PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The Ohio State University Early Psychosis Intervention Center (EPICENTER) Step-Based Care Program for Individuals at Clinical-High Risk for Psychosis: Study Protocol for an Observational Study
AUTHORS	Breitborde, Nicholas J. K.; Guirgis, Hossam; Stearns, Walter; Carpenter, Kristen; Lteif, Ghada; Pine, Jacob; Storey, Nichole; Wastler, Heather; Moe, Aubrey

VERSION 1 – REVIEW

REVIEWER	Carolyn S. Dewa, MPH, PhD University of California, Davis US
REVIEW RETURNED	16-Oct-2019

GENERAL COMMENTS	This is a clearly written protocol. It would be helpful if the authors added a table with the outcome measures that included a bit more detail such as the number of items, time period, and information source.

REVIEWER	Dr Nina R Schooler SUNY Downstate Medical Center/Department of Psychiatry & Behavioral Sciences/USA My research involves centers that provide services that are seen as meeting criteria for Continuing Specialty Care
REVIEW RETURNED	30-Oct-2019

GENERAL COMMENTS	The protocol addresses an important question – design of step-based care for individuals at high risk for psychosis. Such services need to be tailored for individuals and will include multiple domains. The problem then is how to evaluate “success”. But, first services need to be defined. In the protocol the model includes four “track” or domains of service and it is posited that individuals will receive services in all tracks (except for pharmacologic which is limited to higher levels of distress/impairment. A Figure presents the model. The problem with it is that there are no definitions provided for level of distress/severity. There are no criteria provided to determine which treatments would be provided. In fact, the only way to know what level of severity/distress a person exhibited would be to examine, which services that person, had received. By definition a person who received CBT targeted for CHR has a high level of severity. A second problem is that despite the great degree to which services are personalized, the primary outcome measure is exactly

	the same – remission of SIPS symptoms and improvement in the PSP. Some CHR individuals at low levels of severity /distress may show very little impairment on the PSP which was designed for use with much more severely impaired individuals. A table that listed measures that are part of usual care and those that are part of the research protocol would improve the MS. From my read, it appears as though even the usual care battery requires considerable time and effort on the part of participants. Given the extensive battery even in usual care, consideration of how to handle missing data in the statistical analysis plan would be helpful.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1) This is a clearly written protocol. It would be helpful if the authors added a table with the outcome measures that included a bit more detail such as the number of items, time period, and information source.

We thank the Reviewer for this suggestion and have added a Table to the manuscript that outlines the assessments included in the clinical and research assessment battery as well as the domains assessed by specific measures.

Reviewer: 2

1) The protocol addresses an important question – design of step-based care for individuals at high risk for psychosis. Such services need to be tailored for individuals and will include multiple domains. The problem then is how to evaluate "success". But, first services need to be defined. In the protocol the model includes four "track" or domains of service and it is posited that individuals will receive services in all tracks (except for pharmacologic which is limited to higher levels of distress/impairment. A Figure presents the model. The problem with it is that there are no definitions provided for level of distress/severity. There are no criteria provided to determine which treatments would be provided. In fact, the only way to know what level of severity/distress a person exhibited would be to examine, which services that person, had received. By definition a person who received

CBT targeted for CHR has a high level of severity.

We apologize for the lack of clarity with regard to this point. For the step based care model, individuals start at the lowest intensity treatment within a specific intervention track. Disease/severity guidelines are used to assess response to this treatment--as opposed to what specific treatment a person would start with on a given intervention track. Individuals who do not respond to a given treatment based on these disease/severity guidelines progress onto a the next (i.e., higher intensity) intervention within a given intervention track. We have revised the following text in the "Step-Based Care Model" section to improve clarity with regard to the description of this aspect of the model:

"Disease distress/severity guidelines for movement through the step-based care program will be modeled after the proposed guidelines from Nelson and colleagues[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 ≤ 2 and (ii) there is a 5-point increase on the Personal and Social Performance scale (PSP)[54] as compared to baseline assessment or the PSP score is ≥ 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."

2) A second problem is that despite the great degree to which services are personalized, the primary outcome measure is exactly the same – remission of SIPS symptoms and improvement in the PSP. Some CHR individuals at low levels of severity /distress may show very little impairment on the PSP which was designed for use with much more severely impaired individuals.

We agree with regard to the challenges associated with selecting a single primary outcome measure for a multi-intervention study. However, given that (i) the design of the study was approved by our funders and (ii) the study is ongoing, it would be problematic to make changes to our primary outcome measure at this time.

3) A table that listed measures that are part of usual care and those that are part of the research protocol would improve the MS. From my read, it appears as though even the usual care battery requires considerable time and effort on the part of participants. Given the extensive battery even in usual care, consideration of how to handle missing data in the statistical analysis plan would be helpful.

We thank the Reviewer for this suggestion and have added a Table to the manuscript that outlines the assessments included in the clinical and research assessment battery as well as the domains assessed by specific measures.

We appreciate the Reviewer noting the importance of pre-existing plans for addressing missing data and direct the Reviewer to our "Proposed Analyses" section where we include this information: "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."

VERSION 2 – REVIEW

REVIEWER	Nina R Schooler Psychiatry & Behavioral Sciences SUNY Downstate Medical Center United States of America
REVIEW RETURNED	30-Nov-2019

GENERAL COMMENTS	IN my initial review I questioned whether the single outcome measure was equally applicable to all study participants as the intervention can vary very widely depending on participant needs. The authors' agreed with the point but stated response that since this is a protocol and the study is already ongoing, that the outcome measure cannot be changed. That response is a fair one but even if the outcome measure cannot be changed, it behooves the authors to state this concern as a limitation of the study.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

1) In my initial review I questioned whether the single outcome measure was equally applicable to all study participants as the intervention can vary very widely depending on participant needs. The authors' agreed with the point but stated response that since this is a protocol and the study is already ongoing, that the outcome measure cannot be changed. That response is a fair one but even if the

outcome measure cannot be changed, it behooves the authors to state this concern as a limitation of the study.

We thank the reviewer from noting this omission from the manuscript. To address this concern, we have made two changes to the manuscript. First, in the Strengths and Limitations Section (p. 3), we have added the following bullet point:

- A single primary outcome variable may be insufficient to capture improvements within a highly heterogeneous pool of participants who are each participating in a personalized intervention program. As such, several secondary outcome variables will be assessed as part of this study.

Second, we have added the following sentence to the beginning the "Secondary Outcomes" section of the manuscript (p. 9):

> "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 personalized intervention program, several secondary outcome variables will also be assessed as part of the current study."