psychosocial therapies for an average of 3 years.[14] Patients are assigned to the next available and/or most appropriate psychiatrist and case manager (nurse, social worker, or occupational therapist) for a joint consultation appointment, typically within 2 weeks, and are contacted by phone by the EPI program administrator to book and confirm their appointment. After the initial appointment is confirmed, patients receive a phone call reminder the day before their scheduled appointment. As part of routine care, patients who do not attend their scheduled first appointment receive follow-up calls to reschedule an appointment for up to 30 days from the initial referral.

Eligibility criteria

Study inclusion criteria mirror the intake criteria for the CAMH EPI program. Participants will be eligible for the study if they: 1) are between 16 and 29 years old and 2) have been referred by the CAMH ED to CAMH EPI services for suspected psychosis. Our only exclusion criterion is inability to communicate in basic written English. In our pilot SMS study at CAMH, fewer than 5% of potential participants were excluded for lacking a phone; we have budgeted to offer 5% of participants access to a prepaid cellphone for the duration of the study.[27]

Intervention procedures

Study participants will be recruited at the time of EPI referral for a trial of an SMS intervention designed to engage them during the waiting period for their consultation appointment. They will be randomized to receive either sham or active SMS intervention. Sham SMS will consist of 1 message sent just after enrolment indicating that they will be contacted for an appointment. The sham SMS group will not be denied any part of usual clinical care. Thus, the clinic administrator will call patients in both groups to book and remind them of the consultation appointment. Active SMS intervention will include the initial message sent to the control group, plus a series of subsequent messages. These will include the following content: 1) appointment reminders and instructions, 2) psychoeducational material, and 3) 2-way communication check-ins to rate distress (Figure 1). Intervention components were developed based on feedback from a survey of youth in the same EPI program,[30] as well as psychosocial interventions with evidence in early psychosis, including cognitive-behavioural therapy (psychoeducation, behavioural activation) and illness self management (reminders, distress check-in).[31 32] See Supplementary File 1 for a comprehensive description of the intervention. Messages sent back by participants will be monitored by the research team, and the case manager assigned to their consultation appointment will be notified and will respond accordingly if there are indicators of elevated distress. The intervention will continue until the patient attends the first consultation appointment, or for up to 30 days if the patient does not attend, which reflects the program's practice of closing referrals for non-attending patients.

Messages will be sent through CAMH's in-house Research Electronic Data Capture (REDCap) platform via a third-party plug-in, Twilio, which supports routing of SMS messages to participant devices.[33-35] All data is stored securely on CAMH's REDCap servers or in a locked office and password-protected database on CAMH's secure network. The purpose of the sham intervention is to separate out the content of the intervention (i.e. reminders, psychoeducation, 2-way check-ins) from the effect of simply receiving SMS messages, decreasing participant bias.

Assignment of intervention

Immediately after informed consent, participants will be randomized by REDCap to the active or sham intervention. Generation of the randomization sequence will be managed by the

study biostatistician who is not involved in enrolling participants or assigning intervention arms. Randomization will be stratified by sex (male or female) and referral source (ED or Bridging Clinic), using a computer algorithm to determine a randomized, blocked allocation of participants into intervention groups within strata. Once randomized, treatment assignment will be known only by the study personnel involved in managing the SMS intervention and the case manager monitoring text message responses; the principal investigator and study personnel involved in the chart review and the ICES analysis will remain blind to treatment assignment. Study personnel involved in the qualitative interviews and analysis will also be aware of treatment assignment since only individuals receiving the active intervention will participate in this component of the project.

Sample size

Our sample size calculations are based on the primary outcome of rate of attendance at the EPI program consultation appointment. The current rate of attendance at the first consultation appointment for patients referred from the ED and Bridging Clinic is 50%; we have powered our study to detect the treatment effect with an anticipated rate of attendance of 70%, which is the average for all referral sources other than the ED and Bridging Clinic. A total of 186 participants (93 per group) will provide >80% power to detect a change in attendance from 50% to 70% at alpha <0.05. Non-compliance and loss to follow-up are not a concern for our primary outcome since these are counted in the outcome as nonattendance at the consultation. Adjusting analyses for covariates expected to affect attendance (e.g., age, sex) is expected to further increase power.

Study procedures

We will recruit 186 patients consecutively referred from the CAMH ED and Bridging Clinic to the CAMH EPI program at the time of discharge. During business hours and into the evening, research staff will be on call to the ED to recruit patients as soon as they are identified for the study. Eligible participants who present after hours may be identified by ED staff and referred to the research team who will send them an e-consent form via SMS or email. See Supplementary File 2 for patient consent form. Additionally, potential participants who are missed in the ED/Bridging clinic may be identified by the EPI clinic administrator who will approach them over the phone and send them an e-consent form via SMS or email. We have used the approach of having clinical and administrative staff obtain verbal consent to send e-consent forms in other studies with this population.[19]

As part of informed consent, participants will be asked to consent to a review of their chart, a follow-up web-based survey, and linkage of their information to data held at ICES. They will also be given the option to provide consent to be re-contacted for participation in a qualitative interview. There will be no additional in-person assessments for the quantitative component of this study. CAMH uses an electronic health record, which facilitates data abstraction from multiple clinical programs (i.e., both the ED and Bridging Clinic and EPI program). Research staff and students will be trained by the clinician principal investigators to abstract data into a structured database.

All study participants will receive a $10 e-giftcard once the baseline e-visit is complete. Participants in the active intervention group who complete a web-based survey will receive another $10 e-giftcard and those who complete a qualitative interview will receive a $50 e-giftcard. It will be clarified through the consent process that honoraria are to compensate participants for their time and will not be tied to clinical appointment attendance. For the majority of participants, their initial recruitment and consent will be their only interaction with the research team, with a small subgroup completing qualitative interviews.

Outcome measures

Chart review

Outcome measures are shown in Table 1. CAMH uses many standardized assessment forms which increases the completeness of patient data. Demographic variables, clinical diagnoses, substance use, duration of untreated psychosis (measured as the period of time from first onset of psychotic symptoms to initiation of EPI services and initiation of treatment with an antipsychotic or mood-stabilizing medication), characteristics of the ED visit from which they were referred (urgent presentation – brought by police, involuntary status; timing of visit), and family involvement in care are routinely recorded in the clinical chart by clinicians and will be abstracted from the chart at the time of consultation. Additional variables will likely be available but only for patients accepted into the EPI program, and this will be reflected in the data analysis. These include several assessments that are performed routinely in the EPI program. The Service Engagement Scale (SES)[36] is a brief validated tool designed to measure engagement with community mental health services. In 14 items, it assesses patients' availability for treatment, collaboration, help-seeking behaviours and treatment adherence on a four-point Likert scale with higher scores indicating difficulties in service engagement. The Brief Psychiatric Rating Scale (BPRS)[37] is a clinician or interviewer-rated measure of psychiatric symptoms commonly used as an outcome measure for psychotic disorders and collected monthly in CAMH's EPI program. It includes items related to suicidality and hostility. The Clinical Global Impression (CGI)[38] is a clinician-rated measure of the patient's global severity of illness prior to and after initiating a medication. It includes subscales for Severity and Improvement. Medication and appointment nonadherence will also be assessed over 6 months of treatment. Lastly, after 6 months, current EPI enrolment status will be assessed and categorized as: not offered or enrolled in treatment (e.g., because they did not ultimately have psychosis), enrolled but disengaged prematurely, accepted for treatment but transitioned to other services, or continued in treatment.

Administrative data

Primary data collected for the study will be linked deterministically to data sources held at ICES via participants' unique health card numbers. The information available for each participant will be de-identified, stored, and analyzed onsite at ICES following procedures approved by Ontario's Information and Privacy Commissioner. The following ICES data sources will be used: the Ontario Mental Health Reporting System (OMHRS), capturing hospitalizations on adult inpatient mental health units,[39] the Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), capturing all hospital admissions including hospitalizations on child and adolescent inpatient mental health units,[40 41] National Ambulatory Care Reporting System (NACRS) which captures all ED visits,[42] Ontario Health Insurance Plan (OHIP) claims database, which captures outpatient physician visits,[40] Registered Persons Database, which contains health card numbers, demographic information, and deaths, and Ontario Drug Benefits (ODB) claims database, which provides information on all covered prescriptions (based on financial need for those under age 65 and for young people up to age 25 who lack private insurance). These data will also be used for cost effectiveness analysis. Outcomes examined in the linked ICES data are listed in Table 1.

Table 1. Summary of outcome measures and covariates

Type	Variables	Data Source	Timing

Demographic characteristics	Age	Chart review for all demographic characteristics (CAMH Health Equity form and notes)	Baseline[a]
	Sex and gender		
	Sexual orientation		
	Race/ethnicity		
	Born in Canada		
	Religious/spiritual affiliation		
	Highest level of education		
	Source of income and family income		
	Number of people supported by income		
	Employment status		
	Legal history		
	Housing status		
	Living situation		
	Experience of homelessness		
	Relationship status		
Clinical characteristics	Clinical diagnoses	Chart review for all clinical characteristics (consultation and progress notes)	Baseline
	Substance use		Baseline
	DUP		Baseline
	Family involvement in care		Baseline
	Urgent status at ED visit (brought by police, involuntary) Timing of ED visit		
	BPRS[37]		Baseline and 6 months
	CGI[38]		Baseline and 6 months
Service engagement	Attendance at consultation appointment	Chart review for all service engagement measures	30 days
	SES[36]		6 months (completed around 3 months in treatment)

	Medication and appointment nonadherence		6 months
	EPI enrolment status		6 months
System-level outcomes[b]	Number of ED visits	NACRS[42]	6 months and up to 2 years
	Number of inpatient mental health hospitalizations	OMHRS,[39] CIHI-DAD[40 41]	
	Number of days in inpatient mental health hospitalizations	OMHRS,[39] CIHI-DAD[40 41]	
	Number of outpatient mental health visits	OHIP[40]	
	Prescription drugs – psychiatric medications, continuously vs. noncontinuously prescribed	ODB	
	Mortality including cause of death	Registered Persons Database	

[a] Items may be extracted from the ED note or EPI consultation note
[b]Administrative data held at ICES
CAMH, Centre for Addiction and Mental Health; DUP, duration of untreated psychosis; BPRS, Brief Psychiatric Rating Scale; CGI, Clinical Global Impression; SES, Service Engagement Scale; EPI, early psychosis intervention; ED, emergency department; OMHRS, Ontario Mental Health Reporting System; CIHI-DAD, Canadian Institute of Health Information Discharge Abstract Database; NACRS, National Ambulatory Care Reporting System; OHIP, Ontario Health Insurance Plan; ODB, Ontario Drug Benefits.

Statistical analysis

Primary analysis

Descriptive and graphical statistics will be used to summarize the data on all randomized participants and to confirm that there are no group differences in baseline demographics and clinical characteristics. Distributional assumptions will be inspected and appropriate transformations or non-parametric methods will be applied as necessary. In general, generalized linear models[43] will be used throughout. These models account for deviation from normal assumption of the outcome variables and control for covariates.

Our analysis of the primary outcome will be a logistic regression to examine the likelihood of attendance at the EPI consultation with treatment assignment using risk ratios.[44] We will carefully select demographic variables and factors known to influence treatment engagement (e.g., substance use, family involvement in care)[45] to be included in the model as covariates. A difference in attendance between groups will be declared at a significance level of 0.05. Similar models will be used to address the secondary hypotheses, with specific types of models appropriate to each outcome, including time-to-event analysis to examine premature disengagement from services. Administrative data outcomes will be examined using generalized linear models with proper distribution assumptions.

Additional analyses: moderation and generalizability

We plan to conduct two additional exploratory analyses. First, we will run moderation analyses on potential effect modifiers by adding an interaction term between the potential moderator and the treatment assignment indicator in the generalized linear models. We are specifically interested in the moderation effects of health equity factors including gender, race/ethnicity, and housing status. A significant interaction will provide evidence that the treatment effects may be different in the subgroups. A second exploratory analysis will be conducted to evaluate the impact of selection bias of the study sample and estimate the population average treatment effects by employing weighted analysis using propensity scores.[46]

Missing data

The risk of missing data is mitigated through the use of chart review and analysis of administrative data. While the primary outcome will not suffer from attrition, other outcomes will, as some follow-up data will only be available for participants who attended their consultation appointment and those who are enrolled in CAMH EPI services. For these additional outcomes, we plan to use multiple imputation methods developed by Schafer to correct potential bias that could be introduced by missing data.[47]

Economic evaluation

Full details of the economic evaluation appear in Supplementary File 3. We will undertake a cost-effectiveness analysis, where the outcome of interest is consultation appointment attendance, adopting the perspective of the public third-party payer (i.e., the Ontario Ministry of Health). We will collect data on the costs of delivering both arms of the intervention. In addition, using a costing algorithm available at ICES,[48] we will estimate all direct patient-level healthcare costs incurred by the public third-party payer for the intervention and control groups, which will include costs of hospitalizations, ED visits, physician services (i.e., primary care, psychiatry and other) and diagnostic tests, outpatient prescription drugs for individuals covered under the provincial public drug insurance plan, and other hospital-based care. We will use a net benefit regression approach to model probabilities of cost effectiveness for each additional patient referred who attends their consultation appointment in the intervention compared with control group. In addition, we will undertake relevant sensitivity analyses to test the robustness of findings by varying relevant parameters, such as the discount rate. Finally, we will examine the real-world budget impact of implementing the intervention across Ontario, to estimate the cost to the Ministry of Health of implementing this model of care across the province and the potential cost-savings to the system associated with this.

Understanding patient experiences: Survey and qualitative analysis

Participants in the active intervention group will receive a one-time survey sent as a web-link to their phone or email address. Survey topics include user experience, attitudes toward the SMS intervention, its perceived benefits and challenges, acceptability, and suggestions for improvements. Those who consent to participate in the qualitative research component will be re-contacted by phone or email to participate in semi-structured interviews to gain a more in-depth understanding of survey topics. A subsample of 10-15 participants in the active intervention group will be purposively selected to maximize diversity of age, gender, and service attendance. We will use critical realist theory as an underlying framework to guide our interviews, surveys, and analysis.[49] Interviews will be completed until thematic saturation is achieved, estimated at 12 participants. Interviews will be digitally audio-recorded and transcribed verbatim. Surveys will be completed and stored in REDCap. Transcriptions and survey responses will be analyzed using thematic content analysis in NVivo-11. Research participants will be invited to assist with member checking to confirm that themes reflect their experiences. The analysis can inform future

improvements to the intervention and considerations for broader implementation, privileging the experiences of the patients attending these programs.

PATIENT AND PUBLIC INVOLVEMENT

A youth and family member who previously received EPI services have been engaged in helping shape the intervention and study design from project inception. They are active members of the project's Steering Committee that meets monthly to inform study design, implementation, evaluation, and dissemination of results. They will have key roles in the plan to spread the intervention, if successful, to other EPI programs by working with patients and families to adapt the intervention to local contexts. Additional youth with lived experience of receiving EPI services have been consulted on an ad hoc basis through the CAMH Youth Engagement Initiative to provide detailed feedback on the SMS intervention. Patient and family representatives on the research team are compensated for their time.

ETHICS AND DISSEMINATION

The study was approved by the Research Ethics Board (REB) at the Centre for Addiction and Mental Health. The study protocol was prepared according to SPIRIT guidelines[50] and registered with clinicaltrials.gov on March 6, 2020 (NCT04298450; https://clinicaltrials.gov/ct2/show/NCT04298450?term=ed+to+epi&draw=2&rank=1). REB-approved protocol amendments will be posted on the site. The principal investigators and study team will meet regularly to review accrued data, data confidentiality, any adverse events, adherence to protocol design, recruitment and implementation. This intervention has been designed to have high likelihood of adoption and readiness for spread and scale-up because it responds to a critical need, has a strong evidentiary basis, has advantages over existing practice and is both low complexity and low cost.[51] The study team is well-positioned to support widespread implementation of the intervention if successful. We have used an integrated knowledge translation approach that leverages input from stakeholders, including patients, clinicians (both from the ED and EPI services), policymakers, and relevant organizations throughout the study to champion the spread of the intervention to other EPI programs and youth mental health services more broadly. This trial focuses on a particularly vulnerable population—young people transitioning from adolescence to adulthood and from the ED to EPI services—but the basic intervention is widely applicable. The software platform utilized to coordinate this intervention is available at no charge, and the SMS functionality for sending and receiving messages carries a nominal fee, supporting broad uptake.

The results of the trial will be reported in scientific journal articles and shared with key stakeholders as they become available. Our study team includes the co-chair of the Early Psychosis Intervention Ontario Network, a network of over 50 EPI programs across Ontario, and several members of the Canadian Consortium for Early Intervention in Psychosis, providing a durable and established community of practice for immediate spread. De-identified participant data will be available upon reasonable request other than system-level data held at ICES. Requests can be made by contacting the principal investigator Dr. Nicole Kozloff at nicole.kozloff@camh.ca and will be managed by the Steering Committee.

This pragmatic randomized-controlled trial of a low-cost, low-complexity SMS intervention aims to improve the transition from the ED to EPI services for young people with psychosis. It targets a brief but critical period: if young people cannot even get in the door to EPI services, there is no way for them to reap the many known benefits of EPI care. Improving the ED to EPI transition has the potential to result in more young people with psychosis getting appropriate treatment earlier. The proposed intervention is also likely to be easily adaptable to

other referral pathways to EPI services and youth mental health services more broadly. At potentially lower cost to the health system, applying this SMS intervention to the ED to EPI transition has the potential to lead to improved short-term symptoms and functioning, long-term disease trajectories, decreased burden on patients and families, and fewer deaths among young people with psychosis.

Figures

Figure 1. Study intervention schedule*
*This figure represents a summary of the intervention schedule and is not exhaustive of text message content
SMS, short message service; Right arrow, incoming text messages received by participants; Left arrow, outgoing text messages sent by participants

Author contributions

NK is the principal investigator who conceived the original study design and obtained funding, with most of the current authors having contributed to the funding application, and all authors having participated in revisions to the study design for important intellectual content. AP, GF, AW, AA, VS, JD'A, LD, ANV, and NK sit on the project's Steering Committee. AP, GF, JD'A, and NK form the Data Management Committee. AP leads the survey and qualitative analysis. GF, AW, SB, and ANV have administrative roles in the clinical programs and will support the acquisition and interpretation of data. AA and LD act as patient and public consultants. VS acts as a Health System Decision-Maker on the project. KKA, CdO, PK, and NK consult on the ICES analysis. CdO is a health economist who consults on the economic analysis. VS, JH and SK provide knowledge translation expertise. JZ provides consultation on the qualitative interviews and analysis. WW acts as the biostatistical consultant. AP and NK drafted the protocol. All authors read, revised and approved the final version of the manuscript.

Funding statement

This work was supported by the Canadian Institutes of Health Research Transitions in Care Team Grant #165726 as well as by the CAMH Foundation (Award/Grant Number Not Applicable). The funders were not involved in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities.

Competing interests statement

The authors declare no competing interests.

REFERENCES

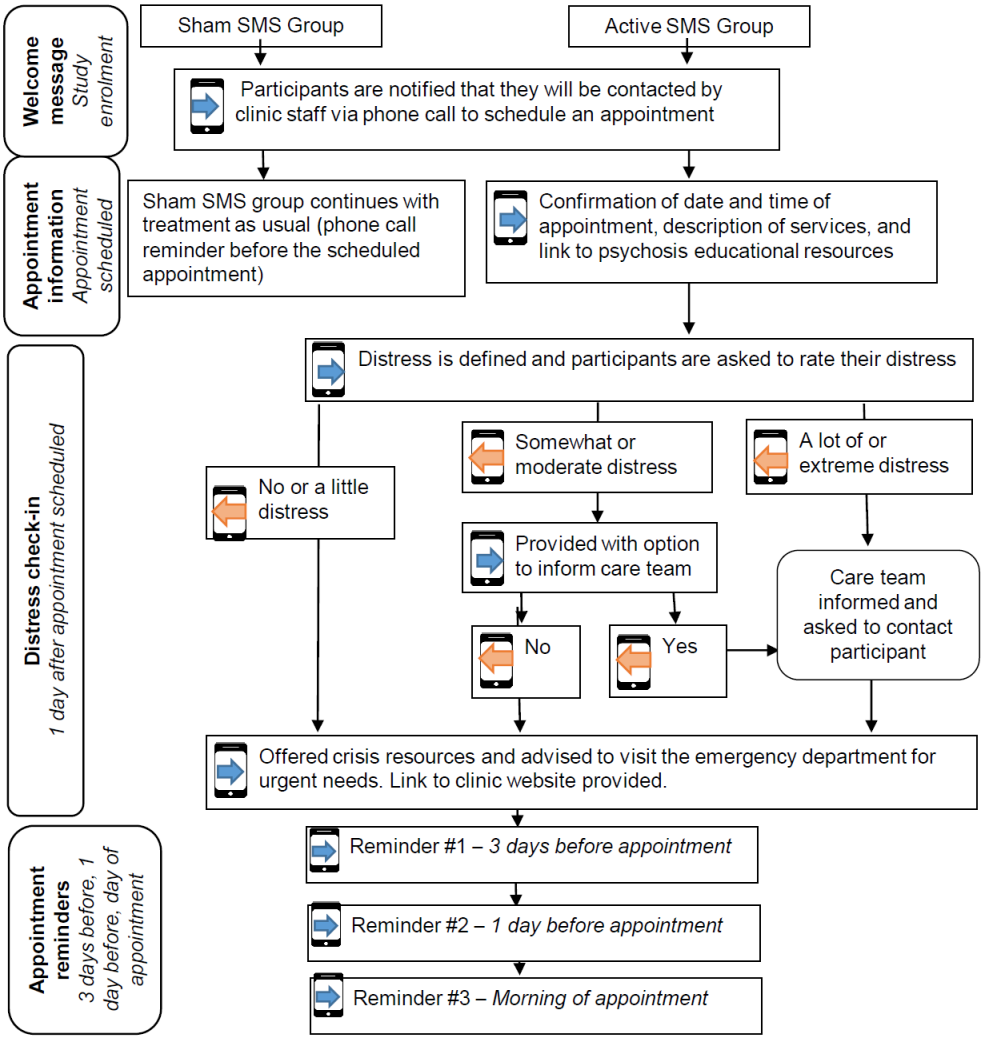
1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. - 5th ed. Arlington, VA: American Psychiatric Publishing 2013.
2. Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013;382(9904):1575-86. doi: 10.1016/s0140-6736(13)61611-6
3. Schoenbaum M, Sutherland JM, Chappel A, et al. Twelve-month health care use and mortality in commercially insured young people with incident psychosis in the United States. *Schizophr Bull* 2017;43(6):1262-72. doi: 10.1093/schbul/sbx009
4. Zaheer J, Olfson M, Mallia E, et al. Predictors of suicide at time of diagnosis in schizophrenia spectrum disorder: A 20-year total population study in Ontario, Canada. *Schizophr Res* 2020 doi: 10.1016/j.schres.2020.04.025 [published Online First: 2020/06/09]
5. Lieberman JA, First MB. Psychotic disorders. *N Engl J Med* 2018;379(3):270-80. doi: 10.1056/nejmra1801490

6. de Oliveira C, Cheng J, Rehm J, et al. The economic burden of chronic psychotic disorders in ontario. *J Ment Health Policy Econ* 2016;19(4):181-92. [published Online First: 2016/12/20]
7. Goeree R, Farahati F, Burke N, et al. The economic burden of schizophrenia in Canada in 2004. *Curr Med Res Opin* 2005;21(12):2017-28. doi: 10.1185/030079905x75087
8. Penttila M, Jaaskelainen E, Hirvonen N, et al. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2014;205(2):88-94. doi: 10.1192/bjp.bp.113.127753
9. Anderson KK, Norman R, Macdougall A, et al. Effectiveness of early psychosis intervention: comparison of service users and nonusers in population-based health administrative data. *Am J Psychiatry* 2018;175(5):443-52. doi: 10.1176/appi.ajp.2017.17050480
10. Craig TK, Garety P, Power P, et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ* 2004;329(7474):1067. doi: 10.1136/bmj.38246.594873.7C [published Online First: 2004/10/16]
11. Petersen L, Jeppesen P, Thorup A, et al. A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ* 2005;331(7517):602. doi: 10.1136/bmj.38565.415000.E01 [published Online First: 2005/09/06]
12. Malla A, Schmitz N, Norman R, et al. A multisite Canadian study of outcome of first-episode psychosis treated in publicly funded early intervention services. *Can J Psychiatry* 2007;52(9):563-71. doi: 10.1177/070674370705200904 [published Online First: 2007/10/24]
13. Bond GR, Drake RE, Luciano A. Employment and educational outcomes in early intervention programmes for early psychosis: a systematic review. *Epidemiol Psychiatr Sci* 2015;24(5):446-57. doi: 10.1017/S2045796014000419 [published Online First: 2014/07/16]
14. Ontario Ministry of Health and Long-Term Care. Early Psychosis Intervention Program Standards. Toronto, ON, 2011.
15. Anderson KK, Norman R, Macdougall AG, et al. Estimating the incidence of first-episode psychosis using population-based health administrative data to inform early psychosis intervention services. *Psychol Medicine* 2018:1-9. doi: 10.1017/s0033291718002933
16. Anderson KK, Fuhrer R, Wynant W, et al. Patterns of health services use prior to a first diagnosis of psychosis: the importance of primary care. *Soc Psychiatry Psychiatr Epidemiol* 2013;48(9):1389-98. doi: 10.1007/s00127-013-0665-3
17. Kozloff N, Jacob B, Voineskos AN, et al. Care of youth in their first emergency presentation for psychotic disorder: a population-based retrospective cohort study. *J Clin Psychiatry* 2018;79(6) doi: 10.4088/JCP.17m11947 [published Online First: 2018/11/13]
18. Lal S, Dell'Elce J, Tucci N, et al. Preferences of young adults with first-episode psychosis for receiving specialized mental health services using technology: a survey study. *JMIR Ment Health* 2015;2(2):e18. doi: 10.2196/mental.4400 [published Online First: 2015/11/07]
19. Patient and Family Perspectives on Improving Engagement in Early Psychosis Intervention. Congress of the Schizophrenia International Research Society; 2019; Orlando, Florida, USA.
20. Using REDCap to evaluate youth and family perspectives on engagement in early psychosis intervention. REDCap Con December 2019; Toronto, Ontario, Canada.
21. Firth J, Torous J. Smartphone apps for schizophrenia: a systematic review. *JMIR mHealth uHealth* 2015;3(4):e102. doi: 10.2196/mhealth.4930 [published Online First: 06.11.2015]

22. D'Arcey J, Collaton J, Kozloff N, et al. The use of text messaging to improve clinical engagement for individuals with psychosis: systematic review. *JMIR Ment Health* 2020;7(4):e16993. doi: 10.2196/16993
23. Alvarez-Jimenez M, Alcazar-Corcoles MA, Gonzalez-Blanch C, et al. Online, social media and mobile technologies for psychosis treatment: a systematic review on novel user-led interventions. *Schizophr Res* 2014;156(1):96-106. doi: 10.1016/j.schres.2014.03.021 [published Online First: 2014/04/22]
24. Ennis L, Rose D, Denis M, et al. Can't surf, won't surf: the digital divide in mental health. *J Ment Health* 2012;21(4):395-403. doi: 10.3109/09638237.2012.689437 [published Online First: 2012/06/21]
25. Kauppi K, Kannisto KA, Hatonen H, et al. Mobile phone text message reminders: measuring preferences of people with antipsychotic medication. *Psychol Med* 2015;168(1-2):514-22. doi: 10.1016/j.schres.2015.07.044
26. Thomas IF, Lawani AO, James BO. Effect of short message service reminders on clinic attendance among outpatients with psychosis at a psychiatric hospital in Nigeria. *Psychiatr Serv* 2017;68(1):75-80. doi: 10.1176/appi.ps.201500514
27. Using short message service as a means of engagement in early psychosis. IEPA 11th International Conference on Early Intervention in Mental Health - "Prevention and Early Intervention: Broadening the Scope"; October 7-10 2018; Boston, Massachusetts, USA. Early Interv Psychiatry.
28. Meinecke AK, Welsing P, Kafatos G, et al. Series: pragmatic trials and real world evidence: paper 8. data collection and management. *J Clin Epidemiol* 2017;91:13-22. doi: 10.1016/j.jclinepi.2017.07.003
29. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clinical Epidemiol* 2009;62(5):464-75. doi: 10.1016/j.jclinepi.2008.12.011
30. Improving Youth Engagement in Early Psychosis Intervention Programs: Preliminary Results From a Youth Survey. 66th Annual Meeting of the American Academy of Child and Adolscent Psychiatry; 2019 October 17, 2019; Chicago, IL, USA.
31. Lecomte T, Abidi S, Garcia-Ortega I, et al. Canadian Treatment Guidelines on Psychosocial Treatment of Schizophrenia in Children and Youth. *Can J Psychiatry* 2017;62(9):648-55. doi: 10.1177/0706743717720195 [published Online First: 2017/09/10]
32. American Psychiatric Association. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia, Third Edition. Washington DC: American Psychiatric Association 2020.
33. Vanderbilt University. REDCap (research electronic data capture) 2018 [Available from: https://www.project-redcap.org accessed April 2 2020.
34. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010 [published Online First: 2008/10/22]
35. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208 [published Online First: 2019/05/13]
36. Tait L, Birchwood M, Trower P. A new scale (SES) to measure engagement with community mental health services. *J Ment Health* 2002;11(2):191-8. doi: 10.1080/09638230020023570-2 [published Online First: 2002/01/01]
37. Flemenbaum A, Zimmermann RL. Inter- and intra-rater reliability of the Brief Psychiatric Rating Scale. *Psychol Rep* 1973;32(3):783-92. [published Online First: 1973/06/01]
38. Guy W. Clinical Global Impressions. ECDEU Assessment Manual for Psychopharmacology. Rockville, Maryland: National Institute for Mental Health 1976:218-22.

39. Canadian Institute for Health Information. Ontario Mental Health Reporting System, Data Quality Documentation, 2015-2016. Ottawa, ON: CIHI, 2017.
40. Williams JI, Young W. A Summary of Studies on the Quality of Health Care Administrative Databases in Canada. In: Goel V, Williams JI, Anderson GM, et al., eds. Patterns of Health Care in Ontario The ICES Practice Atlas. 2nd ed. ed. Ottawa, ON: Canadian Medical Association 1996.
41. Juurlink DN, Preyra C, Croxford R, et al. Canadian Institute for Health Information Discharge Abstract Database: A Validation Study. Toronto, ON: Institute for Clinical Evaluative Sciences, 2006.
42. Canadian Institute for Health Information. CIHI Data Quality Study of Ontario Emergency Department Visits for Fiscal Year 2004-2005--Executive Summary. Ottawa, ON: CIHI, 2008.
43. McCullagh P, Nelder JA. Generalized Linear Models, Second Edition;. London, UK: Chapman and Hall 1989.
44. McNutt LA, Wu C, Xue X, et al. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003;157(10):940-3. [published Online First: 2003/05/15]
45. Doyle R, Turner N, Fanning F, et al. First-episode psychosis and disengagement from treatment: a systematic review. *Psychiatr Serv* 2014;65(5):603-11. doi: 10.1176/appi.ps.201200570 [published Online First: 2014/02/19]
46. Wang W, Ma Y, Huang Y, et al. Generalizability analysis for clinical trials: a simulation study. *Stat Med* 2017;36(10):1523-31. doi: 10.1002/sim.7238 [published Online First: 2017/01/27]
47. Schafer JL. Analysis of incomplete multivariate data;. London, UK: Chapman & Hall 1997.
48. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188(3):182-88. doi: 10.1503/cmaj.150064 [published Online First: 2016/01/13]
49. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa
50. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583 [published Online First: 2013/01/09]
51. Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009;4:50. doi: 10.1186/1748-5908-4-50 [published Online First: 2009/08/12]

Figure 1. SMS intervention schedule*



*This figure represents a summary of the intervention schedule and is not exhaustive of text message content

SMS, short message service; Right arrow, incoming text messages received by participants; Left arrow, outgoing text messages sent by participants

BOTH ACTIVE AND SHAM GROUPS

At Time of Enrolment

Hi [First Name], this is [Clinic]. If you haven't yet been given an appointment, one of our clinic staff will contact you in the next few days. Just so you're aware, our number comes up as private. Please text '1' to confirm you received this message.

(If 1 texted back): Thanks for confirming!

ACTIVE GROUP

After appointment scheduled via phone

Hi [First Name], thank you for booking your first visit with [Clinic] on [date] at [time]. If you need to reschedule, please call [Clinic Phone]. At your appointment, you will meet with a psychiatrist and a case manager who will work with you to figure out how we can best support you. Experiencing psychosis can be difficult and knowing more about mental health may help you cope. If you'd like to learn more about mental health and psychosis, please visit: www.camh.ca/psychosis

Two-way distress check-in

Next day**

Hi [First Name], while you wait for your upcoming appointment with us at [Clinic], we wanted to check in! How are you doing this week? Please send back '1' for well, '2' for okay, or '3' for bad.

If response = 1

Thanks for letting us know. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 2 or 3

We say people are experiencing distress when they are feeling anxious, depressed, worried, or hopeless. Can you please rate your distress for us? '0' for no distress, '1' for a little distressed, '2' for somewhat distressed, '3' for moderately distressed, '4' for a lot of distress, or '5' for extreme distress (urgent).

If response = 1

If response = 2-3

Thanks for letting us know. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Would you like us to pass this information on to your care team? They may reach out to you during business hours. Please text back: '1' for yes, or '2' for no. We won't pass this information on unless you text back '1'.

If response = 1: Thanks for letting us know. We have passed this onto your care team who may reach out during business hours. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 2: Thanks for letting us know. We won't pass this information on. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 4

Thanks for letting us know, we have passed this information on to your care team, who may reach out during business hours. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 5

Thanks for letting us know. We have passed this information on to your care team, who may reach out during business hours. We urge you to consider trying these resources: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 1

Thanks for confirming! For more information about our services, please visit: www.camh.ca/sceis.

Reminder #1

3 days pre-appointment**

Hi, this is a reminder that your appointment at [Clinic] is coming up on [date] at [time].

Reminder #2

1 day pre-appointment

Hi, this is a reminder of your appointment tomorrow at [time]. The care team is looking forward to meeting you. If you need to reschedule, call [Clinic Phone].

Reminder #3

Morning of appointment

Hi, your appointment with [Clinic] is today at [time]. Please call us at [Clinic Phone] if you need any assistance.

If participant does not show, they receive the following message, and then the process starts over from the check-in until participant shows up or 30 days have passed:

Hi, we understand you didn't make it to your [Clinic] appointment. To reschedule, please call [Clinic Phone].

If 30 days have passed and participant has not attended

Hi, you have now finished receiving text messages from the research study. Thank you for your participation!

**Timing of messages and logistical content may vary depending on the date and current context of the consult appointment.

camh
Centre for Addiction and Mental Health

ED to EPI: Using SMS (Text) Messaging to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis
Online Version - Informed Consent Form

Principal Investigator: Dr. Nicole Kozloff
Dr. George Foussias
Dr. Vicky Stergiopoulos
Dr. Aristotle Voineskos

Co-Investigators:
Augustina Ampofo
Dr. Kelly Anderson
Sarah Bromley
Jessica D'Arcey
Dr. Jeff Daskalakis
Dr. Claire de Oliveira
Lillian Duda
Dr. Joanna Henderson
Dr. Sean Kidd
Dr. Paul Kurdyak
Dr. Alexia Polillo
Dr. Brittany Poynter
Dr. Wei Wang
Dr. Albert Wong
Dr. Juveria Zaheer

Sponsor: Canadian Institutes of Health Research, CAMH Foundation

Purpose of the Study:

We invite you to participate in this study because you have been referred to the Slaight Centre for Early Intervention Services. The Slaight Centre is an outpatient program for young people experiencing a first episode of psychosis and their families. In this study we will examine if text messaging can improve the transition from the emergency department to early intervention services for youth. We hope that this study will eventually lead to young people getting appropriate treatment earlier and improve their long-term outcomes. Your participation in this study is voluntary. The following information is provided to help you make an informed decision whether or not to participate.

What will I be asked to do as part of this study?

If you decide to participate in this study, you will be asked to do the following:

1) Intervention: You are being invited to take part in a study. If you consent to participate, you will be randomly assigned to receive one of two types of text messages. Random assignment means that you have an equal chance of being assigned to each text message group. If you are assigned to the text message intervention, you will receive text messages at a time of your choosing (e.g., morning, evening). You will be sent text messages with information about appointment details, education about psychosis, an opportunity to rate your distress, and appointment reminders. These text messages will continue until you attend your first consultation appointment, or for up to 30 days if you did not attend. If you are assigned to the other group, you will receive a one-time text message. If you do not have a phone, one will be offered to you for the duration of the study with the expectation that it is returned at your first consultation appointment.

camh
Centre for Addiction and Mental Health

Please note that text messages are NOT being monitored constantly and if you are experiencing an urgent issue, this information should not be sent by text message. Instead, please visit your nearest emergency department. Additionally, this is not a direct line of communication with your care team and it is not a secure form of communication. You should not send any personal health information that is not requested by the text messages.

2) Collection of data**:** We will also review your medical chart to obtain additional information about you. Information collected through this study will be transferred to the Institute for Clinical Evaluative Sciences (ICES). ICES is an organization that holds routinely collected data on health care use in Ontario. ICES is committed to protecting the privacy and security of health information. ICES is an approved unit under Ontario's Personal Health Information Protection Act and follows the policies and procedures for privacy protection and data security approved by Ontario's Information and Privacy Commissioner. Linking the data will involve using personal identifiers such as your name, date of birth, and OHIP number to identify your health service use. These identifiers will be removed as soon as the data is connected to ICES. The data will then be replaced by a scrambled code in order to decrease the likelihood of a data breach (when people get access to private information without permission)

3) Follow up survey: You may be asked to complete a brief survey following your participation in the text message intervention. Your participation in the survey is voluntary. If you consent to study participation, you may receive a link to the online survey at the contact information of your choice (text message or email). The survey takes approximately 5 to 10 minutes to complete. If you complete the survey, you will be compensated with a $10 e-gift card sent to you by email or text message from your choice of a list of retailers. The survey contains questions about your experiences with the text message intervention.

Are there risks involved?

There are no known harms associated with participation in this study. If your text messaging plan does not include unlimited texting, you may incur additional charges on your cell phone bill. The study will not reimburse you for these charges. You may also feel emotional discomfort and fatigue from receiving recurrent text messages with appointment reminders and questions about how you are feeling. If you do feel this way, you may refuse to answer any question, or terminate your participation in this study at any point in time. You may be asked some questions during the survey that might make you feel somewhat uncomfortable. If you do feel uncomfortable, you may indicate this in the comments or skip the question. You can also pause the survey and continue at another time. Please be advised that if the researcher or study personnel sees that there is a risk to your safety or the safety of others, then steps will be taken to ensure your safety and the safety of others. Lastly, the security of information sent by email/text cannot be guaranteed.

Are there benefits involved?

No direct benefits to your health will likely result from this study. It is possible that the results of this study will increase engagement in early intervention services and may benefit other people now or

camh
Centre for Addiction and Mental Health

in the future. You will also receive compensation for your time and participation in the study. The investigators responsible for this study or CAMH are not conducting this study to receive commercial benefit. However, if this research produces financial returns from a commercialization of the results in the future, you will not receive any benefit from these returns.

Can participation in this study end early?

Participation in any research study is voluntary. Your decision whether or not to participate will not interfere with your right to healthcare or other services to which you are otherwise entitled. You can contact the research team through email or phone to withdraw from the study at any time. After data is anonymized your responses cannot be withdrawn, however, no new data will be collected. Throughout your participation in this study, you will continue to receive usual care as agreed upon by you and your treatment team. In the event of research-related harm, you have not waived any legal rights/rights to legal recourse.

Are study participants paid to participate in this study?

Everyone who participates in the text messaging intervention will receive a $10 e-gift card by email or text message from your choice of a list of retailers. If you decide to withdraw before study end, you will still be paid for your time and participation. Those participants selected to participate in the follow up survey will receive another $10 e-gift card by email or text message from their choice of retailers for completing the survey.

Will personal information about me be kept confidential?

- The research data will be kept confidential from the inception of the study.
- Any information about you obtained from this research will be kept as confidential (private) as possible unless disclosure is required by law. It is important to note that confidentiality will be protected to the extent permitted by law. However, there are 3 exceptions to our confidentiality policy. In any of the following situations, we are obligated by law to contact authorities: 1) if there is a serious possibility that you may harm yourself or others; 2) if you have been involved in any form of child abuse or neglect; 3) if you have been the victim of abuse by a healthcare worker
- All data obtained from this research will be kept in a locked office and secured password database with limited access only to study personnel and authorized CAMH personnel.
- To protect your identity and confidentiality, all personal identifiers (such as your name, birth date) will be removed (de-identified and replaced with a specific code number; the research records and data will be indicated by a case number rather than your name, and the information linking these case numbers with your identity will be kept separate from the research records. This information will be kept in a separate, secure location and will only be accessible to study personnel.
- Study personnel may also access your health records for research purposes; your medical records will be kept confidential.
- All electronic files will be stored on CAMH's secure hospital or institutional network and will be password protected.

camh
Centre for Addiction and Mental Health

- Other Canadian research centres (other than CAMH) may be involved in analyzing the data, and if so this will be confidential, and your name will not be given out.
- Following the completion of the study, the researchers intend to publish the results in scientific journals. You will not be identified in any of these reports. A report of the results of this project will be given to you if you request it.
- The information you provide will not affect the usual care that you receive.
- The investigators on this study will keep the data as long as necessary to fulfill the research purposes and in accordance with the applicable laws and regulations and will use enhanced security measures to store it.
- De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share.
- Your de-identified research data (information about your diagnosis, symptoms, and study evaluations) may be shared with investigators at other Canadian research centres (other than CAMH).

Will this research study involve the use or disclosure of my identifiable medical information?

- Study personnel will retrieve information about your demographics and clinical care from your medical chart. This will be stored in a secure database with a case number rather than your personal identifiers.

Who will have access to identifiable information related to my participation in this research study?

Personal Health Information (PHI) is information about your physical or mental health or the health care that you receive that could identify you. In addition to the investigators listed on the first page of this consent form and their research staff, the following individual and/or programs will or may have access to identifiable information (which may include your identifiable medical information):

a. Institute for Clinical Evaluative Sciences (ICES) is a prescribed entity under Ontario's Personal Health Information Protection Act and adheres to policies and procedures for privacy protection and data security approved by Ontario's Information and Privacy Commissioner.

b. *As part of the Research Services Quality Assurance Program, this study may be monitored and/or audited by a member of the Quality Assurance Team. Your research records and CAMH records may be reviewed during which confidentiality will be maintained as per CAMH policies and extent permitted by law.*

c. As a part of continuing review of the research, your study records may be assessed on behalf of the Research Ethics Board. A person from the research ethics team may contact you (if your contact information is available) to ask you questions about the research study and your consent

camh
Centre for Addiction and Mental Health

to participate. The person assessing your file or contacting you must maintain their confidentiality to the extent permitted by law.

Offer to Answer Questions

We have used some technical terms in this form. Please feel free to ask about anything that you do not understand. Consider this research and the consent form carefully as long as you feel necessary before you make a decision.

Dr. Nicole Kozloff is responsible for this study. If you have any questions, please contact Dr. Nicole Kozloff at 416-535-8501 x 30769.

If you have any questions about your rights as a participant in a research study, you may contact Dr. Robert Levitan, Chair, Research Ethics Board, Centre for Addiction and Mental Health, at 416-535-8501 x 34020.

Consent to Participate: My signature below indicates that:

- I acknowledge that the research study described above has been explained to me and that any questions that I have asked have been answered to my satisfaction.
- I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of medical care for me and for other members of my family.
- I have been informed of the potential risks/harms and discomforts and I also understand the benefits of participating in this study.
- I know that I may ask now, or in the future, any questions that I may have about the study or the research procedures.
- I have been assured that records relating to my research participation and to me will be kept confidential and that no information will be printed that would disclose my identity without my permission, unless required by law.
- I have been given sufficient time to read and understand the above information
- I understand and consent that my records and research data may also be shared with other investigators for analysis and future projects (this would include only de-identified data).

Please check one:

☐ **Yes, I consent to participating in this study**

☐ **No, I do not consent to participating in this study**

Optional – Future Contact:

Do you agree to be re-contacted by our study team for an in-person interview or other follow up? You will be compensated for your participation.

camh
Centre for Addiction and Mental Health

☐ Yes, I agree to be contacted about study follow-up

☐ No, I do not wish to be contacted about study follow-up

Texting Preferences:

If you agreed to participate in the study:

At what phone number would you like to receive text messages?

_____

At what phone number or email address would you like to receive other links related to the study (e.g., your e-giftcard, the survey, and future communications)?

_____

What time of day would you prefer to receive text messages?

☐ Morning ☐ Afternoon ☐ Evening

What first name would you like us to call you in your text messages?

_____

Compensation Preferences:

Which e-giftcard would you like to receive as compensation for participating? It may take up to 10 business days to receive your compensation.

☐ Tim Hortons ☐ Amazon

Please contact 416-535-8501 x 30677 if you do not receive a text message from us within 24 hours.

The security of information sent by e-mail/text cannot be guaranteed. Please do not communicate personal sensitive information by e-mail/text. Let the research team know if you do not want to be contacted by e-mail/text. Email/Text is not routinely monitored outside of work hours. Please do not use e-mail/text to communicate emergency or urgent health matters – please contact your clinician or family doctor. If it is a medical emergency, call 911.

Supplementary File 3

We will undertake a cost-effectiveness analysis, where the outcome of interest is consultation appointment attendance, adopting the perspective of the public third-party payer (i.e., the Ontario Ministry of Health). Using a costing algorithm developed in SAS and available at ICES,[1] we will be able to estimate all direct patient-level healthcare costs incurred by the public third-party payer for both the intervention and control groups. In particular, we will include costs of hospitalizations, ED visits, physician services (i.e. primary care, psychiatry and other) and diagnostic tests, outpatient prescription drugs for individuals covered under the provincial public drug insurance plan, home care, long-term care, and other hospital-based care (which includes rehabilitation and complex continuing care). The costing methodology used in the algorithm includes a bottom-up/micro-costing approach to cost services at the individual level. This makes use of individual episodes of care or utilization in the healthcare system and their associated prices (or costs or amounts paid). A top-down approach, which allocates corporate aggregate (i.e. institutional) costs to individual visits or cases/episodes of care, will be applied in cases where individual unit costs are not available (e.g., for institutional care settings). In addition, we will include all costs associated with delivering both arms of the intervention. Costs will be reported in 2023 using the Consumer Price Index for Health and personal care (Statistics Canada). All costs and outcomes will be discounted at a rate of 1.5% per year, in line with the Canadian Agency for Drugs and Technologies in Health guidelines.[2] The incremental cost-effectiveness ratio (ICER) will be calculated as the difference in discounted mean costs between the intervention and control groups divided by the difference in attendance rates. We will use a net benefit regression approach to model probabilities of cost-effectiveness for each additional patient referred who attends their consultation appointment in the intervention compared with control group. In addition, we will undertake relevant sensitivity analyses to test the robustness of findings by varying relevant parameters, such as the discount rate. Finally, we will examine the real-world budget impact of implementing the intervention across Ontario, to estimate the cost to the Ministry of Health of implementing this model of care across the province and the potential cost-savings to the system associated with this.

REFERENCES

1. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188(3):182-88. doi: 10.1503/cmaj.150064 [published Online First: 2016/01/13]
2. Guidelines for the Economic Evaluation of Health Technologies. 4th ed. Ottawa, ON, 2017.

Supplementary File 1: Protocol reporting checklist based on SPIRIT guidelines

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	12
Funding	#4	Sources and types of financial, material, and other support	13
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	13

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	13
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5

Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5-6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose	6-7

		change in response to harms, participant request, or improving / worsening disease)	
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	8-11
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6-7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8-10
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7-10
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7-8

Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	7

Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	7-10
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	7-9, 12
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10-12

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	12
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12

Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	12
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	12
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7-8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	7-8, 12
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7-8
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	13

Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	12-13
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12-13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	12-13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	12-13
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	7-8, 12
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	12

BMJ Open

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042751.R2
Article Type:	Protocol
Date Submitted by the Author:	19-Nov-2020
Complete List of Authors:	Polillo, Alexia; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Foussias, George; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Wong, Albert; Centre for Addiction and Mental Health, Campbell Family Mental Health Research Institute; University of Toronto, Psychiatry Ampofo, Augustina; Centre for Addiction and Mental Health Stergiopoulos, Vicky; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Anderson, Kelly; Western University, Epidemiology & Biostatistics Bromley, Sarah; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition D'Arcey, Jessica; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Institute of Medical Science de Oliveira, Claire; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Institute of Health Policy, Management and Evaluation Duda, Lillian; Centre for Addiction and Mental Health Henderson, Joanna; Centre for Addiction and Mental Health, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health; University of Toronto Faculty of Medicine, Psychiatry Kidd, Sean; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Kurdyak, Paul; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Wang, Wei; Centre for Addiction and Mental Health; University of Toronto, Psychiatry Zaheer, Juveria; Centre for Addiction and Mental Health, Institute for Mental Health Policy Research; University of Toronto, Psychiatry Voineskos, Aristotle; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry Kozloff, Nicole; Centre for Addiction and Mental Health, Slaight Family Centre for Youth in Transition; University of Toronto, Psychiatry
Primary Subject Heading:	Mental health

Secondary Subject Heading:	Health services research
Keywords:	Schizophrenia & psychotic disorders < PSYCHIATRY, Clinical trials < THERAPEUTICS, Child & adolescent psychiatry < PSYCHIATRY, Information technology < BIOTECHNOLOGY & BIOINFORMATICS

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title

ED to EPI: Protocol for a Pragmatic Randomized Controlled Trial of an SMS (Text) Messaging Intervention to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis

Authors

Alexia Polillo, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

George Foussias, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Albert H.C. Wong, MD, PhD, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Augustina Ampofo, BA, Centre for Addiction and Mental Health, Toronto, Canada

Vicky Stergiopoulos, MD, MHSc, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Kelly K. Anderson, PhD, Department of Epidemiology and Biostatistics, Western University, London, Canada

Sarah Bromley, OT, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health, Toronto, Canada

Jessica D'Arcey, MSc (candidate), Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Institute of Medical Science, University of Toronto, Toronto, Canada

Claire de Oliveira, MA, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Lillian Duda, MPA, Centre for Addiction and Mental Health, Toronto, Canada

Joanna Henderson, PhD, Margaret and Wallace McCain Centre for Child, Youth and Family Mental Health, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Sean A. Kidd, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Paul Kurdyak, MD, PhD, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Wei Wang, PhD, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Juveria Zaheer, MD, MSc, Institute for Mental Health Policy Research, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Aristotle N. Voineskos, MD, PhD, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Nicole Kozloff, MD, SM, Slaight Family Centre for Youth in Transition, Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, Canada

Corresponding author
Nicole Kozloff, Centre for Addiction and Mental Health
250 College Street, 7th floor
Toronto, ON M5T 1R8
n.kozloff@mail.utoronto.ca
416-535-8501

Word count
4339/4000 words

Keywords
Schizophrenia and psychotic disorders
Early psychosis intervention
Mobile health interventions
Patient and family engagement
Pragmatic clinical trials

ABSTRACT

Introduction

While nearly half of all new psychotic disorders are diagnosed in the emergency department (ED), most young people who present to the ED with psychosis do not receive timely follow-up with a psychiatrist, and even fewer with evidence-based early psychosis intervention (EPI) services. We aim to test an intervention delivered using short message service (SMS), a low-cost, low-complexity, youth-friendly approach, to improve transitions from the ED to EPI services.

Methods and analysis

This is a protocol for a pragmatic randomized, single blind, controlled trial with accompanying economic and qualitative evaluations conducted at the Centre for Addiction and Mental Health (CAMH) in Toronto, Canada. A consecutive series of 186 participants aged 16 to 29 referred by the ED to CAMH's EPI program will be recruited for a trial of a 2-way intervention involving reminders, psychoeducation, and check-ins delivered via SMS. The primary outcome will be attendance at the first consultation appointment within 30 days of study enrolment assessed through chart reviews in the electronic health record. We will also extract routine clinical measures, including the Brief Psychiatric Rating Scale, Clinical Global Impression, and Service Engagement Scale, and link with provincial health administrative data to examine system-level outcomes, including ED visits and psychiatric hospitalizations, 6 months and up to 2 years after baseline. We will perform a cost-effectiveness analysis of the primary study outcome and costs incurred, calculating an incremental cost effectiveness ratio. Web-based surveys and qualitative interviews will explore intervention user experience. Patients and families with lived experience will be engaged in all aspects of the project.

Ethics and dissemination
Research ethics board approval has been obtained. Findings will be reported in scientific journal articles and shared with key stakeholders including youth, family members, knowledge users, and decision makers.

Trial registration number clinicaltrials.gov #NCT04298450

ARTICLE SUMMARY

Strengths and limitations of this study

- Pragmatic randomized controlled trial leveraging mobile health technology, chart reviews, routinely collected administrative data, and economic and qualitative evaluations.
- Intervention well-positioned for local adoption as well as scale and spread to other EPI programs and youth mental health services more broadly.
- Collaboration with health system decision-makers, clinical stakeholders, knowledge users, team members with clinical and research expertise, people with lived experience of psychosis, and key relationships with organizations well-positioned to support widespread implementation.
- Conducting the trial at a single site will support streamlined recruitment but may limit generalizability of our findings.
- The pragmatic data collection methods being utilized, particularly chart review, may be subject to unreliable extraction and missing data.

INTRODUCTION

Psychosis, characterized by delusions and/or hallucinations, typically manifests during adolescence or early adulthood. It is the characteristic presentation of schizophrenia and schizoaffective disorder, and often occurs in bipolar disorder.[1] These disorders can cause significant dysfunction: in disability weighting surveys used to establish global disease burden, participants rated schizophrenia as the disorder most disabling for individuals.[2] Young people experience greater mortality by up to 24-fold in the year following a first psychotic disorder diagnosis compared to peers in the general population.[3] In the long term, psychotic disorders are associated with ongoing increased mortality particularly by suicide,[4] substance use disorders, homelessness, victimization, acts of violence,[5] and high economic costs due to healthcare use as well as lost productivity.[6 7] Early psychosis intervention (EPI) is a model developed to provide treatment early in the course of illness to improve patients' long-term trajectories and reduce the burden on individuals and their families. The rationale for EPI has been strengthened by consistent findings that long duration of untreated psychosis is associated with greater symptom burden, lower likelihood of remission and poor social functioning and global outcomes.[8] Members of our team have shown that EPI service use is associated with a four-fold reduction in all-cause mortality for young people with psychosis compared to those who do not access EPI services.[9] EPI services have also been associated with improved access to psychiatric care, reduced risk of relapse, fewer hospital readmissions, and increased employment rates.[9-13] EPI can be a lifechanging and lifesaving intervention for young people with psychosis.

EPI programs are well-established in Ontario and provide services to young people with early psychosis across the province.[14] Despite this, and the clear mandate for EPI programs to promote their services and minimize barriers to care, many youth with psychosis in Ontario either never access these services, or enter them far later than indicated.[15] In Canada, nearly half of all new psychotic disorders are diagnosed in the ED.[16] We recently found that among young people across Ontario presenting with psychotic disorders to the ED for the first time, 40% received no outpatient mental health follow-up within 30 days and only 45% saw a psychiatrist.[17] The reasons young people with psychosis discharged from the ED did not receive follow-up were unclear in this study: both issues of access (availability and awareness of services) and engagement (youth following through on referrals) are potential explanations. Our experience at the Centre for Addiction and Mental Health (CAMH) in Toronto, where our EPI program sees referred patients for consultation within 2 weeks on average, suggests a problem of engagement: according to clinic data, 50% of the youth referred from the ED do not attend their first EPI consultation appointment (compared with approximately 30% from all other referral sources). It is clear that new approaches are required to engage this population in accessing evidence-based care that is life-saving and improves illness outcomes. In surveys of patients and families in EPI services, appointment reminders are cited as a top factor that would improve service engagement, with a preference for email and text communication.[18-20]

Mobile health technologies are increasingly being tested to improve outcomes, including symptoms, appointment attendance, and medication adherence, among young people with mental illness, particularly psychosis.[21-23] Short message service (SMS) or text message is a commonly used mode of communication by adolescents and young adults: in a survey of users of community mental health services, access to mobile phones approached 100%.[24] SMS is associated with low user and financial burden. SMS does not require people to own a smartphone, have data plans, or have access to wireless internet. In a study of people with psychosis, participants were found to be highly engaged with an SMS intervention.[25] SMS reminders have been associated with improved service engagement in psychosis across studies,[22] including twice the attendance rates for initial appointments in an EPI program.[26] An

ongoing pilot study at CAMH investigating the effect of a weekly 2-way SMS intervention on service engagement during the first year of EPI treatment found this approach to be feasible and valued by participants.[27] We are unaware of any studies examining interventions specifically to improve the transition in care from the ED to EPI for young people with psychosis, using mobile health technologies or otherwise.

Objectives and Hypotheses

"ED to EPI," a pragmatic randomized, single blind, controlled trial[28] with accompanying economic and qualitative evaluations, aims to improve the transition from the ED to EPI services for youth with psychosis using an SMS text messaging intervention. It is pragmatic in its participant eligibility criteria (broad and inclusive), comparison intervention (usual care), follow-up intensity (low), primary trial outcome (objective, meaningful and assessed under usual conditions), measurement of participant compliance and practitioner adherence to study protocol (unobtrusive), and analysis of primary outcome (inclusive, i.e. intention-to-treat).[29] We also leverage linked routinely collected data through ICES (previously known as the Institute for Clinical Evaluative Sciences), which holds data on all hospital and physician visits for the province. We will also evaluate the cost effectiveness of the intervention and explore young people's perspectives on its various components. Our study team, in addition to clinicians and researchers, includes a patient and family member with lived experience of using EPI services and key decision-makers to increase the relevance and uptake of the intervention. Specifically, our primary objectives are to:

1. Evaluate the effect of an SMS intervention on attendance at the first consultation appointment within 30 days of study enrolment;
Hypothesis 1: The SMS intervention will increase rate of attendance at the consultation appointment.
2. Assess indicators of longer-term service engagement 6 months following study enrolment;
Hypothesis 2: The SMS intervention will lead to improved indicators of longer-term service engagement (Service Engagement Scale scores and dropout rates).
3. Determine system-level outcomes, including ED visits and psychiatric hospitalizations, as a function of receiving the SMS intervention, and its cost effectiveness, factoring costs of the intervention and cost offsets of health service utilization;
Hypothesis 3: The SMS intervention will lead to decreased use of acute care services (ED visits and psychiatric hospitalizations) and will be cost-effective relative to the control condition, based on improved rate of transition from the ED to EPI services and anticipated reductions in use of costly acute care services.
4. Explore young people's experiences of the intervention and their perspectives on its various components.
This is an exploratory research question that seeks to understand how young people experience the SMS intervention and how they perceive its various components impact their service engagement.

METHODS AND ANALYSIS

Study setting

The study setting will be the Gerald Sheff and Shanitha Kachan Emergency Department at CAMH, Ontario's only 24-hour stand-alone psychiatric emergency service. The ED also houses a drop-in "Bridging Clinic" which provides care to less acute patients who are diverted after ED triage, and rapid follow-up care for patients discharged from the ED and CAMH inpatient units. Together, they serve approximately 1,200 patients each month. The EPI program at CAMH receives over 600 referrals for suspected psychosis annually, approximately 25% of which are from the ED and Bridging Clinic. Reflecting the Ontario EPI Program

Standards, CAMH EPI services are delivered by multidisciplinary teams, employ strategies to promote early entry and ongoing engagement, and provide pharmacotherapy and psychosocial therapies for an average of 3 years.[14] Patients are assigned to the next available and/or most appropriate psychiatrist and case manager (nurse, social worker, or occupational therapist) for a joint consultation appointment, typically within 2 weeks, and are contacted by phone by the EPI program administrator to book and confirm their appointment. After the initial appointment is confirmed, patients receive a phone call reminder the day before their scheduled appointment. As part of routine care, patients who do not attend their scheduled first appointment receive follow-up calls to reschedule an appointment for up to 30 days from the initial referral.

Eligibility criteria

Study inclusion criteria mirror the intake criteria for the CAMH EPI program. Participants will be eligible for the study if they: 1) are between 16 and 29 years old and 2) have been referred by the CAMH ED to CAMH EPI services for suspected psychosis. Our only exclusion criterion is inability to communicate in basic written English. In our pilot SMS study at CAMH, fewer than 5% of potential participants were excluded for lacking a phone; we have budgeted to offer 5% of participants access to a prepaid cellphone for the duration of the study.[27]

Intervention procedures

Study participants will be recruited at the time of EPI referral for a trial of an SMS intervention designed to engage them during the waiting period for their consultation appointment. They will be randomized to receive either sham or active SMS intervention. Sham SMS will consist of 1 message sent just after enrolment indicating that they will be contacted for an appointment. The sham SMS group will not be denied any part of usual clinical care. Thus, the clinic administrator will call patients in both groups to book and remind them of the consultation appointment. Active SMS intervention will include the initial message sent to the control group, plus a series of subsequent messages. These will include the following content: 1) appointment reminders and instructions, 2) psychoeducational material, and 3) 2-way communication check-ins to rate distress (Figure 1). Intervention components were developed based on feedback from a survey of youth in the same EPI program,[30] as well as psychosocial interventions with evidence in early psychosis, including cognitive-behavioural therapy (psychoeducation, behavioural activation) and illness self management (reminders, distress check-in).[31 32] See Supplementary File 1 for a comprehensive description of the intervention. Messages sent back by participants will be monitored by the research team, and the case manager assigned to their consultation appointment will be notified and will respond accordingly if there are indicators of elevated distress. The intervention will continue until the patient attends the first consultation appointment, or for up to 30 days if the patient does not attend, which reflects the program's practice of closing referrals for non-attending patients.

Messages will be sent through CAMH's in-house Research Electronic Data Capture (REDCap) platform via a third-party plug-in, Twilio, which supports routing of SMS messages to participant devices.[33-35] All data is stored securely on CAMH's REDCap servers or in a locked office and password-protected database on CAMH's secure network. The purpose of the sham intervention is to separate out the content of the intervention (i.e. reminders, psychoeducation, 2-way check-ins) from the effect of simply receiving SMS messages, decreasing participant bias.

Assignment of intervention

Immediately after informed consent, participants will be randomized by REDCap to the active or sham intervention. Generation of the randomization sequence will be managed by the

study biostatistician who is not involved in enrolling participants or assigning intervention arms. Randomization will be stratified by sex (male or female) and referral source (ED or Bridging Clinic), using a computer algorithm to determine a randomized, blocked allocation of participants into intervention groups within strata. Once randomized, treatment assignment will be known only by the study personnel involved in managing the SMS intervention and the case manager monitoring text message responses; the principal investigator and study personnel involved in the chart review and the ICES analysis will remain blind to treatment assignment. Study personnel involved in the qualitative interviews and analysis will also be aware of treatment assignment since only individuals receiving the active intervention will participate in this component of the project.

Sample size

Our sample size calculations are based on the primary outcome of rate of attendance at the EPI program consultation appointment. The current rate of attendance at the first consultation appointment for patients referred from the ED and Bridging Clinic is 50%; we have powered our study to detect the treatment effect with an anticipated rate of attendance of 70%, which is the average for all referral sources other than the ED and Bridging Clinic. A total of 186 participants (93 per group) will provide >80% power to detect a change in attendance from 50% to 70% at alpha <0.05. Non-compliance and loss to follow-up are not a concern for our primary outcome since these are counted in the outcome as nonattendance at the consultation. Adjusting analyses for covariates expected to affect attendance (e.g., age, sex) is expected to further increase power.

Study procedures

We will recruit 186 patients consecutively referred from the CAMH ED and Bridging Clinic to the CAMH EPI program at the time of discharge. During business hours and into the evening, research staff will be on call to the ED to recruit patients as soon as they are identified for the study. Eligible participants who present after hours may be identified by ED staff and referred to the research team who will send them an e-consent form via SMS or email. See Supplementary File 2 for patient consent form. Additionally, potential participants who are missed in the ED/Bridging clinic may be identified by the EPI clinic administrator who will approach them over the phone and send them an e-consent form via SMS or email. We have used the approach of having clinical and administrative staff obtain verbal consent to send e-consent forms in other studies with this population.[19]

As part of informed consent, participants will be asked to consent to a review of their chart, a follow-up web-based survey, and linkage of their information to data held at ICES. They will also be given the option to provide consent to be re-contacted for participation in a qualitative interview. There will be no additional in-person assessments for the quantitative component of this study. CAMH uses an electronic health record, which facilitates data abstraction from multiple clinical programs (i.e., both the ED and Bridging Clinic and EPI program). Research staff and students will be trained by the clinician principal investigators to abstract data into a structured database.

All study participants will receive a $10 e-giftcard once the baseline e-visit is complete. Participants in the active intervention group who complete a web-based survey will receive another $10 e-giftcard and those who complete a qualitative interview will receive a $50 e-giftcard. It will be clarified through the consent process that honoraria are to compensate participants for their time and will not be tied to clinical appointment attendance. For the majority of participants, their initial recruitment and consent will be their only interaction with the research team, with a small subgroup completing qualitative interviews.

Outcome measures

Chart review

Outcome measures are shown in Table 1. CAMH uses many standardized assessment forms which increases the completeness of patient data. Demographic variables, clinical diagnoses, substance use, duration of untreated psychosis (measured as the period of time from first onset of psychotic symptoms to initiation of EPI services and initiation of treatment with an antipsychotic or mood-stabilizing medication), characteristics of the ED visit from which they were referred (urgent presentation – brought by police, involuntary status; timing of visit), and family involvement in care are routinely recorded in the clinical chart by clinicians and will be abstracted from the chart at the time of consultation. Additional variables will likely be available but only for patients accepted into the EPI program, and this will be reflected in the data analysis. These include several assessments that are performed routinely in the EPI program. The Service Engagement Scale (SES)[36] is a brief validated tool designed to measure engagement with community mental health services. In 14 items, it assesses patients' availability for treatment, collaboration, help-seeking behaviours and treatment adherence on a four-point Likert scale with higher scores indicating difficulties in service engagement. The Brief Psychiatric Rating Scale (BPRS)[37] is a clinician or interviewer-rated measure of psychiatric symptoms commonly used as an outcome measure for psychotic disorders and collected monthly in CAMH's EPI program. It includes items related to suicidality and hostility. The Clinical Global Impression (CGI)[38] is a clinician-rated measure of the patient's global severity of illness prior to and after initiating a medication. It includes subscales for Severity and Improvement. Medication and appointment nonadherence will also be assessed over 6 months of treatment. Lastly, after 6 months, current EPI enrolment status will be assessed and categorized as: not offered or enrolled in treatment (e.g., because they did not ultimately have psychosis), enrolled but disengaged prematurely, accepted for treatment but transitioned to other services, or continued in treatment. Data abstractors will undergo rigourous training and monitoring, use standardized extraction forms, and calculate inter-rater reliability.

Administrative data

Primary data collected for the study will be linked deterministically to data sources held at ICES via participants' unique health card numbers. The information available for each participant will be de-identified, stored, and analyzed onsite at ICES following procedures approved by Ontario's Information and Privacy Commissioner. The following ICES data sources will be used: the Ontario Mental Health Reporting System (OMHRS), capturing hospitalizations on adult inpatient mental health units,[39] the Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), capturing all hospital admissions including hospitalizations on child and adolescent inpatient mental health units,[40 41] National Ambulatory Care Reporting System (NACRS) which captures all ED visits,[42] Ontario Health Insurance Plan (OHIP) claims database, which captures outpatient physician visits,[40] Registered Persons Database, which contains health card numbers, demographic information, and deaths, and Ontario Drug Benefits (ODB) claims database, which provides information on all covered prescriptions (based on financial need for those under age 65 and for young people up to age 25 who lack private insurance). These data will also be used for cost effectiveness analysis. Outcomes examined in the linked ICES data are listed in Table 1.

Table 1. Summary of outcome measures and covariates

Type	Variables	Data Source	Timing

Demographic characteristics	Age	Chart review for all demographic characteristics (CAMH Health Equity form and notes)	Baseline[a]
	Sex and gender		
	Sexual orientation		
	Race/ethnicity		
	Born in Canada		
	Religious/spiritual affiliation		
	Highest level of education		
	Source of income and family income		
	Number of people supported by income		
	Employment status		
	Legal history		
	Housing status		
	Living situation		
	Experience of homelessness		
	Relationship status		
Clinical characteristics	Clinical diagnoses	Chart review for all clinical characteristics (consultation and progress notes)	Baseline
	Substance use		Baseline
	DUP		Baseline
	Family involvement in care		Baseline
	Urgent status at ED visit (brought by police, involuntary) Timing of ED visit		
	BPRS[37]		Baseline and 6 months
	CGI[38]		Baseline and 6 months
Service engagement	Attendance at consultation appointment	Chart review for all service engagement measures	30 days
	SES[36]		6 months (completed around 3 months in treatment)

	Medication and appointment nonadherence		6 months
	EPI enrolment status		6 months
System-level outcomes[b]	Number of ED visits	NACRS[42]	6 months and up to 2 years
	Number of inpatient mental health hospitalizations	OMHRS,[39] CIHI-DAD[40 41]	
	Number of days in inpatient mental health hospitalizations	OMHRS,[39] CIHI-DAD[40 41]	
	Number of outpatient mental health visits	OHIP[40]	
	Prescription drugs – psychiatric medications, continuously vs. noncontinuously prescribed	ODB	
	Mortality including cause of death	Registered Persons Database	

[a] Items may be extracted from the ED note or EPI consultation note
[b]Administrative data held at ICES
CAMH, Centre for Addiction and Mental Health; DUP, duration of untreated psychosis; BPRS, Brief Psychiatric Rating Scale; CGI, Clinical Global Impression; SES, Service Engagement Scale; EPI, early psychosis intervention; ED, emergency department; OMHRS, Ontario Mental Health Reporting System; CIHI-DAD, Canadian Institute of Health Information Discharge Abstract Database; NACRS, National Ambulatory Care Reporting System; OHIP, Ontario Health Insurance Plan; ODB, Ontario Drug Benefits.

Statistical analysis

Primary analysis

Descriptive and graphical statistics will be used to summarize the data on all randomized participants and to confirm that there are no group differences in baseline demographics and clinical characteristics. Distributional assumptions will be inspected and appropriate transformations or non-parametric methods will be applied as necessary. In general, generalized linear models[43] will be used throughout. These models account for deviation from normal assumption of the outcome variables and control for covariates.

Our analysis of the primary outcome will be a logistic regression to examine the likelihood of attendance at the EPI consultation with treatment assignment using risk ratios.[44] We will carefully select demographic variables and factors known to influence treatment engagement (e.g., substance use, family involvement in care)[45] to be included in the model as covariates. A difference in attendance between groups will be declared at a significance level of 0.05. Similar models will be used to address the secondary hypotheses, with specific types of models appropriate to each outcome, including time-to-event analysis to examine premature disengagement from services. Administrative data outcomes will be examined using generalized linear models with proper distribution assumptions.

Additional analyses: moderation and generalizability

We plan to conduct two additional exploratory analyses. First, we will run moderation analyses on potential effect modifiers by adding an interaction term between the potential moderator and the treatment assignment indicator in the generalized linear models. We are specifically interested in the moderation effects of health equity factors including gender, race/ethnicity, and housing status. A significant interaction will provide evidence that the treatment effects may be different in the subgroups. A second exploratory analysis will be conducted to evaluate the impact of selection bias of the study sample and estimate the population average treatment effects by employing weighted analysis using propensity scores.[46]

Missing data

The risk of missing data is mitigated through the use of chart review and analysis of administrative data. While the primary outcome will not suffer from attrition, other outcomes will, as some follow-up data will only be available for participants who attended their consultation appointment and those who are enrolled in CAMH EPI services. For these additional outcomes, we plan to use multiple imputation methods developed by Schafer to correct potential bias that could be introduced by missing data.[47]

Economic evaluation

Full details of the economic evaluation appear in Supplementary File 3. We will undertake a cost-effectiveness analysis, where the outcome of interest is consultation appointment attendance, adopting the perspective of the public third-party payer (i.e., the Ontario Ministry of Health). We will collect data on the costs of delivering both arms of the intervention. In addition, using a costing algorithm available at ICES,[48] we will estimate all direct patient-level healthcare costs incurred by the public third-party payer for the intervention and control groups, which will include costs of hospitalizations, ED visits, physician services (i.e., primary care, psychiatry and other) and diagnostic tests, outpatient prescription drugs for individuals covered under the provincial public drug insurance plan, and other hospital-based care. We will calculate the incremental cost-effectiveness ratio (ICER) as the difference in discounted mean costs between the intervention and control group sdivided by the difference in attendance rates. We will use a net benefit regression approach to model probabilities of cost effectiveness for each additional patient referred who attends their consultation appointment in the intervention compared with control group. In addition, we will undertake relevant sensitivity analyses to test the robustness of findings by varying relevant parameters, such as the discount rate. Finally, we will examine the real-world budget impact of implementing the intervention across Ontario, to estimate the cost to the Ministry of Health of implementing this model of care across the province and the potential cost-savings to the system associated with this.

Understanding patient experiences: Survey and qualitative analysis

Participants in the active intervention group will receive a one-time survey sent as a web-link to their phone or email address. Survey topics include user experience, attitudes toward the SMS intervention, its perceived benefits and challenges, acceptability, and suggestions for improvements. Those who consent to participate in the qualitative research component will be re-contacted by phone or email to participate in semi-structured interviews to gain a more in-depth understanding of survey topics. A subsample of 10-15 participants in the active intervention group will be purposively selected to maximize diversity of age, gender, and service attendance. We will use critical realist theory as an underlying framework to guide our interviews, surveys, and analysis.[49] Interviews will be completed until thematic saturation is achieved, estimated at 12 participants. Interviews will be digitally audio-recorded and transcribed verbatim. Surveys will be completed and stored in REDCap. Transcriptions and survey responses will be analyzed using

thematic content analysis in NVivo-11. Research participants will be invited to assist with member checking to confirm that themes reflect their experiences. The analysis can inform future improvements to the intervention and considerations for broader implementation, privileging the experiences of the patients attending these programs.

PATIENT AND PUBLIC INVOLVEMENT

A youth and family member who previously received EPI services have been engaged in helping shape the intervention and study design from project inception. They are active members of the project's Steering Committee that meets monthly to inform study design, implementation, evaluation, and dissemination of results. They will have key roles in the plan to spread the intervention, if successful, to other EPI programs by working with patients and families to adapt the intervention to local contexts. Additional youth with lived experience of receiving EPI services have been consulted on an ad hoc basis through the CAMH Youth Engagement Initiative to provide detailed feedback on the SMS intervention. Patient and family representatives on the research team are compensated for their time.

ETHICS AND DISSEMINATION

The study was approved by the Research Ethics Board (REB) at the Centre for Addiction and Mental Health. The study protocol was prepared according to SPIRIT guidelines[50] and registered with clinicaltrials.gov on March 6, 2020 (NCT04298450; https://clinicaltrials.gov/ct2/show/NCT04298450?term=ed+to+epi&draw=2&rank=1). REB-approved protocol amendments will be posted on the site. The principal investigators and study team will meet regularly to review accrued data, data confidentiality, any adverse events, adherence to protocol design, recruitment and implementation. This intervention has been designed to have high likelihood of adoption and readiness for spread and scale-up because it responds to a critical need, has a strong evidentiary basis, has advantages over existing practice and is both low complexity and low cost.[51] The study team is well-positioned to support widespread implementation of the intervention if successful. We have used an integrated knowledge translation approach that leverages input from stakeholders, including patients, clinicians (both from the ED and EPI services), policymakers, and relevant organizations throughout the study to champion the spread of the intervention to other EPI programs and youth mental health services more broadly. This trial focuses on a particularly vulnerable population—young people transitioning from adolescence to adulthood and from the ED to EPI services—but the basic intervention is widely applicable. The software platform utilized to coordinate this intervention is available at no charge, and the SMS functionality for sending and receiving messages carries a nominal fee, supporting broad uptake.

The results of the trial will be reported in scientific journal articles and shared with key stakeholders as they become available. Our study team includes the co-chair of the Early Psychosis Intervention Ontario Network, a network of over 50 EPI programs across Ontario, and several members of the Canadian Consortium for Early Intervention in Psychosis, providing a durable and established community of practice for immediate spread. De-identified participant data will be available upon reasonable request other than system-level data held at ICES. Requests can be made by contacting the principal investigator Dr. Nicole Kozloff at nicole.kozloff@camh.ca and will be managed by the Steering Committee.

This pragmatic randomized-controlled trial of a low-cost, low-complexity SMS intervention aims to improve the transition from the ED to EPI services for young people with psychosis. It targets a brief but critical period: if young people cannot even get in the door to EPI services, there is no way for them to reap the many known benefits of EPI care. Improving the

ED to EPI transition has the potential to result in more young people with psychosis getting appropriate treatment earlier. The proposed intervention is also likely to be easily adaptable to other referral pathways to EPI services and youth mental health services more broadly. At potentially lower cost to the health system, applying this SMS intervention to the ED to EPI transition has the potential to lead to improved short-term symptoms and functioning, long-term disease trajectories, decreased burden on patients and families, and fewer deaths among young people with psychosis.

Figures

Figure 1. Study intervention schedule*

*This figure represents a summary of the intervention schedule and is not exhaustive of text message content

SMS, short message service; Right arrow, incoming text messages received by participants; Left arrow, outgoing text messages sent by participants

Author contributions

NK is the principal investigator who conceived the original study design and obtained funding, with most of the current authors having contributed to the funding application, and all authors having participated in revisions to the study design for important intellectual content. AP, GF, AW, AA, VS, JD'A, LD, ANV, and NK sit on the project's Steering Committee. AP, GF, JD'A, and NK form the Data Management Committee. AP leads the survey and qualitative analysis. GF, AW, SB, and ANV have administrative roles in the clinical programs and will support the acquisition and interpretation of data. AA and LD act as patient and public consultants. VS acts as a Health System Decision-Maker on the project. KKA, CdO, PK, and NK consult on the ICES analysis. CdO is a health economist who consults on the economic analysis. VS, JH and SK provide knowledge translation expertise. JZ provides consultation on the qualitative interviews and analysis. WW acts as the biostatistical consultant. AP and NK drafted the protocol. All authors read, revised and approved the final version of the manuscript.

Funding statement

This work was supported by the Canadian Institutes of Health Research Transitions in Care Team Grant #165726 as well as by the CAMH Foundation (Award/Grant Number Not Applicable). The funders were not involved in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities.

Competing interests statement

The authors declare no competing interests.

REFERENCES

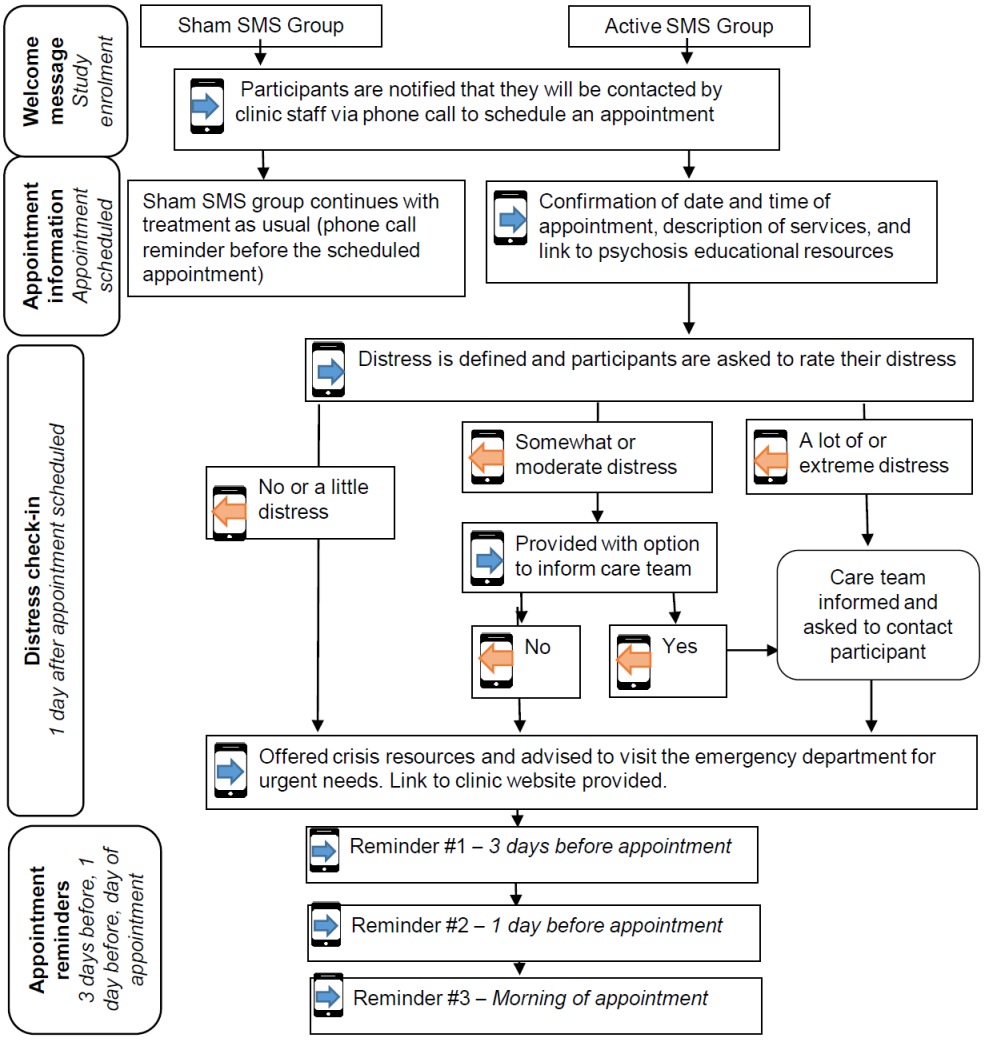
1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. - 5th ed. Arlington, VA: American Psychiatric Publishing 2013.
2. Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013;382(9904):1575-86. doi: 10.1016/s0140-6736(13)61611-6
3. Schoenbaum M, Sutherland JM, Chappel A, et al. Twelve-month health care use and mortality in commercially insured young people with incident psychosis in the United States. *Schizophr Bull* 2017;43(6):1262-72. doi: 10.1093/schbul/sbx009
4. Zaheer J, Olfson M, Mallia E, et al. Predictors of suicide at time of diagnosis in schizophrenia spectrum disorder: A 20-year total population study in Ontario, Canada. *Schizophr Res* 2020 doi: 10.1016/j.schres.2020.04.025 [published Online First: 2020/06/09]

5. Lieberman JA, First MB. Psychotic disorders. *N Engl J Med* 2018;379(3):270-80. doi: 10.1056/nejmra1801490
6. de Oliveira C, Cheng J, Rehm J, et al. The economic burden of chronic psychotic disorders in ontario. *J Ment Health Policy Econ* 2016;19(4):181-92. [published Online First: 2016/12/20]
7. Goeree R, Farahati F, Burke N, et al. The economic burden of schizophrenia in Canada in 2004. *Curr Med Res Opin* 2005;21(12):2017-28. doi: 10.1185/030079905x75087
8. Penttila M, Jaaskelainen E, Hirvonen N, et al. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2014;205(2):88-94. doi: 10.1192/bjp.bp.113.127753
9. Anderson KK, Norman R, Macdougall A, et al. Effectiveness of early psychosis intervention: comparison of service users and nonusers in population-based health administrative data. *Am J Psychiatry* 2018;175(5):443-52. doi: 10.1176/appi.ajp.2017.17050480
10. Craig TK, Garety P, Power P, et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ* 2004;329(7474):1067. doi: 10.1136/bmj.38246.594873.7C [published Online First: 2004/10/16]
11. Petersen L, Jeppesen P, Thorup A, et al. A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ* 2005;331(7517):602. doi: 10.1136/bmj.38565.415000.E01 [published Online First: 2005/09/06]
12. Malla A, Schmitz N, Norman R, et al. A multisite Canadian study of outcome of first-episode psychosis treated in publicly funded early intervention services. *Can J Psychiatry* 2007;52(9):563-71. doi: 10.1177/070674370705200904 [published Online First: 2007/10/24]
13. Bond GR, Drake RE, Luciano A. Employment and educational outcomes in early intervention programmes for early psychosis: a systematic review. *Epidemiol Psychiatr Sci* 2015;24(5):446-57. doi: 10.1017/S2045796014000419 [published Online First: 2014/07/16]
14. Ontario Ministry of Health and Long-Term Care. Early Psychosis Intervention Program Standards. Toronto, ON, 2011.
15. Anderson KK, Norman R, Macdougall AG, et al. Estimating the incidence of first-episode psychosis using population-based health administrative data to inform early psychosis intervention services. *Psychol Medicine* 2018:1-9. doi: 10.1017/s0033291718002933
16. Anderson KK, Fuhrer R, Wynant W, et al. Patterns of health services use prior to a first diagnosis of psychosis: the importance of primary care. *Soc Psychiatry Psychiatr Epidemiol* 2013;48(9):1389-98. doi: 10.1007/s00127-013-0665-3
17. Kozloff N, Jacob B, Voineskos AN, et al. Care of youth in their first emergency presentation for psychotic disorder: a population-based retrospective cohort study. *J Clin Psychiatry* 2018;79(6) doi: 10.4088/JCP.17m11947 [published Online First: 2018/11/13]
18. Lal S, Dell'Elce J, Tucci N, et al. Preferences of young adults with first-episode psychosis for receiving specialized mental health services using technology: a survey study. *JMIR Ment Health* 2015;2(2):e18. doi: 10.2196/mental.4400 [published Online First: 2015/11/07]
19. Patient and Family Perspectives on Improving Engagement in Early Psychosis Intervention. Congress of the Schizophrenia International Research Society; 2019; Orlando, Florida, USA.
20. Using REDCap to evaluate youth and family perspectives on engagement in early psychosis intervention. REDCap Con December 2019; Toronto, Ontario, Canada.
21. Firth J, Torous J. Smartphone apps for schizophrenia: a systematic review. *JMIR mHealth uHealth* 2015;3(4):e102. doi: 10.2196/mhealth.4930 [published Online First: 06.11.2015]

22. D'Arcey J, Collaton J, Kozloff N, et al. The use of text messaging to improve clinical engagement for individuals with psychosis: systematic review. *JMIR Ment Health* 2020;7(4):e16993. doi: 10.2196/16993
23. Alvarez-Jimenez M, Alcazar-Corcoles MA, Gonzalez-Blanch C, et al. Online, social media and mobile technologies for psychosis treatment: a systematic review on novel user-led interventions. *Schizophr Res* 2014;156(1):96-106. doi: 10.1016/j.schres.2014.03.021 [published Online First: 2014/04/22]
24. Ennis L, Rose D, Denis M, et al. Can't surf, won't surf: the digital divide in mental health. *J Ment Health* 2012;21(4):395-403. doi: 10.3109/09638237.2012.689437 [published Online First: 2012/06/21]
25. Kauppi K, Kannisto KA, Hatonen H, et al. Mobile phone text message reminders: measuring preferences of people with antipsychotic medication. *Psychol Med* 2015;168(1-2):514-22. doi: 10.1016/j.schres.2015.07.044
26. Thomas IF, Lawani AO, James BO. Effect of short message service reminders on clinic attendance among outpatients with psychosis at a psychiatric hospital in Nigeria. *Psychiatr Serv* 2017;68(1):75-80. doi: 10.1176/appi.ps.201500514
27. Using short message service as a means of engagement in early psychosis. IEPA 11th International Conference on Early Intervention in Mental Health - "Prevention and Early Intervention: Broadening the Scope"; October 7-10 2018; Boston, Massachusetts, USA. Early Interv Psychiatry.
28. Meinecke AK, Welsing P, Kafatos G, et al. Series: pragmatic trials and real world evidence: paper 8. data collection and management. *J Clin Epidemiol* 2017;91:13-22. doi: 10.1016/j.jclinepi.2017.07.003
29. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clinical Epidemiol* 2009;62(5):464-75. doi: 10.1016/j.jclinepi.2008.12.011
30. Improving Youth Engagement in Early Psychosis Intervention Programs: Preliminary Results From a Youth Survey. 66th Annual Meeting of the American Academy of Child and Adolscent Psychiatry; 2019 October 17, 2019; Chicago, IL, USA.
31. Lecomte T, Abidi S, Garcia-Ortega I, et al. Canadian Treatment Guidelines on Psychosocial Treatment of Schizophrenia in Children and Youth. *Can J Psychiatry* 2017;62(9):648-55. doi: 10.1177/0706743717720195 [published Online First: 2017/09/10]
32. American Psychiatric Association. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia, Third Edition. Washington DC: American Psychiatric Association 2020.
33. Vanderbilt University. REDCap (research electronic data capture) 2018 [Available from: https://www.project-redcap.org accessed April 2 2020.
34. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010 [published Online First: 2008/10/22]
35. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208 [published Online First: 2019/05/13]
36. Tait L, Birchwood M, Trower P. A new scale (SES) to measure engagement with community mental health services. *J Ment Health* 2002;11(2):191-8. doi: 10.1080/09638230020023570-2 [published Online First: 2002/01/01]
37. Flemenbaum A, Zimmermann RL. Inter- and intra-rater reliability of the Brief Psychiatric Rating Scale. *Psychol Rep* 1973;32(3):783-92. [published Online First: 1973/06/01]
38. Guy W. Clinical Global Impressions. ECDEU Assessment Manual for Psychopharmacology. Rockville, Maryland: National Institute for Mental Health 1976:218-22.

39. Canadian Institute for Health Information. Ontario Mental Health Reporting System, Data Quality Documentation, 2015-2016. Ottawa, ON: CIHI, 2017.
40. Williams JI, Young W. A Summary of Studies on the Quality of Health Care Administrative Databases in Canada. In: Goel V, Williams JI, Anderson GM, et al., eds. Patterns of Health Care in Ontario The ICES Practice Atlas. 2nd ed. ed. Ottawa, ON: Canadian Medical Association 1996.
41. Juurlink DN, Preyra C, Croxford R, et al. Canadian Institute for Health Information Discharge Abstract Database: A Validation Study. Toronto, ON: Institute for Clinical Evaluative Sciences, 2006.
42. Canadian Institute for Health Information. CIHI Data Quality Study of Ontario Emergency Department Visits for Fiscal Year 2004-2005--Executive Summary. Ottawa, ON: CIHI, 2008.
43. McCullagh P, Nelder JA. Generalized Linear Models, Second Edition;. London, UK: Chapman and Hall 1989.
44. McNutt LA, Wu C, Xue X, et al. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003;157(10):940-3. [published Online First: 2003/05/15]
45. Doyle R, Turner N, Fanning F, et al. First-episode psychosis and disengagement from treatment: a systematic review. *Psychiatr Serv* 2014;65(5):603-11. doi: 10.1176/appi.ps.201200570 [published Online First: 2014/02/19]
46. Wang W, Ma Y, Huang Y, et al. Generalizability analysis for clinical trials: a simulation study. *Stat Med* 2017;36(10):1523-31. doi: 10.1002/sim.7238 [published Online First: 2017/01/27]
47. Schafer JL. Analysis of incomplete multivariate data;. London, UK: Chapman & Hall 1997.
48. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188(3):182-88. doi: 10.1503/cmaj.150064 [published Online First: 2016/01/13]
49. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa
50. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583 [published Online First: 2013/01/09]
51. Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009;4:50. doi: 10.1186/1748-5908-4-50 [published Online First: 2009/08/12]

Figure 1. SMS intervention schedule*



*This figure represents a summary of the intervention schedule and is not exhaustive of text message content

SMS, short message service; Right arrow, incoming text messages received by participants; Left arrow, outgoing text messages sent by participants

BOTH ACTIVE AND SHAM GROUPS

At Time of Enrolment

Hi [First Name], this is [Clinic]. If you haven't yet been given an appointment, one of our clinic staff will contact you in the next few days. Just so you're aware, our number comes up as private. Please text '1' to confirm you received this message.

(If 1 texted back): Thanks for confirming!

ACTIVE GROUP

After appointment scheduled via phone

Hi [First Name], thank you for booking your first visit with [Clinic] on [date] at [time]. If you need to reschedule, please call [Clinic Phone]. At your appointment, you will meet with a psychiatrist and a case manager who will work with you to figure out how we can best support you. Experiencing psychosis can be difficult and knowing more about mental health may help you cope. If you'd like to learn more about mental health and psychosis, please visit: www.camh.ca/psychosis

Two-way distress check-in

Next day**

Hi [First Name], while you wait for your upcoming appointment with us at [Clinic], we wanted to check in! How are you doing this week? Please send back '1' for well, '2' for okay, or '3' for bad.

If response = 1

Thanks for letting us know. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 2 or 3

We say people are experiencing distress when they are feeling anxious, depressed, worried, or hopeless. Can you please rate your distress for us? '0' for no distress, '1' for a little distressed, '2' for somewhat distressed, '3' for moderately distressed, '4' for a lot of distress, or '5' for extreme distress (urgent).

If response = 1

If response = 2-3

Thanks for letting us know. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Would you like us to pass this information on to your care team? They may reach out to you during business hours. Please text back: '1' for yes, or '2' for no. We won't pass this information on unless you text back '1'.

If response = 1: Thanks for letting us know. We have passed this onto your care team who may reach out during business hours. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 2: Thanks for letting us know. We won't pass this information on. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 4

Thanks for letting us know, we have passed this information on to your care team, who may reach out during business hours. Here are some resources if you're experiencing a crisis: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 5

Thanks for letting us know. We have passed this information on to your care team, who may reach out during business hours. We urge you to consider trying these resources: www.camh.ca/crisis-resources. If you need urgent support, please see your nearest emergency department. Please text '1' to confirm you received this message.

If response = 1

Thanks for confirming! For more information about our services, please visit: www.camh.ca/sceis.

Reminder #1

3 days pre-appointment**

Hi, this is a reminder that your appointment at [Clinic] is coming up on [date] at [time].

Reminder #2

1 day pre-appointment

Hi, this is a reminder of your appointment tomorrow at [time]. The care team is looking forward to meeting you. If you need to reschedule, call [Clinic Phone].

Reminder #3

Morning of appointment

Hi, your appointment with [Clinic] is today at [time]. Please call us at [Clinic Phone] if you need any assistance.

If participant does not show, they receive the following message, and then the process starts over from the check-in until participant shows up or 30 days have passed:

Hi, we understand you didn't make it to your [Clinic] appointment. To reschedule, please call [Clinic Phone].

If 30 days have passed and participant has not attended

Hi, you have now finished receiving text messages from the research study. Thank you for your participation!

**Timing of messages and logistical content may vary depending on the date and current context of the consult appointment.

camh
Centre for Addiction and Mental Health

ED to EPI: Using SMS (Text) Messaging to Improve the Transition from the Emergency Department to Early Psychosis Intervention for Young People with Psychosis
Online Version - Informed Consent Form

Principal Investigator: Dr. Nicole Kozloff
Dr. George Foussias
Dr. Vicky Stergiopoulos
Dr. Aristotle Voineskos

Co-Investigators:
Augustina Ampofo
Dr. Kelly Anderson
Sarah Bromley
Jessica D'Arcey
Dr. Jeff Daskalakis
Dr. Claire de Oliveira
Lillian Duda
Dr. Joanna Henderson
Dr. Sean Kidd
Dr. Paul Kurdyak
Dr. Alexia Polillo
Dr. Brittany Poynter
Dr. Wei Wang
Dr. Albert Wong
Dr. Juveria Zaheer

Sponsor: Canadian Institutes of Health Research, CAMH Foundation

Purpose of the Study:

We invite you to participate in this study because you have been referred to the Slaight Centre for Early Intervention Services. The Slaight Centre is an outpatient program for young people experiencing a first episode of psychosis and their families. In this study we will examine if text messaging can improve the transition from the emergency department to early intervention services for youth. We hope that this study will eventually lead to young people getting appropriate treatment earlier and improve their long-term outcomes. Your participation in this study is voluntary. The following information is provided to help you make an informed decision whether or not to participate.

What will I be asked to do as part of this study?

If you decide to participate in this study, you will be asked to do the following:

1) Intervention: You are being invited to take part in a study. If you consent to participate, you will be randomly assigned to receive one of two types of text messages. Random assignment means that you have an equal chance of being assigned to each text message group. If you are assigned to the text message intervention, you will receive text messages at a time of your choosing (e.g., morning, evening). You will be sent text messages with information about appointment details, education about psychosis, an opportunity to rate your distress, and appointment reminders. These text messages will continue until you attend your first consultation appointment, or for up to 30 days if you did not attend. If you are assigned to the other group, you will receive a one-time text message. If you do not have a phone, one will be offered to you for the duration of the study with the expectation that it is returned at your first consultation appointment.

camh
Centre for Addiction and Mental Health

Please note that text messages are NOT being monitored constantly and if you are experiencing an urgent issue, this information should not be sent by text message. Instead, please visit your nearest emergency department. Additionally, this is not a direct line of communication with your care team and it is not a secure form of communication. You should not send any personal health information that is not requested by the text messages.

2) Collection of data**:** We will also review your medical chart to obtain additional information about you. Information collected through this study will be transferred to the Institute for Clinical Evaluative Sciences (ICES). ICES is an organization that holds routinely collected data on health care use in Ontario. ICES is committed to protecting the privacy and security of health information. ICES is an approved unit under Ontario's Personal Health Information Protection Act and follows the policies and procedures for privacy protection and data security approved by Ontario's Information and Privacy Commissioner. Linking the data will involve using personal identifiers such as your name, date of birth, and OHIP number to identify your health service use. These identifiers will be removed as soon as the data is connected to ICES. The data will then be replaced by a scrambled code in order to decrease the likelihood of a data breach (when people get access to private information without permission)

3) Follow up survey: You may be asked to complete a brief survey following your participation in the text message intervention. Your participation in the survey is voluntary. If you consent to study participation, you may receive a link to the online survey at the contact information of your choice (text message or email). The survey takes approximately 5 to 10 minutes to complete. If you complete the survey, you will be compensated with a $10 e-gift card sent to you by email or text message from your choice of a list of retailers. The survey contains questions about your experiences with the text message intervention.

Are there risks involved?

There are no known harms associated with participation in this study. If your text messaging plan does not include unlimited texting, you may incur additional charges on your cell phone bill. The study will not reimburse you for these charges. You may also feel emotional discomfort and fatigue from receiving recurrent text messages with appointment reminders and questions about how you are feeling. If you do feel this way, you may refuse to answer any question, or terminate your participation in this study at any point in time. You may be asked some questions during the survey that might make you feel somewhat uncomfortable. If you do feel uncomfortable, you may indicate this in the comments or skip the question. You can also pause the survey and continue at another time. Please be advised that if the researcher or study personnel sees that there is a risk to your safety or the safety of others, then steps will be taken to ensure your safety and the safety of others. Lastly, the security of information sent by email/text cannot be guaranteed.

Are there benefits involved?

No direct benefits to your health will likely result from this study. It is possible that the results of this study will increase engagement in early intervention services and may benefit other people now or

in the future. You will also receive compensation for your time and participation in the study. The investigators responsible for this study or CAMH are not conducting this study to receive commercial benefit. However, if this research produces financial returns from a commercialization of the results in the future, you will not receive any benefit from these returns.

Can participation in this study end early?

Participation in any research study is voluntary. Your decision whether or not to participate will not interfere with your right to healthcare or other services to which you are otherwise entitled. You can contact the research team through email or phone to withdraw from the study at any time. After data is anonymized your responses cannot be withdrawn, however, no new data will be collected. Throughout your participation in this study, you will continue to receive usual care as agreed upon by you and your treatment team. In the event of research-related harm, you have not waived any legal rights/rights to legal recourse.

Are study participants paid to participate in this study?

Everyone who participates in the text messaging intervention will receive a $10 e-gift card by email or text message from your choice of a list of retailers. If you decide to withdraw before study end, you will still be paid for your time and participation. Those participants selected to participate in the follow up survey will receive another $10 e-gift card by email or text message from their choice of retailers for completing the survey.

Will personal information about me be kept confidential?

- The research data will be kept confidential from the inception of the study.
- Any information about you obtained from this research will be kept as confidential (private) as possible unless disclosure is required by law. It is important to note that confidentiality will be protected to the extent permitted by law. However, there are 3 exceptions to our confidentiality policy. In any of the following situations, we are obligated by law to contact authorities: 1) if there is a serious possibility that you may harm yourself or others; 2) if you have been involved in any form of child abuse or neglect; 3) if you have been the victim of abuse by a healthcare worker
- All data obtained from this research will be kept in a locked office and secured password database with limited access only to study personnel and authorized CAMH personnel.
- To protect your identity and confidentiality, all personal identifiers (such as your name, birth date) will be removed (de-identified and replaced with a specific code number; the research records and data will be indicated by a case number rather than your name, and the information linking these case numbers with your identity will be kept separate from the research records. This information will be kept in a separate, secure location and will only be accessible to study personnel.
- Study personnel may also access your health records for research purposes; your medical records will be kept confidential.
- All electronic files will be stored on CAMH's secure hospital or institutional network and will be password protected.
- Other Canadian research centres (other than CAMH) may be involved in analyzing the data,

camh
Centre for Addiction and Mental Health

and if so this will be confidential, and your name will not be given out.

- Following the completion of the study, the researchers intend to publish the results in scientific journals. You will not be identified in any of these reports. A report of the results of this project will be given to you if you request it.
- The information you provide will not affect the usual care that you receive.
- The investigators on this study will keep the data as long as necessary to fulfill the research purposes and in accordance with the applicable laws and regulations and will use enhanced security measures to store it.
- De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share.
- Your de-identified research data (information about your diagnosis, symptoms, and study evaluations) may be shared with investigators at other Canadian research centres (other than CAMH).

Will this research study involve the use or disclosure of my identifiable medical information?

- Study personnel will retrieve information about your demographics and clinical care from your medical chart. This will be stored in a secure database with a case number rather than your personal identifiers.

Who will have access to identifiable information related to my participation in this research study?

Personal Health Information (PHI) is information about your physical or mental health or the health care that you receive that could identify you. In addition to the investigators listed on the first page of this consent form and their research staff, the following individual and/or programs will or may have access to identifiable information (which may include your identifiable medical information):

a. Institute for Clinical Evaluative Sciences (ICES) is a prescribed entity under Ontario's Personal Health Information Protection Act and adheres to policies and procedures for privacy protection and data security approved by Ontario's Information and Privacy Commissioner.

b. *As part of the Research Services Quality Assurance Program, this study may be monitored and/or audited by a member of the Quality Assurance Team. Your research records and CAMH records may be reviewed during which confidentiality will be maintained as per CAMH policies and extent permitted by law.*

c. As a part of continuing review of the research, your study records may be assessed on behalf of the Research Ethics Board. A person from the research ethics team may contact you (if your contact information is available) to ask you questions about the research study and your consent to participate. The person assessing your file or contacting you must maintain their confidentiality to the extent permitted by law.

camh
Centre for Addiction and Mental Health

Offer to Answer Questions

We have used some technical terms in this form. Please feel free to ask about anything that you do not understand. Consider this research and the consent form carefully as long as you feel necessary before you make a decision.

Dr. Nicole Kozloff is responsible for this study. If you have any questions, please contact Dr. Nicole Kozloff at 416-535-8501 x 30769.

If you have any questions about your rights as a participant in a research study, you may contact Dr. Robert Levitan, Chair, Research Ethics Board, Centre for Addiction and Mental Health, at 416-535-8501 x 34020.

Consent to Participate: My signature below indicates that:

- I acknowledge that the research study described above has been explained to me and that any questions that I have asked have been answered to my satisfaction.
- I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of medical care for me and for other members of my family.
- I have been informed of the potential risks/harms and discomforts and I also understand the benefits of participating in this study.
- I know that I may ask now, or in the future, any questions that I may have about the study or the research procedures.
- I have been assured that records relating to my research participation and to me will be kept confidential and that no information will be printed that would disclose my identity without my permission, unless required by law.
- I have been given sufficient time to read and understand the above information
- I understand and consent that my records and research data may also be shared with other investigators for analysis and future projects (this would include only de-identified data).

Please check one:

☐ **Yes, I consent to participating in this study**

☐ **No, I do not consent to participating in this study**

Optional – Future Contact:

Do you agree to be re-contacted by our study team for an in-person interview or other follow up? You will be compensated for your participation.

☐ Yes, I agree to be contacted about study follow-up

camh
Centre for Addiction and Mental Health

☐ No, I do not wish to be contacted about study follow-up

Texting Preferences:

If you agreed to participate in the study:

At what phone number would you like to receive text messages?

_____

At what phone number or email address would you like to receive other links related to the study (e.g., your e-giftcard, the survey, and future communications)?

_____

What time of day would you prefer to receive text messages?

☐ Morning ☐ Afternoon ☐ Evening

What first name would you like us to call you in your text messages?

_____

Compensation Preferences:

Which e-giftcard would you like to receive as compensation for participating? It may take up to 10 business days to receive your compensation.

☐ Tim Hortons ☐ Amazon

Please contact 416-535-8501 x 30677 if you do not receive a text message from us within 24 hours.

The security of information sent by e-mail/text cannot be guaranteed. Please do not communicate personal sensitive information by e-mail/text. Let the research team know if you do not want to be contacted by e-mail/text. Email/Text is not routinely monitored outside of work hours. Please do not use e-mail/text to communicate emergency or urgent health matters – please contact your clinician or family doctor. If it is a medical emergency, call 911.

Supplementary File 3

We will undertake a cost-effectiveness analysis, where the outcome of interest is consultation appointment attendance, adopting the perspective of the public third-party payer (i.e., the Ontario Ministry of Health). Using a costing algorithm developed in SAS and available at ICES,[1] we will be able to estimate all direct patient-level healthcare costs incurred by the public third-party payer for both the intervention and control groups. In particular, we will include costs of hospitalizations, ED visits, physician services (i.e. primary care, psychiatry and other) and diagnostic tests, outpatient prescription drugs for individuals covered under the provincial public drug insurance plan, home care, long-term care, and other hospital-based care (which includes rehabilitation and complex continuing care). The costing methodology used in the algorithm includes a bottom-up/micro-costing approach to cost services at the individual level. This makes use of individual episodes of care or utilization in the healthcare system and their associated prices (or costs or amounts paid). A top-down approach, which allocates corporate aggregate (i.e. institutional) costs to individual visits or cases/episodes of care, will be applied in cases where individual unit costs are not available (e.g., for institutional care settings). In addition, we will include all costs associated with delivering both arms of the intervention. Costs will be reported in 2023 using the Consumer Price Index for Health and personal care (Statistics Canada). All costs and outcomes will be discounted at a rate of 1.5% per year, in line with the Canadian Agency for Drugs and Technologies in Health guidelines.[2] The incremental cost-effectiveness ratio (ICER) will be calculated as the difference in discounted mean costs between the intervention and control groups divided by the difference in attendance rates. We will use a net benefit regression approach to model probabilities of cost-effectiveness for each additional patient referred who attends their consultation appointment in the intervention compared with control group. In addition, we will undertake relevant sensitivity analyses to test the robustness of findings by varying relevant parameters, such as the discount rate. Finally, we will examine the real-world budget impact of implementing the intervention across Ontario, to estimate the cost to the Ministry of Health of implementing this model of care across the province and the potential cost-savings to the system associated with this.

REFERENCES

1. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188(3):182-88. doi: 10.1503/cmaj.150064 [published Online First: 2016/01/13]
2. Guidelines for the Economic Evaluation of Health Technologies. 4th ed. Ottawa, ON, 2017.

Supplementary File 1: Protocol reporting checklist based on SPIRIT guidelines

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	12
Funding	#4	Sources and types of financial, material, and other support	13
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	13

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	13
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5

Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5-6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose	6-7

		change in response to harms, participant request, or improving / worsening disease)	
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	8-11
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6-7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8-10
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7-10
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7-8

Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	7

Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	7-10
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	7-9, 12
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10-12

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	12
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12

Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	12
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	12
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7-8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	7-8, 12
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7-8
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	13

Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	12-13
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12-13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	12-13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	12-13
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	7-8, 12
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	12