The Ohio State University Early Psychosis Intervention Center (EPICENTER) step-based care programme for individuals at clinical high risk for psychosis: study protocol for an observational study

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ABSTRACT

Introduction In October 2018, the Substance Abuse and Mental Health Services Administration funded 21 sites throughout the USA to develop, implement and evaluate specialised care programmes for individuals at clinical high risk for developing a psychotic disorder (CHR-P). Per the funding requirements, such programmes were required to provide ‘step-based care’—a model in which individuals are initially provided with low-intensity, non-psychosis-specific and more benign (ie, least side effects) interventions and only progress onto higher-intensity, psychosis-specific interventions with a greater risk of more severe side effects should they not meet a priori criteria for clinical response to such lower-intensity interventions. Here, we outline the evaluation component of the step-based care programme for individuals at CHR-P at The Ohio State University Early Psychosis Intervention Center (EPICENTER).

Methods and analyses The EPICENTER CHR-P programme provides a step-based care model comprising psychotherapy, medication management, family support/education, peer support and vocational/educational support. All participants who opt to receive care at the EPICENTER will complete a standardised assessment battery as part of usual care. This battery will be administered on enrolment and will be re-administered at 6-month intervals throughout individuals’ participation in EPICENTER clinical services. Participants will have the opportunity to allow for data from these usual care assessments to be used as part of an evaluation project for this new clinical service. The primary outcome for this evaluation project is time to remission of symptomatic and functional deficits commonly experienced by individuals at CHR-P. Participants will also have the opportunity to participate in a supplemental research project designed to further evaluate treatment outcomes and patient characteristics among individuals participating in EPICENTER clinical services.

Ethics and dissemination This project was approved by The Ohio State University Institutional Review Board. Results from this project will be disseminated through publications and presentations.

Trial registration number NCT03970005; Pre-results.

INTRODUCTION

In the absence of cure therapeutics for psychotic disorders, growing attention has been directed towards developing tertiary prevention strategies designed to minimise and/or ameliorate the morbidity and mortality typically associated with psychotic disorders.1 Within the USA, such work has focused primarily on the development of a national network of clinical programmes providing specialised, multicompartment care for individuals with first-episode psychosis (ie, Coordinated Specialty Care). Facilitated primarily via funds provided by block grants from the Substance Abuse and Mental Health...
Services Administration (SAMHSA), this network provides youth and young adults with first-episode psychosis with access to a care model shown to produce greater improvements in symptomatology, quality of life and functional outcomes as compared with usual care.3–4

Yet, the development of reliable and valid assessment strategies for identifying the early warning signs of a burgeoning psychotic disorder (eg, the Structured Interview for Psychosis Risk Syndromes5 and the Comprehensive Assessment of At-Risk Mental States6) now offers opportunities for the development of clinical services providing secondary prevention strategies designed to reduce the incidence rate of psychotic disorders.7 8 Available data suggest that, if successful, such programmes would offer significant societal benefits both with regard to reductions of the human suffering and also the economic costs associated with psychotic disorders.9 10 To date, several trials have been completed of specialised care strategies for individuals at clinical high risk for psychosis (CHR-P). Previous meta-analyses of these trials suggest that such interventions (and, in particular, cognitive-behavioural therapy) may offer benefits with regard to reduced rates of transition to psychotic disorders.11–15 However, more recent meta-analyses have concluded that no single specialised intervention is more effective than any other intervention (including usual care) in reducing rates of transition to psychosis,16 with available specialised psychosocial or pharmacological treatments appearing to be largely ineffective in promoting improvement in social functioning,17 attenuated positive symptoms,18 or negative symptoms.19

In response to the need for improved treatment strategies for individuals at CHR-P, SAMHSA funded 21 sites throughout the USA to develop, implement and evaluate specialised care programmes for these individuals. Per the funding requirements, such programmes were required to provide ‘step-based care’—a model in which individuals are initially provided with low-intensity, non-psychosis-specific and more benign (ie, least side effects) interventions and only progress onto higher-intensity, psychosis-specific interventions with a greater risk of more severe side effects should they not meet a priori criteria for clinical response to such lower-intensity interventions. Such work builds off of the ongoing (and pioneering) study by Nelson et al.,20 which was the first trial designed to test the benefits of step-based models of care for individuals at CHR-P. The benefits of such a staged-based approach to CHR care include: (i) limiting the use of more intensive and potentially less safe (ie, greater side effects) interventions to individuals who do not respond to more benign treatments and (ii) possible reductions of stigma by limiting the application of psychosis-specific treatments to individuals with more severe and distressing symptoms.20

For this study protocol, we outline the design of the evaluation component of the step-based care programme for individuals at CHR-P at The Ohio State University Early Psychosis Intervention Centre (EPICENTER)—one of the 21 sites funded by SAMHSA to develop, implement and evaluate such specialised care programme. Such work is critical given the relatively low growth of published evaluations of specialised treatment programme for individuals at CHR-P over the past three decades.21

METHODS AND ANALYSIS

This study outlines a naturalistic, observational evaluation of response to a specific step-based care model for individuals at clinical high risk for developing a psychotic disorder. Online supplementary figure 1 highlights how the methodology for this study is consistent with guidelines for cohort studies developed by the Strengthening the Reporting of Observational Studies in Epidemiology group.22

Participants

All individuals participating in care at the EPICENTER CHR-P programme will be invited to participate in the evaluation component of the project. Eligibility criteria for participation in services at the CHR-P programme include: (i) meeting clinical high-risk criteria for psychosis as determined using the Structured Interview for Psychosis Risk States (SIPS)5; (ii) being between the age of 12 and 25 years and (iii) no evidence of intellectual disability as defined as a premorbid IQ>70 as estimated using the Reading subtest of the Wide Range Achievement Test-4.23 With regard to eligibility criterion (i), we will enrol individuals meeting any of the three CHR syndromes assessed by the SIPS (ie, attenuated psychotic symptoms; brief intermittent psychosis and genetic risk and functional deterioration). We will also enrol people at all four current status specifiers for the SIPS (ie, progression, persistence, partial remission and full remission) given evidence that future worsening of symptoms and/or progression to psychosis is possible for individuals in each current status specifier category.24 25 With regard to eligibility criterion (ii), we will limit eligibility to individuals at least 12 years of age given questions about the validity of the SIPS among individuals younger than 12 years. We will plan to enrol patients from a variety of settings including outpatient, inpatient and emergency room referrals. We are also planning on more proactive recruitment strategies in the community by partnering with paediatricians, family doctors, schools and various community agencies.

Prior to the launch of the North American Prodrome Longitudinal Study, single site programmes for individuals meeting CHR criteria funded by the National Institute of Mental Health reported an average enrolment of 18 individuals per year.26 Drawing on these data, we anticipate enrolling 18 unduplicated individuals per year over the course of the study. The exception to this will be year 1. As we will open the CHR programme for enrolment in month 5 of year 1, we anticipate enrolling only nine unduplicated individuals during year 1.
Step-based care model

Data from existing treatment trials have suggested important factors to consider in designing such step-based care models for individuals at CHR-P. For example, while cognitive behavioural therapy for clinical high-risk symptoms (CBT CHR) has been suggested as ‘the first-choice treatment’ in individuals at CHR-P,\textsuperscript{15,27} CBT CHR may not be an ideal first-line psychotherapy for certain individuals given that (i) among individuals meeting CHR criteria, the most common reason for seeking care is to address anxiety and depression—not clinical high-risk symptoms of psychosis,\textsuperscript{28,29} and (ii) CBT CHR does not appear to address the functional deficits experienced by individuals meeting CHR criteria.\textsuperscript{14,17} With regard to pharmacotherapy, available data suggest that antipsychotics are not an appropriate first-line treatment during the CHR phase and should be reserved for individuals at the highest level of distress/severity.\textsuperscript{30} Conversely, selective serotonin reuptake inhibitors (SSRIs) show promise in reducing rates of transition to a frank psychotic disorder, have a less severe side-effect profile and are perceived as less stigmatising as compared with antipsychotic medication,\textsuperscript{31–35} although their efficacy in this population has not been firmly established. Family psychoeducation and peer support are recognised as essential components of early intervention services for psychosis,\textsuperscript{34} with the former shown possibly to produce improvements in attenuated positive symptoms of psychosis\textsuperscript{35,36} and the latter potentially leading to improvements in empowerment and recovery.\textsuperscript{37} Finally, difficulties in cognitive abilities\textsuperscript{38–40} and social and role functioning\textsuperscript{41–45} are common among individuals at CHR-P and may represent key treatment targets given their possible association with increased risk for transition to psychosis.\textsuperscript{40,44,45}

The resulting step-based care model inspired by these data is displayed in figure 1. The psychotherapy track was influenced by the step-based model of psychotherapy proposed by Nelson \textit{et al}\textsuperscript{20} and ranges from (i) brief psychoeducation on the clinical high-risk phase and substance use reduction programme to (ii) the unified protocol (i.e., a transdiagnostic CBT protocol developed by Barlow \textit{et al}\textsuperscript{46} to address emotional disorders such as anxiety and depression) to (iii) targeted psychotherapies designed specifically to address attenuated psychotic symptoms (CBT CHR) and functional difficulties and cognitive deficits (metacognitive remediation therapy).\textsuperscript{47} Pharmacological interventions are provided only at later stages of the care model with SSRIs considered first and antipsychotic medication reserved for the highest levels of illness distress/severity. Family support will be delivered using the step-based model developed by Breitborde and Srihari\textsuperscript{48} and later revised by Breitborde.\textsuperscript{49} Peer support activities will range in intensity from a non-specific activity group for programme participants designed to facilitate socialisation\textsuperscript{50} to participation in the Programme for Enrichment and Education of Relational Skills (PEERS).\textsuperscript{51} Originally developed for individuals with autism, PEERS is an evidence-based manualised social skills intervention designed to target the specific developmental needs of children, adolescents and young adults. In our application of PEERS among individuals receiving inpatient care for psychosis, we have found significant improvements in both self-report (\(d=0.9\)) and performance-based (\(d=0.8\)) measures of social functioning.\textsuperscript{52} Consistent with the supported employment principal of ‘eligibility based on consumer choice’,\textsuperscript{53} vocational and educational support will be available at all stages of the care model.

Selection of what interventions/tracks individuals will receive will be determined via a shared decision-making process between patients and members of the clinical team. This process will be facilitated through the completion of a standardised assessment battery administered as part of usual care on enrolment in EPICENTER and will be re-administered at 6-month intervals throughout individuals’ participation in clinical services at EPICENTER. Moreover, individuals will not be required to participate in all interventions/tracks included within the step-based care model. For example, an individual could participate in vocational/education support but decline to participate in any form of psychotherapy.

Disease distress/severity guidelines for movement through the step-based care programme will be modelled after the proposed guidelines from Nelson \textit{et al}\textsuperscript{20} with regard to step-based care for individuals meeting CHR criteria. These guidelines define response as concurrent remission of CHR positive symptoms and functional improvement. More specifically, individuals will start at the lowest intensity intervention within a given intervention track and will have the option to continue to transition to higher levels of care until (i) all SIPS positive symptoms score \(\leq 2\) and (ii) there is a 5-point increase on the Personal and Social Performance scale (PSP)\textsuperscript{54} as compared with baseline assessment or the PSP score is \(\geq 70\). In situations in which individuals request to remain at lower levels of care or progress to higher levels of care in the absence of supporting distress/severity data, patient preference will always be the determining factor in selecting level of care.

![Figure 1](image-url) The Ohio State University Early Psychosis Intervention Center clinical high risk for psychosis step-based care model. CBT CHR, cognitive behavioural therapy for clinical high-risk symptoms; MCR, metacognitive remediation therapy; PEERS, Programme for Enrichment and Education of Relational Skills.

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Assessment battery

All participants who opt to receive care at the EPICENTER CHR programme will complete a standardised assessment battery as part of their usual care. This battery will be administered on enrolment in EPICENTER and will be re-administered at 6-month intervals throughout individuals’ participation in clinical services at EPICENTER. The primary goal of this clinical battery will be to assist in treatment planning, monitoring of response to care among patients and continuous quality improvement activities at the CHR programme. All patients at the EPICENTER CHR programme will also have the opportunity to participate in a research project evaluating treatment outcomes and patient characteristics among individuals participating in EPICENTER CHR clinical services. Individuals who consent to participate in this project will complete an additional set of research measures that will be administered at enrolment in EPICENTER and re-administered at 6-month intervals for up to 2 years during their participation in EPICENTER care. With the exception of the measures administered at each clinical visit (ie, SIPS positive symptom items and PSP), all measures will be administered by an individual not involved in the provision of care for the specific participant. Measures included in the clinical and research batteries are included in table 1.

Primary outcome

Time to remission: the primary outcome for this evaluation project is time to remission of symptomatic and functional deficits commonly experienced by individuals at clinical high risk for developing a psychotic disorder. Using criteria modelled in the study by Nelson et al of clinical high risk for developing a psychotic disorder, remission will be defined as a state in which a participant concurrently experiences (i) all SIPS positive symptoms score ≤ 2 and (ii) there is a 5-point increase on the PSP as compared with baseline assessment or the PSP score is ≥ 70. These scales will be administered to participants at every intervention visit that they complete over the course of their participation in step-based care.

Secondary outcomes

Measures administered as part of usual care

As a single primary outcome variable may be insufficient to capture improvements within a highly heterogeneous pool of participants who are each participating in a personalised intervention programme, several secondary outcome variables will also be assessed as part of the current study. Current cognitive functioning will be assessed using the MATRICS Consensus Cognitive Battery (MCCB), and premorbid cognitive functioning will be estimated using the reading subtest of the Wide Range Achievement Test. As the MCCB norms are only applicable to adults aged 20–59 years, scores for study participants aged 12–19 years will be calculated using standardised MCCB data for adolescents developed by Smelror et al. Quality of life will be assessed using the WHO Quality of Life Scale-Brief and the RAND 36-Item Health Survey. Scores from the RAND-36 will also be used to calculate quality-adjusted life years to facilitate comparison of our results with results from other studies using this common health metric. The Service Utilisation and Resources Form (SURF) will be administered to track healthcare and social services utilisation during the course of the study, and data from the SURF will be used in conjunction with local cost estimates of healthcare and social services for economic evaluations of the CHR programme. Social and role functioning will be measured using the Global Functioning: Social Scale, Global Functioning: Role Scale, and PSP. The HABITS inventory, and Alcohol Use Scale/Drug Use Scale will be administered to assess severity of current substance use behaviours. The Columbia Suicide Severity Rating Scale will be used to characterise the severity of suicidal ideation and behaviour over the past 6 months. Severity of attenuated psychotic symptoms will be measured using the SIPS, and the severity of depression and anxiety will be assessed using the Calgary Depression Scale for Schizophrenia and the Hamilton Anxiety Scale. Of note, the latter will be administered using the Hamilton Anxiety Rating Scale Interview Guide to facilitate improved reliability between study raters. The Medication Adherence Rating Scale will be used to assess adherence to psychiatric medication among study participants, and adherence to psychosocial interventions offered as part of the step-based care model will be measured using the Treatment Adherence and Acceptability Scale. Finally, trauma exposure will be evaluated using the Adverse Childhood Experiences questionnaire and the Brief Trauma Questionnaire.

Measures administered for research purposes

Constructs associated with increased suicidality (ie, thwarted belongingness, perceived burdensomeness and capacity for suicide) will be assessed using the Interpersonal Needs Questionnaire and the Acquired Capacity for Suicide Scale-Fearlessness about Death Scale. Metacognitive abilities will be assessed using both self-report (ie, Metacognition Awareness Inventory) and performance-based measures (Modified Zoo Task). The Delis-Kaplin Executive Function System will be used to measure components of executive functioning, and the Hinting Task and the Movie for the Assessment of Social Cognition will be used to evaluate theory of mind. Motor functioning will be evaluated using the grooved pegboard test, finger tapping test and MovAlyzeR handwriting assessment. Various aspects of the quality of social functioning will be assessed using the Quality of Socialisation Questionnaire, Social Responsiveness Scale and the UCLA Loneliness Scale. Exposure to illness-related stigma will be assessed using the Stigma Questionnaire and internalisation of illness-related stigma will be assessed using the Internalised Stigma of Mental Illness questionnaire. Severity of referential thinking will be measured using the Referential Thinking Scale. Beliefs about substance use will be evaluated.
| Domain                      | Clinical battery                                                                 | Research battery                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| **Cognition**               | MATRICS Consensus Cognitive Battery Wide Range Achievement Test                  | Delis-Kaplin Executive Functioning System Metacognition Awareness Inventory       |
|                             |                                                                                  | Modified Zoo Task                                                                |
| **Social and role functioning** | Global Functioning: Social Scale Global Functioning: Role Scale                  | Quality of Socialisation Questionnaire Social Responsiveness Scale                |
| **Quality of life**         | WHO Quality of Life Scale-Brief                                                  | UCLA Loneliness Scale                                                             |
| **Service utilisation and perception of care** | Service Utilisation and Resources Form Medication Adherence Rating Scale          | The Treatment Motivation Questionnaire                                            |
|                             | Treatment Adherence and Acceptability Scale                                      |                                                                                  |
| **Substance use**           | HABITS Inventory                                                                 | Alcohol Expectancy Questionnaire-Brief                                             |
|                             | Alcohol Use Scale/Drug Use Scale                                                 | Marijuana Effect Expectancy Questionnaire-Brief                                   |
|                             |                                                                                  | PATH Assessment of Tobacco Use                                                   |
| **Suicidality**             | Columbia Suicide Severity Rating Scale                                          | Acquired Capability for Suicide Scale-Fearlessness about Death                    |
|                             |                                                                                  | Interpersonal Needs Questionnaire                                                 |
| **Symptoms**                | Structured Interview for Psychosis Risk States                                   |                                                                                  |
|                             | Calgary Depression Scale for Schizophrenia                                       |                                                                                  |
|                             | Hamilton Anxiety Scale                                                           |                                                                                  |
| **Trauma**                  | Adverse Childhood Experiences Questionnaire                                      | PTSD Checklist-5                                                                  |
|                             | Brief Trauma Questionnaire                                                       |                                                                                  |
| **Personality factors**     |                                                                                  | Ten-Item Personality Inventory                                                    |
| **Motor functioning**       |                                                                                  | Pegboard Test                                                                      |
|                             |                                                                                  | Finger Tapping Test                                                                |
|                             |                                                                                  | MovAlyzeR Handwriting Assessment                                                   |
| **Social cognition**        |                                                                                  | Hinting Task                                                                      |
| **Physical activity**       |                                                                                  | Movie for Assessment in Social Cognition                                          |
| **Stigma**                  |                                                                                  | International Physical Activity Questionnaire                                     |
|                             |                                                                                  | Internalised Stigma of Mental Illness Questionnaire                                |
|                             |                                                                                  | Stigma Questionnaire                                                               |
| **Cognitive biases**        |                                                                                  | Referential Thinking Scale                                                        |
|                             |                                                                                  | Brief Core Schema Scale                                                           |
|                             |                                                                                  | Cognitive Biases Questionnaire for Psychosis                                      |
| **Insight**                 |                                                                                  | Measure of Insight into Cognition-Self Report                                     |
| **Self/Agency**             |                                                                                  | Beck Cognitive Insight Scale                                                      |
|                             |                                                                                  | Assessment of Self-Descriptions                                                   |
|                             |                                                                                  | Computerised action prime task                                                     |

PTSD, post-traumatic stress disorder.
using the Alcohol Expectancy Questionnaire-Brief and the Marijuana Effect Expectancy Questionnaire-Brief. Utilisation of tobacco products, including e-cigarettes, will be assessed using the PATH Assessment of Tobacco Use. Core schemas will be assessed using the Brief Core Schema Scale and cognitive biases will be assessed using the Cognitive Biases Questionnaire for Psychosis. Insight into cognitive functioning will be assessed using the Measure of Insight into Cognition-Self Report, and recognition of experience of common thinking errors will be assessed using the Beck Cognitive Insight Scale. The Treatment Motivation Questionnaire will be used to track participants’ motivation with regard to participation in the step-based care programme. Level of physical activity among study participants will be measured using the International Physical Activity Questionnaire. The PTSD Checklist will be used to assess symptoms associated with post-traumatic stress disorder, and the Ten-Item Personality Inventory will be administered to assess Big five personality traits among study participants. Narrative aspects of self, agency and relatedness will be evaluated using the Assessment of Self Descriptions employing the analytical techniques developed by Moe and Docherty. Sense of agency for motor actions—and how agency may be influenced by action primes—will be assessed using a modified version of the computerised action prime task developed by Damen et al.

Proposed analyses

Prior to completion of data analyses, all data will be inspected for outliers and departures from a normal distribution. Missing data will be addressed via multiple imputation unless factors arise during the course of the study that lead to missing data occurring not at random. Descriptive data will be presented using means and SD. Should the data be found to deviate significantly from a normal distribution, medians and IQRs will be presented instead. Cross-sectional analyses will be completed using Pearson’s correlations for continuous variables and \( \chi^2 \) test for categorical variables. In situations where there is a categorical predictor variable and a continuous outcome variable, between-subject t-test and analysis of variance will be employed. Within-subject longitudinal changes will be evaluated using the regression-based test developed by Hedberg and Ayers for continuous variables, McNemar’s test for two-level categorical variables and Fleiss-Everitt \( \chi^2 \) test for categorical variables with greater than two levels. Linear and logistic regression will be used to evaluate between-subject longitudinal associations. Mediators and moderators of longitudinal associations will be examined using strategies consistent with the guidelines outlined by Breitborde et al. For all analyses, in situations in which data deviate from a normal distribution, non-parametric alternatives will be used instead.

Patient and public involvement

A community advisory board comprised of an individual with lived experience of psychosis, a caregiving relative of an individual with a psychotic disorder, a paediatrician and a director of a mental health advocacy programme will meet 3–4 times per year over the course of the project to review interim findings and provide guidance on how the EPICENTER CHR-P programme can best meet the needs of the community. Prior to the start of the project, the community advisory board reviewed and approved the intervention components included within the step-based care programme. The board also reviewed the assessment battery and identified important outcomes missing from the battery (e.g., e-cigarette use). Measures assessing these topics were added to the programme assessment battery prior to the launch of the step-based clinic.

ETHICS AND DISSEMINATION

Results from this project will be disseminated through publications and presentations.

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Competing interests All authors reports grants from SAMHSA during the conduct of the study. NJKB and AM have completed paid and unpaid consultation for the Institute for Mental Health Research (IMHR) in helping support the launch of specialised clinic for individuals with first-episode psychosis in Phoenix, Arizona.

Patient consent for publication Not required.

Ethics approval This study was approved by The Ohio State University Institutional Review Board (IRB Protocol Number: 2018H0503).

Provenance and peer review Not commissioned; externally peer reviewed.

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