camh
Centre for Addiction and Mental Health
Centre de toxicomanie et de santé mentale

STUDY PROTOCOL

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Study Title: Enhancing Evidence-Based Practice for Youth and Emerging Adults with Early Psychosis: Implementation and Evaluation in Diverse Service Settings

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1. Abstract

Implementation of 'NAVIGATE' in Ontario aims to help youth and emerging adults (YEA) suffering from a first episode of psychosis (FEP). Although Ontario already has early psychosis intervention (EPI) programs, our team's recent work has identified major challenges of delivering coordinated care, particularly those elements of care that enhance recovery. These challenges also exist nationally and internationally. By building on the already existing EPI community of practice through the Early Psychosis Intervention Ontario Network, we will implement NAVIGATE with the help of CAMH's Provincial System Support Program facilitators. The use of tele-videoconferencing through ECHO Mental Health Ontario, and the processes and protocols that ECHO provide us with an opportunity to ensure sustainability. Using health administrative data held at the Institute for Clinical Evaluative Sciences (ICES), we can examine system-level outcomes, including hospitalizations, emergency department visits, and outpatient physician visits of YEA suffering from a FEP who are treated with NAVIGATE compared with those treated in EPI programs without NAVIGATE and those who are not treated in EPI programs. In addition, we can also evaluate health care costs. Prior to initiating this project, we obtained the input of YEA with an FEP and family members. We will also continue to measure engagement across the study. This work fulfills the innovative clinical trial mandate through its implementation and measurement plan, along with the strategy for patient-oriented research through the involvement of patients, family members, and policy makers as equal partners.

2. Introduction and Background/Rationale

2.1. Overview

First Episode Psychosis (FEP) as a Public Health Priority:
An FEP is one of the most frightening and disabling experiences from which a young person can suffer. Onset occurs in nearly all cases in youth and emerging adults (YEA), a crucial transition time, when major developmental milestones (high school graduation, first intimate relationship, maturation of executive function) occur[1,2,3]. An FEP typically occurs in the context of diagnoses of schizophrenia, schizoaffective disorder, psychotic disorder NOS, substance-induced psychosis, and psychotic bipolar disorder, which when taken together are the most disabling disorders (among all medical illnesses) for YEA in OECD countries (causing over 10% of the total disability adjusted life years (DALYs) in this population[4]. Recent evidence from the U.S. shows the lethality of an FEP: associated mortality rates are 24 times greater in the 12 months after diagnosis compared to the general population[5]. Suicide, the second leading cause of death among youth in Canada, remains much higher in early psychosis than in the general population. Even after accounting for suicide, persons suffering from these illnesses have a shortened lifespan that is attributed to early mortality, primarily due to downward socioeconomic drift and poorly treated medical disorders, a reflection of the gross inequity experienced by those with an FEP in relation to the general population[6,7,8].

Early Psychosis Intervention (EPI) Programs: Life-Saving, but Lack of High Quality Care:
The emergence of EPI programs has provided tremendous hope by providing early intervention[9,10,11]. Work by our team, recently published in the American Journal of Psychiatry[12], shows that youth who access an EPI program in Ontario, Canada receive faster psychiatric follow-up, better coordination of care between inpatient and outpatient services, reduced burden on the emergency department, and reduced all-cause mortality. Our system-level data support EPI programs as a critical life-saving intervention. Internationally, EPI has demonstrated significant benefits compared to treatment as usual with respect to engagement, service utilization, and suicide[9,13,14,15].

Despite the initial life-saving benefits of EPI services, provincial, national and international data show that consistent delivery of high-quality, evidence-based care in EPI programs is a major challenge[16]. Recovery rates in EPI programs remain low[17], and associated disability has not improved under routine clinical care[18]. One explanation for these disappointing facts is that a low proportion of patients receive recovery-based services, namely, case management including individualized psychosocial interventions, family education and intervention, supported education and employment. Even in clinical service delivery trials (where service quality is typically superior to real-world settings), recovery-based service is received by 15-56% of patients[9,13] with only 18% receiving comprehensive EPI services[9]. While EPI standards across jurisdictions recommend coordinated and comprehensive recovery-based care[19], effective implementation and sustainability of such care in real-world settings remains poor[20].

Our own work in Ontario, detailed below, has uncovered a startling gap between the evidence-based standard of care, and real-world delivery of care, even in a jurisdiction (Ontario) that has prioritized EPI services. The results of our Ontario survey[21] were mirrored in a national survey of 11 Canadian EPI programs[22]. Similarly, ten years after Australia (a leader in EPI care) published national early psychosis guidelines, surveys demonstrated that implementation of recovery-based care was varied and disappointingly low[23]. This study is designed to improve the delivery of recovery-oriented evidence-based EPI care in Ontario. If successful, we will improve person-, system-, and economic-level outcomes for YEA suffering from an FEP, and offer a potential roadmap for the rest of Canada.

EPI in Ontario: Shows Early Success Through a Community of Practice But Challenges Continue in Delivering Consistent and Sustained High Quality, Evidence-Based Care:
In 2004, the province of Ontario allocated funding for EPI programs based on early evidence of efficacy. Between 2005 and 2007, this new provincial funding led to a major EPI program expansion in Ontario[24], but the absence of provincial standards led to program development in an ad-hoc manner, drawing upon general service delivery experience and advice from established programmes[24]. Concomitantly, the Early Psychosis Intervention Ontario Network (EPION) was established, which has now grown to 52 EPI sites. The establishment of EPI program standards[25] in Ontario in 2011, informed by existing international and national standards, but also by input from clinicians, patients, family-members, and policy makers was a crucial first step toward standardizing care. However, the release of standards alone is not sufficient to ensure effective implementation, practice change, and ongoing quality practice.

The Ontario Ministry of Health and Long Term Care established a Standards Implementation Steering Committee (SISC) within EPION that is supported by the Provincial System Support Program (PSSP), based at the Centre for Addiction and Mental Health (CAMH). The SISC was established due to increasing recognition that active support is required to implement and sustain evidence-based care in routine practice[26]. Key findings from the first survey by the Ontario SISC of 52 EPI program sites in Ontario (92% participation) demonstrated important challenges in delivering evidence-based EPI care[27]. A follow-up survey also identified opportunities for addressing these challenges[21]. Building on the two surveys, we conducted a study[28] to measure fidelity to current EPI standards using the First Episode Psychosis Service – Fidelity Scale (FEPS-FS)[29]. This fidelity project trained EPI staff as peer assessors to document current service delivery approaches, challenges and support needs in self-selected EPION programs. Our most notable finding was lack of delivery of consistent recovery-oriented care, with no structured or manualized process for these elements of care. Through site visits, and in-person interviews with nine Ontario EPI programs, we obtained a richer and clearer picture of the current state, creating an opportunity to implement solutions that can address the major challenges identified in the fidelity study:

Challenge 1. There is variability in the type and frequency of EPI services offered. Variability was particularly noted in aspects of recovery-oriented care, including comprehensive care planning and monitoring, use of psychotherapies (CBT), family support, and employment support. A lack of protocols to guide such delivery and inconsistent documentation was a common theme.

Challenge 2. Programs expressed a need for more tools and protocols to guide service delivery, more consistent access to training, and lack of time for training in the implementation of new practices.

Challenge 3. Programs desired opportunities to learn from peers in a community of practice, and noted resource challenges such as accessing expertise and travel time.

How Will this Study Address the Identified Challenges?
We want to address these challenges in Ontario EPI settings by implementing NAVIGATE, a coordinated and comprehensive multidisciplinary treatment program for FEP that is deliverable in community mental health settings. NAVIGATE is manualized and measurement-based. To maximize affordability, adaptability, spread, and sustainability, the key elements of success for an implementation project as defined by CIHR, we will utilize a) the already-established EPION community of practice, b) the implementation science expertise of PSSP, and c) the sustainability and capacity building approach of The Extension of Community Health Outcomes (ECHO) Ontario Mental Health at CAMH and the University of Toronto (ECHO-ONMH). These are detailed point-by-point below. We first briefly explain, and summarize the evidence for NAVIGATE.

In 2008, the National Institute of Mental Health (NIMH) issued a request for proposals entitled: Recovery After an Initial Schizophrenia Episode (RAISE), with a goal to change the trajectory and prognosis of FEP30. NAVIGATE was developed in consultation with clinical and research experts, biostatisticians, health economists, consumers, family members, advocacy groups, and government officials. It is a form of coordinated specialty care for FEP consisting of 4 key intervention components: (i) individualized medication management using a decision support tool, (ii) a package of psychoeducation and a blend of evidence-based psychotherapies called "individual resiliency training" (IRT); (iii) supported employment and education (SEE); and (iv) a family education program. NAVIGATE was evaluated from 2009-2014 in a cluster randomized controlled trial involving 404 individuals with an FEP in 34 community mental health centers across the United States[20]. Notably, it was delivered by re-allocating existing community mental health resources with no new funding for clinical care. Compared to usual care, NAVIGATE treatment provided greater improvement in symptoms, but more importantly, as prioritized by patients, significantly greater improvement in real-world functioning, including social functioning and engagement in educational and vocational training[20,31]. NAVIGATE was also readily implementable across a broad range of community-based mental health settings, with enhanced engagement and delivery of multidisciplinary care to YEA presenting with psychosis and their families compared to standard care, and with longer and more consistent receipt of mental health services[20]. A recent economic analysis revealed that NAVIGATE treatment was more cost-effective compared to standard community care, driven by the anticipated enhanced health benefits and improvements in quality of life[32].

Challenge 1. Need to Standardize Care, Particularly Recovery-Oriented Care and Manualized Protocols: NAVIGATE operationalizes current EPI standards using manualized protocols, ensuring consistency and reducing variability in care. The four NAVIGATE components (individualized medication management, IRT, SEE, and family education program) are systematically applied in collaboration with the patient[33]. There is an overarching emphasis on the coordinated delivery of these elements of care. Every patient is offered these elements of care, and modules are completed in a systematic time-oriented fashion

that reduces variability in care among sites and team-members within a site. For instance, goal-setting and identification of personal strengths are consistently discussed at the first visit. This ensures that care is systematically oriented and aligned towards patient preference. At each patient visit, a contact/progress note is completed, including the modules delivered, that the team reviews to assess patient progress, fidelity, and determine need for adjustments.

Challenge 2. Need for Consistent Access to Training, To Investigate and Implement New Practices:
Ontario EPI sites have learned about NAVIGATE through didactic sessions and conferences offered through EPION. As new evidence emerges, and network members are interested in how to translate new research to daily practice. Because translation and implementation of evidence-based practice remains challenge, training, implementation expertise, and other resources are required[34]. Implementation science supports a systematic, deliberate and evidence-based process of implementing new practices, and requires key factors and processes for sustainable practice change. The mandate of the CAMH PSSP is to support system change in Ontario by providing implementation, evaluation, knowledge exchange, engagement and information management expertise to organizations and networks across the province. PSSP operates regional offices with implementation teams throughout Ontario, and includes regional oversight of the sites participating in the study. Regional implementation teams work closely with local communities and key partners to implement and sustain system improvements. This approach is aligned with implementation science research showing that a guided implementation process by a group of individuals with specialized skills, dedicated time, and accountability for overall guidance is critical to good implementation and clinical outcomes[35]. PSSP facilitators will guide the implementation process in the study. PSSP has a strong relationship with EPION, providing in-kind support through annual knowledge exchange and training activities. PSSP supported the implementation of the EPI surveys conducted by the SISC. For this project, regional PSSP teams will support implementation and work closely with NAVIGATE content experts from the Slaight Centre (CAMH's EPI program), and community site leads, who are members of EPION.

Challenge 3. Need to Bolster a Community of Practice and Provide Ongoing Access to Expertise:
EPION has identified use of technology to transfer knowledge, and equitable application of the provincial standards as key priorities. ECHO consists of specialist hubs that connect with multiple spoke (learner) teams in remote areas through televideo-conferencing technology, and thus can bridge the geographic gap required to bolster the Ontario EPI community of practice. The goal of ECHO clinics is to extend the reach of best practices in academic settings to the chronic and complex illnesses seen in local settings, thereby reducing variation, increasing access to specialist mentoring and services, and monitoring and improving patient outcomes[36]. Project ECHO is designed to facilitate a community of practice, provide access to expertise, and overcome geographic barriers in relation to specialty coordinated care. In a landmark study, the original Project ECHO demonstrated treatment outcomes for hepatitis C that were comparable to referral to an academic centre for specialist management[37]. As a result of this growing evidence base, the ECHO Act was adopted by the United States Senate in 2016, stating that technology-enabled capacity building interventions, such as ECHO, be used to bridge the gap between specialist care in academic hubs to more rural and remote communities[38]. Initial evaluation data in Ontario has shown high provider satisfaction and engagement with ECHO, and increased knowledge and self-efficacy in managing mental health and addictions in rural and remote settings39.

How is this Study Further Enhanced? From Patient Level to System Level:
i). This project meets the SPOR Mandate through Patient and Family Engagement (using both full participation as equal partners, and more limited commitment, i.e. interviews). Most recently CAMH's youth advisory committee recently selected functioning (i.e. functional outcome) as their preferred outcome

measure in YEA mental health intervention research[44]. In addition, in the direct planning and design of the present study, our own Principal Investigator with lived experience was present at each team meeting, and was an equal partner in decisions regarding all of our outcome measures. Following success at the LOI stage, our co-applicant family member (her son experienced an FEP) joined our team, and she provided input, further refining our research objectives. These collective efforts were predicated on SPOR patient engagement guiding principles of inclusiveness, support, mutual respect, and co-building. If our application is successful, these SPOR principles will be applied across sites, such that our Advisory Committee will grow to include patient/family representation from each site. The Advisory Committee will provide ongoing guidance to the research team in implementation, evaluation, analyses, and dissemination. In addition, at CAMH's Slaight Centre, we undertook a qualitative study[45] that placed an emphasis on experiential knowledge, a desired patient engagement outcome. This study included interviews with 15 patients (men and women) and eight family members (mothers and fathers). Respondents identified that highly integrated coordinated multidisciplinary care that includes the core components of NAVIGATE is essential to engagement and recovery. Patients and families had positive attitudes toward scales and measures, and felt that formalized assessment tools provided them and their care providers an approach to track progress. We will also continue our qualitative work with patients and families to further evaluate NAVIGATE at the participating sites. To date, qualitative research in FEP has focused on patient experiences of hospitalization and medication management, narratives of illness and recovery, or transitions in care[46-49] rather than a program of care[50]. Therefore, the present study provides an opportunity to build on our novel work.

ii). Institute for Clinical and Evaluative Sciences (ICES) Data: A Unique Opportunity to Evaluate System-Level Impact – Meeting the Mandate of the Innovative Clinical Trial (ICT): Using data from ICES, which captures all physician and hospital-provided insured services in Ontario, we will compare population-based outcomes (hospitalizations, emergency department visits, suicide attempts and mortality) with two comparison groups: 1) all EPI program FEP patients who have not been part of the NAVIGATE trial; and 2) all FEP patients who are not attached to EPI programs. All EPI programs in Ontario report their service utilization data through the Ontario Common Assessment of Need (OCAN) dataset (OCAN is linked to ICES data). While accuracy of data within OCAN is variable, we have confirmed that we can accurately ascertain the initiation date of all EPI patients by sex within Ontario through ICES linkage. The ability to link NAVIGATE's primary clinical and implementation data with ICES data, and the capacity to identify all FEP patients in Ontario (whether treated in EPI programs or not) allows for a meaningful, valid, and highly generalizable comparison of outcomes. The use of propensity score methods will address confounding associated with observational studies, and mimics some of the characteristics of a randomized controlled trial[51]. Since outcome data across all comparison groups are routinely collected by ICES, this dramatically reduces the time and cost of a randomized controlled trial (RCT) (thus fulfilling the ICT mandate), because the study does not require costly, extensive follow-up.

ICES has developed a costing macro that we have used to study health care costs among individuals in Ontario with schizophrenia[52]. The costing macro ensures that we have the capacity to determine costs associated with NAVIGATE relative to EPI usual care and no EPI care, a key implementation outcome. Cost estimation adds to the feasibility and policy-relevance of scaling up.

3. Statement of Objectives and Hypotheses

3.1. Primary Objectives

1. Assess whether implementation of NAVIGATE leads to improvement in fidelity to the EPI standard (using the FEPS-FS).

2. Compare system-level outcomes, i.e. days in hospital, emergency department visits, suicide attempts, mortality, and system costs among patients receiving NAVIGATE compared with patients at other EPI sites not receiving NAVIGATE and patients with psychotic disorders who are not enrolled in EPI.

3. Determine longitudinal change in functioning and symptoms in NAVIGATE patients.

4. Evaluate patient and family member engagement according to the SPOR framework.

3.2. Hypotheses

1. Following the implementation of NAVIGATE, program fidelity to the Ontario EPI standard will improve.

2. Compared to patients not receiving NAVIGATE, those who receive NAVIGATE through this implementation study will have fewer days in hospital, fewer ED visits, fewer suicide attempts, lower mortality, and lower costs.

3. Improvements in functioning and symptoms will be comparable to the RAISE study; improvement may be influenced by demographic, socio-economic, geographic, and clinical factors.

4. Our engagement approach will demonstrate that we used the full range of patient engagement based on objectively assessed engagement metrics.

3.3. Study Design/Approach

Description of Sites:
We will include EPI programs, with representation from different geographic regions of Ontario respectively: the south, central-east, and North-east that collectively cover 45% of the province's land area. The North-east is considered one EPI program but does consist of three smaller sub-sites due to geographic spread. All programs are EPION members, participated in the PSSP/SISC survey and in the PSSP/EPION fidelity study. Each site includes health professionals that provide case management support as well as psychiatric care. Each site has unique characteristics or factors that strengthen the diversity and generalizability of this work - site differences may offer the opportunity to evaluate subpopulations, e.g. ethnic/racial minority including Indigenous populations, urban vs. rural location, and variation in service resources.

Assessing outcomes of NAVIGATE patients (obj. #3)
Duration of Study, Recruitment Plan; Inclusion/Exclusion Criteria, Assessment Schedule:
Recruitment: We will recruit consecutive referrals to the EPI programs participating in the study, with representation from three geographic regions of Ontario respectively: the south, central-east, and north-east.

Based on 2016 program data, the total number of new patients across sites was 411. In the RAISE study, 423 patients were randomized to NAVIGATE (n=223) vs. usual care (n=181). We anticipate that we will recruit n=400 patients into the study (based on EPI service sex ratios, we anticipate n=150 women, and n=250 men), with a two year follow-up plan mirroring RAISE. From months 6-12, when we expect 200+ new patients across sites, we will recruit n=100, since we will gradually phase in recruitment (i.e. some sites will be ready earlier than others during this time frame), and since some patients might decline participation. All sites will proceed with full recruitment (i.e. consecutive referral series) from months 12-24. During this time, of the 400+ new patients across sites, we will aim to recruit n=300 (accounting for ~ 25% who might decline or be lost to follow-up prior to first visit). Follow-Up: Of the n=400 who will be recruited between months 6-24, we will complete assessments across a two year period. The first patient will complete the study in month 30 (with n=100 completing by month 36), while the final patient will complete 2 year follow-up at month 48.

Inclusion Criteria / All of the EPI sites follow people experiencing an FEP:

- Age range of 14-35 years;
- any DSM-diagnosis that can manifest as early psychosis (schizophrenia, schizoaffective disorder, schizophreniform disorder, bipolar I disorder, major depressive disorder with psychotic features, substance induced psychotic disorder, or unspecified psychotic disorder);

Exclusion Criteria:

- Absence of psychosis

Clinical Assessments: All patients will be evaluated at baseline, 6 months, 12 months, 18 months, and 24 months with comprehensive assessments of symptom and overall illness severity, and functional outcomes. All patient-level assessment tools chosen are those used in the original NAVIGATE study. At the time of entry all patients will be administered the Structured Clinical Interview for DSM-5 (SCID-5) for formal diagnostic assessment. Functioning will be assessed with the Quality of Life Scale (QLS)[53], consistent with the original RAISE clinical trial[20]. The QLS is the most comprehensive measure of community functioning in schizophrenia populations[54]. Because the QLS is psychosis-specific, we will augment assessment of functioning using the self-report WHO Disability Assessment Schedule 2.0[55] to provide an assessment of health and disability that is utilized across diverse populations and illnesses, and aligns with recent recommendations from the DSM-5 for the use of this instrument across mental illnesses[56]. At the symptom level, psychosis, negative symptoms, and general psychopathology will be assessed using the Brief Psychiatric Rating Scale (BPRS), and the Patient Health Questionnaire – 9 (PHQ-9). The Clinical Global Impression scale (CGI) will be administered to characterize overall illness severity. Using Project-ECHO infrastructure, all interviewer-rated assessments will be administered via live two-way video conferencing by trained interviewers, in a manner identical to the approach utilized in the original NAVIGATE trial[20]. This method of remote assessment is comparable to in-person assessments for both patient acceptability and reliability[57].

Of the participants recruited between months 6-24, we will complete assessments across a two year period. The first participant will complete the study in month 30, while the final participant will complete 2 year follow-up at month 48.

Schedule of Assessments (Timeframe relates to the participants' 2 year timeframe in the clinic)					
Assessments	**Admission to Clinic**	**Month 6**	**Month 12**	**Month 18**	**Month 24**
Screening					
Informed Consent	•				
Demographic form/SES	•				
Eligibility/Termination Checklist	•				
SCID 5 Baseline: Full SCID Month 12 and 24: Mood, Psychosis and Substance Use Disorders Modules	•		•		•
Medical History	•				
Clinical Assessments					
CGI	•	•	•	•	•
PHQ-9	•	•	•	•	•
BPRS	•	•	•	•	•
Service Utilization					
SURF		•	•	•	•
Clinician Contact forms		•	•	•	•
Functional Assessments					
QLS	•	•	•	•	•
WHO DAS 2.0	•	•	•	•	•

Assessment for diagnosis

1. The Structured Clinical Interview for Axis I DSM-5 Disorders. Diagnosis will be confirmed using the Structured Clinical Interview for DSM-5 (SCID-5). Information from the SCID will be supplemented by information from family informants, any previous psychiatrist, and medical records. Demographics and a medical history will also be recorded at baseline. The SCID is a semi-structured diagnostic interview designed to assist clinicians, researchers, and trainees in making reliable DSM-5 psychiatric diagnoses.

Scale to measure clinical psychopathology

1. The Brief Psychiatric Rating Scale (BPRS) (24 item) will be used to assess the severity of positive symptoms, psychosis, negative symptoms, and general psychopathology.
2. The self-report Patient Health Questionnaire – 9 (PHQ-9) will be used to characterize the presence and severity of depressive symptoms.
3. The Intrinsic Motivation Factor of the Quality of Life Scale (QLS) will serve as a specific measure of motivation to augment the above psychopathology measures.

Scale to assess illness severity and improvement

1. The Clinical Global Impressions Scale (CGI) will be administered to characterize overall illness severity. It is designed to rate both illness severity and improvement. It takes into account all available information, including knowledge of the patient's history, psychological circumstances, symptoms, behaviour, and the impact of the symptoms on the patient's ability to function.

Scales to assess functioning

1. Quality of Life Scale (QLS). Functioning will be assessed with the Quality of Life Scale (QLS), which is the most comprehensive measure of community functioning in schizophrenia populations. The scale has been used successfully in studies in prodromal, first episode, and chronically ill participants. It is designed to evaluate the current functioning of nonhospitalized individuals with schizophrenia apart from the presence or absence of florid psychotic symptomatology or need for hospitalization. It is a semi-structured interview. It has 4 subscales: Interpersonal Relations, Instrumental Role, Intrapsychic Foundations and Common Objects and Activities. For the evaluation of community functioning, the Intrapsychic Foundations subscale (which comprises the Intrinsic Motivation factor) will be excluded in order to minimize overlap between assessments of schizophrenia psychopathology and community functioning.

2. WHO Disability Assessment Schedule 2.0: Because the QLS is psychosis-specific, we will augment assessment of functioning using the self-report WHO Disability Assessment Schedule 2.0 to provide an assessment of health and disability that is utilized across diverse populations and illnesses, and aligns with recent recommendations from the DSM-5 for the use of this instrument across mental illnesses.

Scale to determine parental socio-economic status

1. Parental and participant education to be used as indicator of SES.

Measurement of service utilization

1. The Service Use and Resource Form (SURF) will be used to measure utilization of mental health and other medical services across residential, inpatient, and outpatient treatment settings. This will be administered by research staff either over the phone or via email survey, based on participant preference.

2. Data from the NAVIGATE Clinician Contact and Progress Note forms will be collected for all participants. These forms comprise a standard documentation template within NAVIGATE for IRT, SEE, and FEP components of treatment, and capture information about which module was covered during each treatment session.

Other Measures

1. Demographic questionnaire

4. NAVIGATE Implementation Approach

Although each EPI program has existing processes for providing the components of early psychosis care, these are not necessarily delivered in the systematic and intentional manner outlined through NAVIGATE. Building on a large body of practice change evidence supporting a 'make it happen' rather than 'let it happen' approach[34,58], we will guide each program site through a facilitated, staged, change process informed by the Active Implementation Framework and the Quality Implementation Framework[34,59]. A regional PSSP facilitator will have primary responsibility for the implementation, working closely with the CAMH NAVIGATE experts, and EPI program staff lead at each site. The CAMH NAVIGATE experts and PSSP facilitator will bring expertise and momentum to the work. The PSSP facilitator, EPI program staff lead, and ECHO team will assist with site engagement, understanding and preparing the program context, and local problem-solving[60].

Although sites will vary somewhat in their pace of implementation, we expect that installation (see below) will occur across the first six months, that trialing and refining will occur during months 7-12, and that practice will become embedded after month 12. Thus, PSSP involvement and facilitation will be most intense during early and mid-implementation stages as sites plan, trial and refine, and will decrease as delivery practices stabilize and become routine. The facilitators will monitor program progress in a task log based on Meyers[59]. Achievement of key implementation milestones will be reported and areas flagged where more support may be needed. Correspondingly, involvement of ECHO will increase over time to support NAVIGATE as part of routine practice and this will also be monitored. The stages of our implementation process include:

Stage 1. Exploration (to assess site capacity and need, build engagement): This stage is key to successful practice change. As EPION members, who are commitment to this project there is already considerable engagement among participating sites. Additionally, having participated in the prior sector surveys and fidelity reviews, NAVIGATE was identified as a strategy to improve upon current practice at each site. In this stage the CAMH NAVIGATE experts, PSSP facilitators, and ECHO team will met with each site to explain NAVIGATE, learn about their current staffing and service delivery processes, and discuss how NAVIGATE could be integrated into their practice. Staff will complete a site readiness assessment survey and a program fidelity review will be conducted to learn more about site capacities and needs for NAVIGATE implementation.

Stage 2. Installation (to create structures/build capacity for implementation): Intensive staff training over several days will include a didactic component, role playing, and discussions with individual sites to best fit NAVIGATE with each site's current processes. The training will initially require three days at the coordinating site (CAMH, Slaight Centre), co-led by NAVIGATE trainers from the RAISE study. Regular site visits from PSSP facilitators and CAMH Slaight Centre content experts will occur to develop the local implementation plan working with each site lead to prepare staff. Preparation for practice change will include discussions of: role allocation among staff (i.e. IRT vs. SEE vs. family psychoeducation program); whether the program needs to partner with an external service to deliver some elements (particularly the smaller sites); any changes to current patient flow required to deliver NAVIGATE (the care path); how contact and progress note data will be collected and used in meetings to review progress in NAVIGATE delivery; and how to prepare for ECHO sessions (topics and cases). The ECHO team will also work with each site to ensure set-up and ongoing functioning of infrastructure for live video-conferencing.

Stage 3. Initial implementation (trialing and refining) and Evaluation of Implementation Quality: During this stage, each site will begin NAVIGATE delivery and use feedback from various sources, including ECHO training and coaching, contact and progress notes, and staff meetings to make refinements to the implementation and service delivery processes and to address staff support/skill building needs. To increase the quality and consistency of the implementation process across sites (fidelity to the implementation process), we will build on experience of implementing NAVIGATE at the CAMH Slaight Centre, using the Quality Implementation Framework[60] to track implementation steps that have been tailored to our study. The PSSP facilitator will document progress, strategies, and challenges in relation to these tasks in a structured log that they will share in regular meetings with the NAVIGATE experts and other facilitators for continuous improvement. Here, we will be mindful of site-specific factors and population-specific factors (e.g. biological sex, gender, ethnicity, rural vs. urban, LGBTQ status) that may influence implementation. In addition to implementation process tracking data, staff feedback will be used to refine the implementation process.

Stage 4. Full Implementation and Sustainability: At this stage NAVIGATE is fully embedded into the organization and can be sustained with internal resources. The focus on sustainability runs through all stages to ensure capacity building along the way so that additional implementation supports provided by PSSP are eventually no longer needed. The ECHO team will work in collaboration with EPION study sites to create and sustain a community of practice for NAVIGATE implementation and spread beyond the duration of this study, such that it becomes routine practice (care paths, feedback processes). After each ECHO session, questionnaires will be used to evaluate satisfaction and inform ECHO modifications. Additionally, cases discussed during the sessions will generate implementation recommendations, and phone calls at 3-months post-case discussion will be used to evaluate adherence to these recommendations.

Evaluation of Implementation outcomes (Objective 1):
Proctor's implementation outcomes[61] will guide evaluation of implementation outcomes: three of the four CIHR implementation science metrics (adaptability, scalability, sustainability). Specifically we will assess i) fidelity (i.e. adaptability) to examine the extent to which programs operating in different contexts with different resources are able to implement NAVIGATE as intended. Second we will assess ii) penetration (i.e. scalability) the extent to which all eligible program patients receive NAVIGATE. Using the Consolidated Framework for Implementation Research (CFIR)[62], we will assess contextual factors (stakeholder perceptions of acceptability, appropriateness, feasibility) that help or hinder use of NAVIGATE. Learning about these factors including how they relate to unique aspects across settings will inform wider efforts to adapt NAVIGATE and tailor implementation (adaptability and scalability). We will also assess iii) sustainability through uptake of the ECHO model. We address the fourth CIHR implementation science metric (affordability) in the System-Level outcome section further below.

i) Fidelity (ADAPTABILITY): We will use the First Episode Psychosis Service–Fidelity Scale (FEPS-FS)[29] to assess fidelity of service delivery to the current standard of EPI evidence-based practice in relation to 31 program-specific items (individual and team practices) on a 5-point scale from "not implemented" to "fully implemented". Ratings for each site will be made by centrally located trained assessors through a remote assessment process that includes a review of site administrative data, data abstracted from client health records by trained abstractors, and phone interviews with site staff. The FEPS-FS was developed with a formal knowledge synthesis process rather than a single program model. It was used in the Ontario pilot and is relevant to the Ontario EPI standards. Reviews will be conducted at three points in time: during the exploration stage, after full implementation is reached and at the study end to assess sustainability. To examine fidelity results, site will be the unit of analysis. Descriptive statistics (percentages, means, medians,

range) will be reported for the total scale score and for subscale scores that align with NAVIGATE components. With a small number of sites, we cannot quantitatively test changes over time and across sites, but will describe and qualitatively compare findings.

For additional validation of intervention delivery, fidelity scores will be calculated per site in relation to the four core NAVIGATE interventions (medication, IRT, SEE, family education) using the service utilization measures (see description in previous section). The Clinician Contact and Progress Note will provide model adherence data for each patient across the core interventions. This will be augmented by the Service Use and Resource Form (SURF) that research staff will complete with each patient. We will mirror the original study, calculating the percentage of core modules completed per intervention per patient.

ii.a.) Penetration (SCALABILITY): Penetration assesses the extent to which eligible program patients receive the NAVIGATE treatments, and identifies any biases in delivery[61,63]. This is important because a core aim of NAVIGATE is to increase consistency of model delivery across in patients across all programs. Fidelity to NAVIGATE will be calculated from the contact forms (clinician report) and the SURF (client report), and will be used to assess penetration and to identify variations in delivery across patients within sites and across sites. When assessing scalability, the unit of analysis will be the patient (n=400 patients). The outcome will be percentage of modules received for each of the four interventions and will be reported using percentages, means, medians, standard deviations, and interquartile ranges. A linear regression model will be used to identify predictors, with patient baseline characteristics such as sex, age, and illness complexity. The nesting of patients within each site will be accounted for in the analysis. All statistical tests will be two-tailed and statistical significance will be defined as p-values less than 0.05.

ii.b.) Contextual Factors (ADAPTABILITY & SCALABILITY): The Consolidated Framework for Implementation Research (CFIR)[62] will be used to systematically assess contextual factors that are associated with effective implementation. The CFIR offers a comprehensive menu of constructs from published frameworks that influence implementation. The constructs are organized within five major domains: intervention characteristics (e.g., complexity, relative advantage); outer setting (e.g., external policy, patient needs); inner setting (e.g., resources, fit, leadership); staff characteristics (e.g., knowledge, beliefs); and implementation process (e.g., facilitation, planning, coaching). Similar to the Damschroder approach[64,65], the CFIR will be used to develop a semi-structured interview to guide data collection. Interviews will be conducted with stakeholders at each site (EPI staff, organization leaders) at the end of the study, recorded, and transcribed. The CFIR will provide the organizing framework for qualitative data coding and analysis, while being open to new, emergent themes. At each analysis stage, coding and development of themes will be conducted by multiple coders, with consensus achieved through discussion and deliberation. We will develop summary statements of relevant constructs for each site. In combination with fidelity results, we will look for patterns within and across sites related in implementation facilitators and challenges. Qualitative analysis will be supported with NVivo software.

iii) SUSTAINABILITY: ECHO coaching is expected to build staff competencies in delivery of NAVIGATE and to support longer-term sustainability of high quality NAVIGATE delivery. Our evaluation of ECHO will adhere to an established evaluation framework led previously by the ECHO team, building on continuing education program evaluation[66,67]. At each study site we will assess staff participation (engagement and retention); staff satisfaction with ECHO support; and perceived changes in competence to perform NAVIGATE. Staff attendance during ECHO sessions will indicate ECHO engagement and retention. Competency assessment questionnaires will be administered to staff prior to participation in ECHO sessions and at the conclusion of the study to assess changes in attitudes, knowledge and self-efficacy

(self-reported competence) in delivering NAVIGATE components. These questionnaires will be based on pre-existing evaluation questionnaires used for ECHO-ONMH[39].

ECHO pre-post questionnaires will assess participants at stage 1 and stage 4. The staff knowledge and skills questionnaire is based on survey design literature and Bandura's self-efficacy question framework. The questionnaire has been previously used to assess ECHO Ontario Mental Health programs and will be adapted to assess participants' confidence and self-reported capability in delivering NAVIGATE components. Question domains will include Likert scales assessing self-reported knowledge and skill domains specific to the NAVIGATE model. Self-efficacy questions will focus on key competency domains of NAVIGATE and assess confidence in delivering these components in their local settings.

Site implementation of NAVIGATE into practice will be assessed at the end of study CFIR interviews on factors associated with successful implementation will explore the role of ECHO as a support for sustainability, including the formation of a community of practice. Additionally the readiness assessment[68] will assess site capacity at the end of the study to continue NAVIGATE. Site readiness scores will be combined with CFIR and fidelity results for a qualitative examination of patterns within and across sites related in implementation facilitators and challenges.

Implementation evaluation measures and timeline						
Implementation stage		**Explore (stage 1)**	**Install (stage 2)**	**Initial imp. (stage 3)**	**Full implementation & sustainability (stage 4)**	
Measurement domain	**Measure**	**Capacity & needs Ax**	**Plan & prepare**	**Trial & refine**	**Stabilize practice**	**Practice is routine**
		Months 1-3	Months 4-6	Months 7-12	Months 13-24	Months 25-42
Implementation process						
Implementation log (milestones, risk, action)	QIF (adapted)	•	•	•	•	•
ECHO implementation (clinical coaching)	Post-session questionnaires and phone calls	•	•	•	•	•
Implementation outcomes (organizational capacity)						
Staff survey (readiness to implement)	RMT adapted	•			•	•
Fidelity to EPI model	FEPS-FS	•			•	•
Fidelity to NAVIGATE (clinician report)	Clinician contact form		•	•	•	•
Fidelity to NAVIGATE (client report)	SURF		•	•	•	•
Staff interview (value and feasibility)*	CFIR adapted					•
Implementation outcomes (staff capacity)						
Staff survey (knowledge and skills)	ECHO survey	•			•	•

* includes perceptions of ECHO support

System Level Outcomes + Analytic Plan (Objective 2):
Data Sources: The primary data collected for patients of the NAVIGATE protocol will be linked deterministically to data sources held at the Institute for Clinical Evaluative Sciences (ICES) via their unique

health card number. The patient-level outcomes are enhanced by routine system-level outcome measurement and the capacity to compare outcomes among NAVIGATE subjects with two control populations: 1) FEP subjects in Ontario who are not part of the NAVIGATE trial but are receiving EPI services; and 2) FEP patients with no EPI contact. Only NAVIGATE patients who have consented will have their program-level data linked to ICES. The following ICES data sources will be used: the Ontario Health Insurance Plan (OHIP) which covers data for physician billings; the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) which covers all hospitalizations; the Ontario Mental Health Reporting System (OMHRS), covering adult mental health hospitalizations; the National Ambulatory Care Reporting System (NACRS) for emergency department (ED) visits; the Ontario Drug Benefits (ODB) which provides information on all prescriptions covered by the ODB (based on financial need for those under 65 years of age and universally for young people up to age 25); and the Registered Persons Database (RPDB) containing information on patient demographics and deaths. The Ontario Community Assessment of Need (OCAN) database captures all first episode patients attached to EPI programs in Ontario. OCAN will be used to develop a control population of FEP patients who are attached to non-NAVIGATE EPI programs. Statistics Canada estimates will be used to derive neighbourhood income and rurality. These data sources can be linked via the encrypted health card number such that all the information is available for each individual, and de-identified.

Matched Controls: Each NAVIGATE subject will be matched to two types of subjects: 1) FEP patients attached to EPI programs who are not participating in the NAVIGATE trial; and 2) FEP patients with no EPI program attachment. Control cases will be matched to NAVIGATE subjects based on OCAN admission date for patients attached to EPI programs and at time of first diagnosis for those patients not attached to EPI programs. Patients with no EPI attachment will be identified using a validated algorithm that identifies all incident cases of psychotic disorders[69]. The diagnostic codes vary by database and included ICD-9, ICD-10, DSM-IV codes. In order to be a FEP case among the non-EPI attached control group, subjects will not have had a non-affective psychotic disorder diagnosis within five years of the matching date. We will use propensity score matching to create the 2 comparison groups of non-NAVIGATE subjects. Propensity score matching mimics the characteristics of a randomized trial using observational data. A propensity scores defined as the probability that a person is in the "exposed" category. In this case, the exposure condition is access to the NAVIGATE protocol. The propensity score is developed using logistic regression to model exposure to NAVIGATE as a function of observed covariates to yield a probability of NAVIGATE access for each subject. The propensity score model will include sociodemographic characteristics, clinical factors, and prior service use (defined below). We will match non-NAVIGATE to NAVIGATE subjects based on year of index diagnosis and caliper of the propensity score. Non-NAVIGATE Subjects will be assigned the same admission date as NAVIGATE subjects.

System Outcomes (Hospitalization, ED visits, suicide attempts): Our primary outcome is number of psychiatric hospitalization days in the year following NAVIGATE admission. We will include secondary outcomes, such as ED visits and suicide attempts. Hospitalization-based outcomes will include number of psychiatric hospitalizations and time to first psychiatric hospitalization. We will measure psychiatric emergency department visits with a year of admission as well as ED visits for suicide attempts. Visits to psychiatrists and primary care physicians will also be counted[70,71]. Visits to primary care physicians will be stratified as mental health related versus non-mental health related based on a previously validated algorithm[72].

iv) AFFORDABILITY System Outcome – Cost (i.e. Implementation Evaluation Outcome iv):
We will employ a costing algorithm developed in SAS®, and available at ICES[73], to estimate all direct patient-level health care costs incurred by the public third-party payer (Ontario Ministry of Health and Long-Term Care) across the three comparison groups. We will include costs of hospitalizations (both non-psychiatric and psychiatric); ED visits; physician services (i.e. primary care, psychiatry and other care) and diagnostics tests; outpatient prescription drugs for individuals covered under the provincial public drug insurance plan only (for individuals under 65 who receive social assistance and currently universally for individuals under age 25); home care; long-term care; and other care (this includes other ambulatory care, such as same-day surgery/procedures, cancer and dialysis clinic visits, and other hospital-based care, such as rehabilitation and complex continuing care). The costing methodology used in the algorithm will include a bottom-up/micro-costing approach to cost services at the individual level. This approach will make use of individual episodes of care or utilization in the health care system and attached prices (or costs or amounts paid) to each one. 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). Assuming that all subjects will incur health care costs, we will use a generalized linear model with a gamma distribution and log link to model health care costs. Actual model parameters will be determined by the nature of the cost distributions.

Covariates: We will extract information on sociodemographic characteristics, including age, sex, neighborhood-level income quintile, and rurality of residence. Clinical covariates will include type of diagnosis (schizophrenia, schizoaffective disorder, etc.), source of index diagnosis (hospitalization, outpatient visit), and history of visits with alcohol- or substance-related diagnoses. We will also measure prior service use for mental disorders, including the number of prior visits for mental health reasons with the primary care physician, visits to psychiatrist, emergency department visits related to mental health and addiction conditions, and previous psychiatric hospitalizations.

Statistical Analysis: Our primary outcome is days in hospital in the year following NAVIGATE admission. We will compare the three groups (NAVIGATE, non-NAVIGATE EPI, and non-EPI FEP patients) across all covariates listed above. We will subsequently model total hospital days adjusting for covariates. The regression model will be determined by the distribution of the dependent variables. If normally distributed, linear regression; if the distribution assumes a Poisson distribution, we will use Poisson regression. Secondary outcomes will be modeled using logistic regression (for binary outcomes) or Cox Proportional Hazard modelling (for time-to-event outcomes).

Patient-Level Outcomes – Analytic/Statistical Plan (Objective 3):
Since this is an implementation study, based on the already established effectiveness of NAVIGATE, we do not have a comparator arm. We will compare patient level outcome data from our study with the aggregate data from the original NAVIGATE study to assess comparability of the intervention in different jurisdictions, using a matching-adjusted indirect comparison (MAIC) model. In this approach we adjust the population receiving the intervention to match the average baseline characteristics with a reference population. We then compare outcomes across balanced populations. This is facilitated by the use of identical patient-level outcome measures as in the RAISE study, and the collection of similar baseline characteristics that might influence outcome (e.g. age, education, sex, race, baseline illness severity). With a large number of patients, we will also explore sex-stratified analyses. Matching will be based on propensity score weighting. We will compare the primary patient-level outcome (total quality of life score) between our NAVIGATE and the U.S. RAISE study NAVIGATE groups over two years (baseline, 6 months, 12 months, 18 and 24 months). At each time point, we will use percentage change in total QLS score, along with 95%

confidence interval from the RAISE study and the present study. Using the MAIC approach, mean results with overlapping 95% confidence intervals are taken to indicate that the interventions produced equivalent results.

With a sample size n=400 and repeated measures across five time-points (for QLS and BPRS), we will have the opportunity to identify subgroups of patients with different functional outcome and symptom trajectories using complex mixture modeling, namely latent class growth analysis (LCGA) and Latent Growth Mixture Modelling (LGMM). We can also model factors associated with outcomes in key subpopulations of interest. Given that 30% of individuals with first-episode psychosis disengage from services[74], measuring the effectiveness of implementation in specific at-risk subpopulations can help inform future adaptations of the intervention to better serve YEA with an FEP. These at-risk subpopulations include YEA without family involvement[74], those who use substances[74], homeless youth[75], youth from ethno-racial minority populations[76-78], Indigenous youth[79,80], and sexual minority youth[81]. Service in more remote areas (especially at our north-eastern sites) may be an additional vulnerability factor. We have engaged the OSSU's Centre for Rural and Northern Health Research to incorporate some of these considerations. In addition, we have engaged OSSU Women's Xchange given sex-based differences in prevalence and illness severity.

Authentic Engagement of people with lived experience (Objective 4):
Engagement process: Consistent with best practices for both youth[82-84] and patient[85-90] engagement, opportunities for youth and family participation will range from ad hoc, limited commitment (e.g., surveys or interviews) to full, ongoing participation with opportunities for research mentorship, and research team membership. Regarding full, ongoing participation, we will establish an advisory committee that will meet monthly (compensated), and provide guidance to the research team. This committee will guide: recruitment strategies; assessment and treatment protocols; outcome measures; interpretations of findings; knowledge translation goals and strategies to reach youth, families and other stakeholders; dissemination of the trial learnings to knowledge users. This committee will consist of patients and family members from each site and will initially be co-led by our CAMH Slaight Centre patient with lived experience and family member, but where leadership will be determined on an annual basis, to give participating site patient members an opportunity to lead. Leadership of this committee by a patient and family member with lived experience will help facilitate ongoing interaction among research, implementation and patient engagement leads to ensure that project activities are continuously informed by patient priorities.

Preparation for Advisory Group Membership and Participation: In order to prepare patients and family members for advisory group membership, the co-leaders will discuss their readiness for becoming part of the NAVIGATE team (which includes NAVIGATE experts, local site leads, the PSSP facilitator, and an ECHO hub member). Special and specific NAVIGATE training will be held for patients and family representatives that is tailored to their learning needs. In addition, scientific, clinical, and program leaders will receive training on how to include patients and family members on a team in a meaningful manner. Patient and family representatives, i.e. the advisory committee will meet via monthly ECHO teleconference or in person. In addition, all patient and family representatives will have an opportunity to meet monthly over teleconference or in person with each other to discuss their experiences of the implementation process.

Building on Experiential Knowledge to Further Evaluate NAVIGATE from the Patient and Family Perspective: This particular approach will engage patients and family members to build on our qualitative work regarding acceptability, feasibility, and preference for NAVIGATE, i.e. coordinated, manualized EPI care, and will serve to engage those patients and family members who prefer more limited involvement (i.e. through interviews). Patients and family members participating in this process will be different than those

participating on the advisory committee. Semi-structured interviews will be conducted at three stages during the NAVIGATE implementation process: after the first engagement, at the end of the implementation, and at study end. By working alongside patients and families through engagement activities focused on the content and purpose of NAVIGATE, all stakeholders have the opportunity to contribute to the dialogue on its development. We will use a combination of purposive and convenience sampling strategies for the study[91]. Each site will help facilitate the recruitment of approximately three patient and two family member representatives, to ensure recruitment of 20 male and female patients and family members in total. We will aim to include patients and families from diverse demographic, geographic, or socio-economic backgrounds: e.g. LGBTQ, rural, Indigenous, urban socio-economically disadvantaged and newly-immigrated populations.

Evaluation of Patient Engagement: Following consultation with the OSSU Support Unit Innovations Strengthening Primary HealthCare through Research (INSPIRE-PHC) & Patient Engagement Resource Centre (PERC), we reviewed public and patient engagement evaluation tools[92]. We identified the Public and Patient Engagement Evaluation Tool (PPEET)[93] and the PCORI engagement activity inventory[94] as those that might most comprehensively evaluate engagement. In particular, the PPEET had the highest aggregate score on all categories, and includes a patient questionnaire (i.e. for service users, citizens, community representatives, and other stakeholders), a project questionnaire (i.e. for project lead, manager, or director), and an organization questionnaire (i.e. for senior leadership). We will administer the PPEET and PCORI engagement activity inventory in parallel with the semi-structured interviews, i.e. after first engagement, implementation end (end of year one) and study end (end of year four).

5. Study Duration

The estimated length of time needed to complete the entire study (from enrolment of the first participant to completion of the last participant) is four years.

Termination of Participants from the Study:
Reasons for withdrawing individual participants from the study may include one or more of the following:

a) Participant lost to follow-up.
b) Withdrawal of consent: **As this is a two part study, participants are free to withdraw consent in part or in entirety. Their participation in part or the entire study would be terminated accordingly.**

Any participant may be discontinued from the study at the discretion of the investigators if this is deemed to be in the best interest of the participant. The decision may be made either to protect the participant's health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

Any research information recorded for, or resulting from, participation in this research study prior to the date that the participant formally withdrew their consent will be retained and may continue to be used and disclosed by the investigators for research purposes; however, no new data will be collected.

6. Risks/Benefits

6.1. Risks

Assessments can involve emotional discomfort and possibly fatigue. Some of the assessment, in particular the questionnaires, may be upsetting to study participants. We will minimize this by having assessments performed by well-trained research staff with clinical experience and appropriate skills to maximize the participants' comfort and keep their distress to a minimum during each visit.

6.2. Benefits

Past studies have shown that implementation of team-based model of first episode psychosis care, demonstrated significant benefits compared to treatment as usual. This study may benefit participants in that it might help with patient engagement, and greater quality of life. Ontario research has shown that EPI programs in general are associated with more contact with outpatient psychiatry, fewer ED visits, and reduced mortality[12]. The RAISE study found that the NAVIGATE intervention was associated with greater treatment retention, improvement in quality of life and psychopathology and involvement in work or school compared with standard community care[20]. The benefits of this study include the long-term contribution to determine whether the NAVIGATE will lead to improved health outcomes for youth and emerging adults experiencing early psychosis. For the longitudinal assessments, There is a reasonable likelihood that quality of care delivered through NAVIGATE will be superior. Also the use of measurement to assess progress, symptoms and functioning over time has been associated with improved outcomes.

7. Innovation/Impact/KT/Future Plan

Building on Existing Structures: We established new relationships and built on existing ones over the past several months and years to set the stage for this project. Efforts and substantial investment of time with persons with lived experience, family members, front-line clinicians, members and leaders of invested organizations and networks within Ontario, and across Canada along with U.S. EPI and NAVIGATE leadership now position us uniquely to conduct the study.

i) Engagement with Persons with Lived Experience and Family Members: Relationships have been established with men and women with lived experience and family members. The Principal Knowledge User with lived experience has worked closely with the other Principal Applicants from the initial conception of this project, through the weekly planning calls, the teleconferences with community EPION sites, and in the writing and review of the study. Our family member with lived experience has also contributed significantly to the conception of this project based on her own experience across different care settings in Ontario in relation to her son who has experienced psychosis. Her desire to see reduction in variability of care, and better quality care across settings, all crucial patient-oriented goals for this project, is a driving force behind her participation. In addition, the aggregate participation of several persons with lived experience and family members, along with front-line clinicians in our qualitative research study that examined the acceptability and feasibility of manualized, measurement-based care in EPI, further informed our design of the study.

ii) Engagement with Clinician/Front-Line Stakeholders and Community Sites: Key members of the study team arranged meetings with EPION-member EPI programs that participated in the Ontario fidelity study to introduce the concept of the study, obtained feedback on the proposal, and set the stage for ongoing collaborations. Communication was conducted via two-way video conferencing to ensure both verbal and non-verbal relational aspects were evident for all team members. During these meetings, each site asked questions, provided criticisms, and feedback. Our principal applicant with lived experience also participated in all of these meetings to provide his perspective on NAVIGATE, measurement-based care, and other aspects of the study.

Operational Plan

iii) Organizational Engagement - Bringing EPION (and community sites), PSSP, and ECHO-ONMH together: Our team includes the EPION co-Chair (Sarah Bromley) who has already received NAVIGATE training and led NAVIGATE implementation implementer at CAMH. Ms. Bromley is the Principal Knowledge User Clinician. Dr. Janet Durbin Principal Investigator, and scientist at PSSP, and lead scientist for EPION will lead the fidelity implementation and evaluation at each site. Alexia Jaouich, Director of Implementation and Innovation at PSSP will broadly oversee implementation efforts for this project, consistent with her expertise. Dr. Sockalingam, Principal Investigator is the co-lead for ECHO-ONMH, and Dr. Crawford, co-lead ECHO is a co-investigator. Ms. E. Serhal, Project Director, ECHO, Knowledge User will oversee the continued use of ECHO across sites. Through weekly grant planning meetings with other Principal and co-investigators, along with meetings with the community sites, EPION, PSSP, and ECHO-ONMH leadership crystallized their respective roles, in-kind support, and motivation to pursue and succeed in the project.

iv) Canadian and U.S. EPI Leadership: Dr. Voineskos, Director, Slaight Centre, Nominated Principal Investigator, will oversee all aspects of the study, and Dr. George Foussias will provide leadership in clinical training and expertise for participating sites, as well as analyses of the longitudinal patient-level data working with Dr. Haltigan. Dr. Jean Addington co-investigators will provide additional leadership and oversight of training. Dr. John Kane, Principal Investigator of the NIMH-Funded RAISE study who is a collaborator on the study, and along with Dr. J. Addington will ensure RAISE-level NAVIGATE training for all community sites. Dr. Don Addington, chief author of the Canadian Schizophrenia Guidelines is a collaborator and will oversee use of his FEPS-FS scale to evaluate fidelity to the EPI standard. Dr. Phil Tibbo, President of the CCEIP, also a collaborator has interest to scale nationally. The presence of EPI leadership from western and eastern regions of Canada ensures opportunity for future work in other provinces, and unified national leadership.

v) Support from the Ontario Health System: Dr. Kurdyak, one of the Principal Investigators, and Lead of the ICES Mental Health and Addictions Program, will oversee the system-level outcome evaluation, and will work closely with Dr. Anderson co-investigator and Dr. de Oliveira for data and cost analyses. Mr. Patrick Mitchell, Principal Knowledge User, and Director of the Mental Health branch within the Ontario Ministry of Health and Long-term Care (MOHLTC) will ensure that our implementation is aligned with ongoing provincial Mental Health Strategy goals. He has participated in all steps of planning for this work. His team is interested to translate any findings from the present work into policy, and specifically articulated a need for data analyses across the duration of the study, in order to inform policy as early as possible. Mr. Mitchell will also provide advice on shaping the knowledge generated by the project to maximize uptake, and will liaise with other MOHLTC divisions to facilitate discussion on scaling and spreading innovation and evidence from this project. Finally, as described previously, we have engaged the OSSU, and OSSU Units INSPIRE-PHC/PERC (Dahrouge, co-investigator), CRaNHR (Urajnik, co-investigator), and Women's Xchange (Mason, collaborator), to assist with study design and analysis.

8. Data Management and Integrity

The basic protection against risk in this study will be provided by the Principal Investigators. The PIs will have primary responsibility for monitoring of participants during the entire time they participate in the study. The PIs, scientific committee and study team will meet regularly to review accrued data, data confidentiality, and adherence to protocol design, recruitment and implementation During meetings the scientific committee

will also review the enrollment data, the accrual and integrity of clinical data, implementation and fidelity of NAVIGATE and any adverse event associated with the various components of the study.

All data pertaining to a participant's involvement in this study will be coded and stored in locked offices. This information will only be accessible to the research team. In unusual cases, a participant's research records may be released in response to a court order. If the research team learns that a participant or someone with whom the participant is involved with is in serious danger or harm, an investigator will inform the appropriate agencies as per legal or regulatory requirements.

The hard data are stored in a locked filing cabinet stored in a locked office to further protect participant anonymity. Data auditing, entry and quality control will be carried out regularly. Regularly scheduled, and as needed, communications between the study team and the Study PI will clarify any inconsistencies and ambiguities in the data.

Study data will be entered in a secure database (REDCap) web-based electronic data capture platform offered at CAMH and managed by the CAMH Information Management Group and Research IT. At point-of-entry, data values will undergo consistency edits (e.g., ID validation, range verification, duplicate detection) and personnel will be required to correct errors. Data management staff will run logic error programs to check for accuracy and irregularities within and across data structures and within and across sites. Quality assurance checks will be conducted daily and weekly by site personnel, as well as by data management staff. No personal identifiers will be included in any data entry forms, only initials and participant ID. For data collection involving clinician contact forms there will be 3 options: a) REDCap will be used for direct entry by clinicians and then a report emailed to them for entry into their EMR; b) REDCap will be used for direct entry and then a pdf of report will be emailed to the sites so they can scan into their EMR; c) Paper-based form completion by clinicians that is then copied for research team- in this instance, the study RA will go to each site to input data from these forms into REDCap or the forms will be scanned and emailed to CAMH for local data entry into REDCap. Since this is a multi-site study, the data collection processed need to be accommodate the workflow of each site that will have unique needs or preferences. Data collection will be based on individual clinic workflow and hence the above 3 options will be provided with choice being guided by site preferences.

System-level data will be stored at Institute for Clinical Evaluative Sciences (ICES) which has its own protocols for data management. All patient-level records at ICES are de-identified and linked across datasets by a unique identifier number following procedures approved by Ontario's Information and Privacy Commissioner.

9. Study Management and materials

CAMH Investigators will retain a participant identification code list if they need to contact participants after the study. This list will contain the complete name, identification number, address, phone number, and emails (if provided) of all participants and will be held confidentially at the investigators site after completion of the study.

An eCRF will be completed for each participant enrolled in the study. A participant screening log, noting reasons for screen failure, where applicable, will be maintained for all participants. The investigator will document the obtained informed consent and record all medication administration (including concomitant medication(s)), medical history, and efficacy data in the eCRF. Psychopathology scales will be considered source documents and will be incorporated into the eCRF in a confidential manner. Participating sites will send

the coordinating site (CAMH) numbers quarterly (numbers of new intakes in services/clinics); this will be set up as a survey in REDCAP and all of the data would be stored there.

10. Recruitment and Consent

Recruitment for the study will be initiated by the clinical team at each participating site who is treating the potential study participant. The treating physician/clinical care team will not obtain consent to reduce the risk of undue influence in the consent process. They may identify potential research participants and obtain verbal permission from these potential participants for a member of the research team to approach them. Potential participants who indicate a further interest in hearing more about the study and provide assent to be contacted by a member of the research team will then be contacted by a member of the research team who will engage them in an informed consent process. Consent will be obtained in-person or via 2-way videoconference by CAMH research personnel; participants who consent via 2-way videoconference will read the consent form online and will provide digital consent signatures. In instances where consent is obtained in-person a hard copy of the consent will be given to the participant, if consent is obtained via 2-way videoconference, a copy of the signed consent will be emailed to the participant. PII data collected via 2-way videoconference consent process will not be linked to any study data. User rights will also be configured to limit access to any PII containing form to essential staff only

All patients will be given the option to participate. Participation in the study is voluntary. The decision to participate will not affect patients' receipt of treatment or clinical services. Participants will be informed that they have the option of terminating their participation at any time, without consequence and that no new data will be collected on them. Any existing data will be anonymized.

Participants will be provided with a clear explanation of the objectives, procedures, risks and benefits of the study and all questions will be answered. Questions will be asked of participants to ensure that they understand the nature of the research, the risks and potential benefits of study participation, and their rights as research participants prior to obtaining their signature on the informed consent document. Because we believe that consent is an ongoing process in any study, we will continue to educate participants about the nature of the research and address any questions that may arise throughout the course of the study. We are not planning to use proxy consent.

The delegated research staff will access personal health information (PHI) from patient medical records in order to determine eligibility or obtain clinical data for research purposes. We will obtain collateral information (if necessary) from the sites clinical team to confirm diagnosis or obtain other clinically relevant information in the research study. No PHI except MRN will be collected for this purpose and this information will be kept in a secure locked location per Research Standard Operating Procedures SOP# CR501.

11. Confidentiality

There is a potential risk of breach of confidentiality that is inherent in all research protocols. Breach of confidentiality will be minimized by the staff who will maintain research data (identified only by participant code number not related to name, or date of birth) in separate charts and a dedicated password protected electronic database. A list of participant names, their ID numbers, and information about how they can be reached will be kept in a separate locked cabinet with access only to study personnel authorized by the PI. Procedures have been established, and will be followed, to minimize the risk of breach of confidentiality.

Procedures to maintain confidentially include: (1) formal training sessions for all research staff emphasizing the importance of confidentiality; (2) specific procedures developed to protect participants' confidentiality, and (3) formal mechanisms limiting access to information that can link data to individual participants. All information obtained from participants will be kept as confidential as possible. Computer based files/data will be entered into password-secured databases and paper-based files will be stored in a secure location. These data will only be accessible to personnel involved in the study and they will abide by confidentiality regulations of the REB. The ethics committee will be granted direct access to the study participants' original medical records for verification of study procedures and/or data, without violating the confidentiality of the participants, to the extent permitted by the law and regulations.

Participants will not be identified by name in any publication of research results. Results will be published as group data without the use of characteristics that would identify individual participants.

12. Financial Compensation

Longitudinal Assessments: Participants will receive a stipend of $100 to compensate them for their time after they complete all the baseline procedures of the study ($50 for diagnostic assessments and $50 for symptom assessments). At the 6 and 18 month follow-up visit participants will receive $50 for the completion of assessments. At the 12 and 24 month follow-up visits participants will receive $100 ($50 for diagnostic assessments and $50 for symptom assessments). They will also receive $10 for travel compensation at each study visits. However, if they drop out of the study or their participation is terminated, they will be reimbursed at the time of the last scheduled visit based on what they have completed.

CAMH Patient with Lived Experience: Patient of CAMH, who has received early psychosis intervention services, will participate in weekly scientific meetings, and monthly advisory group meetings. He/she will provide input into study design and objectives planning the proposed work and will receive compensation of $25/per hour.

Family Member of CAMH Patient with Lived experience: Mother of a current CAMH patient, who is currently receiving early psychosis intervention at CAMH's Slaight Centre, will provide input and feedback across the duration of the proposed study. She will receive compensation of $25/per hour

Advisory committee (youth and family members with lived experience): In addition to the CAMH youth with lived experience and family members, the team members of the advisory will provide input and feedback for the NAVIGATE program. This advisory group will include one or two patient or family members per site, to ensure that site-specific considerations related to the patient or family member are taken into account across the duration of the study. The advisory committee will meet on a monthly basis, and will receive $89 after each meeting ($25 for time and effort, $30 for travel expenses, and $34 for meal costs).

Qualitative interviews (patients and family members): Separate from the advisory committee we will conduct interviews to obtain experiential knowledge from patients and family members at each site related to the implementation of the NAVIGATE program. 20 interviews will be conducted at the start of implementation/baseline, end of year 1, and at the end of year 4 of the study. The interviews will involve 3 clients and 2 family members from each site and compensation of $40/per interview ($30 for time and $10 for travel).

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