

NCS Formative Research Template for OIRA Clearance

TO BE COMPLETED BY FIELD CONTRACTOR:

LOI #: [LOI3-MHLTH-09](#)
Title of Formative Research: A Methodological Study to Assess Mental Disorders for NCS Birth Parents
Participating Institutions: University of Massachusetts Medical School
Recruitment Study Arms: Worcester County, Massachusetts
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COTR: Eric Lorenzo

Purpose of the Study: The purpose of this study is to 1) test the feasibility of implementing a short, telephone mental health screen called the Parental Mental Health Screen (PMHS, Attach. 4) and then 2) test the validity of the PMHS against the gold standard, the Composite International Diagnostic Interview (Revised CIDI, Attach. 5). The PMHS is a phone-administered questionnaire developed by the National Children's Study (NCS) Mental Health Working Team (MHWT) with an expected duration of approximately 10 minutes. Questionnaire responses from the PMHS that are considered indicative of an aspect of mental illness will be validated against a gold standard instrument, the CIDI. The CIDI is widely used internationally and has known validity and reliability.

Benefit to NCS Vanguard or Main Study: Several research studies have already established the evidence that commonly found mental health disorders in parents (particularly pregnant women) are likely to yield to children's mental and behavioral health problems. These include mood disorders (major depressive disorder, bipolar disorder), anxiety disorders (generalized anxiety disorder, panic disorder, post-traumatic stress disorder), and impulse-control disorders (adult attention/deficit hyperactivity disorder, intermittent explosive disorder). All of these disorders other than bipolar disorder are commonly occurring disorders in the general population.^{1,2} In comparison, bipolar disorder has a prevalence of only about 1% for Bipolar-I and another 1-2% for Bipolar-II, but has a clinically significant sub-threshold spectrum that represents approximately 5% of the US population.³ Overall, parental mental disorders are powerful risk factors for children's mental and behavioral disorders, making it critical to obtain accurate estimates of parental mental disorders in NCS baseline assessments. However, these disorders are usually assessed and diagnosed using very lengthy and complicated instruments.

There are no current measures in the Vanguard (Pilot) Study to measure parental mental health. Validating the PMHS against the longer 30 minute CIDI will benefit the Vanguard and/or Main Study by offering an efficient and less burdensome approach to incorporating comprehensive mental health assessment of NCS birth parents into Vanguard and/or Main Study activities. Since pediatric behavioral and mental disorders account for one in every five office visits to pediatricians and carry enormous medical and societal costs, a short and financially feasible parental mental health screen will be of immense value to the NCS in providing a research platform for future study.

Study Design:

Parental Mental Health Screen

The first step in the study is the implementation of the Parental Mental Health Screen (PMHS). Participants will be invited to participate in PMHS consisting of a series of screens for common mental health disorders (specifically general anxiety disorder, panic disorder, major depression) in order to assess prevalent mental disorders in the general population.

All pregnant women and fathers of the babies who agree to participate in this study will provide a phone number to the PMH interviewer and they will schedule a time for a telephone call. The parent will sign an

¹ Kessler RC, Berglund P, Demler O, Jin R, Merikanga KR, Walters EE. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 2005;62(6):593-602.

² Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 2005;62(6):617-627.

³ Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Arch Gen Psychiatry*, 2007;64(5):543-52.

NCS Formative Research Template for OIRA Clearance

informed consent (Consent Form, Attach. 6) form prior to receiving a phone call from the interviewer. At the agreed-upon time, the interviewer will call the parent and verbally re-consent the parent prior to administering the PMH questionnaire. The interviewer will ask the parent a series of questions from the PMHS. This call will last approximately 10 minutes. At the end of the questionnaire, the interviewer will advise the participant that they may be recontacted in the future for the CIDI interview.

The UMass NCS Study Center location will administer the PMHS via the secure, encrypted, web-based Research Electronic Data Capture (REDCap) platform. REDCap is designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The UMass NCS Center staff will use Federal Information Security Management Act (FISMA)-compliant laptops to enter the data into REDCap. The PMHS will be entered directly into the REDCap system as the interview is conducted by phone in real time (computer-assisted telephone interviewing).

Composite International Diagnostic Interview

The second step of the study is validating the PMHS against the Composite International Diagnostic Interview (CIDI). The CIDI is a comprehensive, fully-structured interview designed to be used by trained lay interviewers for the assessment of mental disorders according to the definitions and criteria of ICD-10 and DSM-IV. It is intended for use in epidemiological studies, has been used extensively for decades in multiple international settings, and has known validity and reliability.

Once a week, diagnostic algorithms (developed in SAS) will be run at the UMass NCS Study Center using the data from REDCap PMH database. Upon completion, a second analytical program will be implemented to obtain a subsample for participation in a second step clinical reappraisal interview using the CIDI. A subset of 400 parents in the study will be randomly chosen to participate in a second phone call.

When a respondent is selected for the clinical reappraisal interview using the CIDI, the CIDI interviewer will verbally re-consent the parent prior to administering the CIDI. This phone call will last approximately 30 minutes. The CIDI interview will use a paper interview form, which will be entered into the REDCap system. The CIDI paper forms will be stored in a locked cabinet in a locked office and only accessed by study staff. The forms will be kept for a minimum of seven years after the date of the last publication.

Staff Training

Both of these activities will be conducted by the PMH interviewers and research assistants. PMH interviewers and recruiter/schedulers will be trained in the administration of all instruments by the project manager and the PI who have extensive experience in mental health research. The CIDI training session is 54 hours. The PMH training program was developed at UMass in collaboration with the University of Michigan. The training program for PMH is 24 hours. The final piece of the training will include a course on crisis intervention. It will include as to how to identify a person and crisis and how to respond. The total amount of training staff will undergo is two weeks and 1 day.

Screening Scales

Many brief screening scales of commonly occurring mental disorders have been developed to facilitate screening in general medical settings. In addition, validated fully-structured psychiatric diagnostic interviews have been developed for use in large-scale community epidemiological surveys. The MHWTS and study collaborators selected from among these scales in constructing a proposed screening battery for the NCS. Lifetime and 30-day prevalence versions of these scales were chosen. The disorders that the working team proposes to assess include mood disorders (major depressive disorder, bipolar disorder), anxiety disorders (generalized anxiety disorder, panic disorder, post-traumatic stress disorder), impulse-control disorders (adult attention/deficit hyperactivity disorder, intermittent explosive disorder), and substance abuse disorders (alcohol and drug abuse and dependence). These disorders other than bipolar disorder are common in the general population. A brief scale of nonspecific psychological distress was selected that could dually serve as a first-stage screen for 30-day prevalence of generalized anxiety and depression and as a dimensional measure of 30-day distress.

NCS Formative Research Template for OIRA Clearance

Pilot Test

In accordance with OMB guidelines, we conducted a pilot study in which we administered a survey to nine participants recruited from South Dakota State University and the University of Mississippi Study Centers from August to September 2011. Data on the nine subjects were used 1) to test for bugs in the REDCap application, 2) to determine the average administration time of the surveys, and 3) obtain feedback from the South Dakota and Mississippi sites in the field activities required for the administration of the questionnaire. In addition, we gathered feedback from Yale regarding Structured Clinical Interview for DSM-IV (SCID). Study Centers recruited subjects from currently-enrolled NCS participants located at their NCS sites. Case Coordinators were provided with a PMH Study Information Flier and PMH Study consent forms. They informed subjects of the PMH Study either (1) in-person upon completion of a pregnancy visit or (2) by phone. If the woman was interested, the Case Coordinator obtained written consent.

In the original application, clinical interviewers were required as part of the protocol due to the training and licensing requirements to administer the SCID. The revised project does not include the SCID; it has been replaced with the CIDI that was developed for field use by trained lay investigators.

Target Respondents: Study subjects will consist of adults of age 18 and older, pregnant women at any stage of gestation, and the male partners of pregnant women. Postpartum (defined as four weeks following birth) mothers and fathers will also be included. The subjects must be English-speaking to participate, though it need not be their first language.

No minors, adults unable to consent, or prisoners will be included in the study.

The total number of participants to be recruited is 1200 with an expectation that the recruitment of mothers and fathers would be 2:1 (800 mothers, 400 fathers). We will use clinical sites, prenatal classes, and nutrition programs that we have identified but are not using for PBS or have used in other formative research involving pregnant parents. That is, those recruited will be non-NCS participants so as not to increase patient or even clinical burden.

Sample Size Calculation: In practice, a larger sample size tends to obtain a better level of precision in making statistical inferences about the population. We will use a convenience sample, which also allows for oversampling of small subgroups of interest, such as race or ethnicity. For the second interview using the CIDI, the sampling methodology will account for the population prevalence of the various psychiatric illnesses. As such, all PMH screen positives for bipolar disorder and schizophrenia will be selected as these are rare disorders in the general population. Depression and anxiety, being the most prevalent conditions, will be selected using a stratified sampling method to include all subgroups identified above.

An estimated 1,200 participants will be utilized in the above analyses with 1,200 of the parents receiving one questionnaire (PMHS) and then a subset 400 of the 1,200 will receive a second questionnaire (CIDI). The sample sizes required for the 80% or 90% power required to detect kappa values significantly different from 0 for a two-tailed test for null at a value of .60 is 149 and 200, which is well within our targeted sample size.

A large number of populations based surveys on the mental health of the U.S. population have documented that the prevalence of any mental disorder is ~30 percent. Thus, in a cohort of 1,200 individuals in the community we expect ~360 persons who will endorse one or more of the screening modules. The remaining 840 people are expected to be screen negatives. Of these we will randomly sample ~40 individuals who are screen negatives. To assess that we do not have any false negatives we will validate the findings of this random sample of ~40 with the CIDI. That leaves 800 individuals who are presumably screen negative. Though we could administer the CIDI to all of them, the gains in power are modest. This would not be a good use of the budget unless we are asked to increase power beyond the usually accepted value of 0.8-0.9 and alpha to a value less than 0.05.

NCS Formative Research Template for OIRA Clearance

Should we find that those screening negative on the Parental Mental Health Screener have a mental health diagnosis as determined by the CIDI, we would increase the sampling rate of screen negatives in order to meet the goals of the study and develop sensitivity and specificity estimates. That would increase the number receiving both the PMHS and CIDI. Though we cannot say until the data are in, we are confident that the design and sample are the most appropriate in meeting the needs of the NCS and are sensitive to feasibility and cost.

Analytic Approach

The approach employed in the Parental Mental Health formative research is based upon use of the Composite International Diagnostic Interview as a gold standard (“truth”) and against which we develop and compare the Parental Mental Health Screener. The analytics that drive the development of a new mental health screener appropriate for the diverse patient groups to be studied in the NCS are based on classical epidemiologic approaches combined with more sophisticated Receiver Operator Curve (ROC) and area under the curve (AUC) analyses. Comparison of the results from the screener against the gold standard CIDI findings will rely upon logistic regression models that will allow us to incorporate patient socioeconomic and demographic characteristics to detect patient variables such as race or ethnicity associated with initial measures of discordance. The logistic regression models will also allow us to develop separate calibration rules to adjust the estimates of predicted probability of diagnosis from screen scale scores for patient subgroups of relevance to the NCS (e.g., Latinos or low socioeconomic status).

In general, comparison of the accuracy of a new screening instrument like the Parental Mental Health screener (PMHS) against an existing diagnostic tool proceeds in a logical sequence. We first use conventional statistical approaches relying on estimates of sensitivity, specificity, and kappas to describe diagnostic consistency between the screen and the standard (in this case the CIDI) at the aggregate level. In addition, we will employ receiver operator curve (ROC) approaches that are a more useful general-purpose measure of consistency and provide more granular information to capture the interplay between sensitivity (fraction of true positives identified by the new screen) and specificity (fraction of true negatives identified by the screen that in ROC graphs is typically depicted as 1-specificity or false positives).

After estimating sensitivity, specificity, kappas and producing ROC curves, we will next employ logistic regression models that allow us to enter specific covariates like race or ethnicity into modeling concordance (yes/no) between the CIDI and the new PMHS, thus allowing us to detect systematic patterns of concordance (or non-concordance) between PMHS and CIDI results. One practical consequence of this analytic approach is that it allows us to develop separate calibration rules for the PMHS such as might be needed for specific patient subgroups if there is a need to do that. In addition, extensions of the logistic regression model will allow us to streamline the PMHS by detecting items that contribute little information to the scale and could be eliminated without comprising the diagnostic detection signal. This is of considerable importance for the value of the PMHS as a tool that will be used as part of a larger set of questionnaires for the main NCS in which patient burden, time of administration and cost are key drivers of feasibility.

In sum, the analytic plan employs classical and state-of-the-art statistical approaches. Work is led by a team with decades of experience in conducting population and clinically based epidemiologic mental health surveys as well as a track record in translating advances in statistics into useful research applications.

Method of Recruiting: The UMass NCS Study Center will recruit parents from throughout Worcester County utilizing NCS Community Advisory Board, birth education classes, and advertisements on community message boards.

Eligible women and men (1) can self-select into the study by calling the study phone number or website. This information will be available through advertisements on message boards or study flyers (Flyers, Attach. 7) and brochures materials (Brochure, Attach. 8), or (2) will be informed of the project by a brief presentation by a NCS staff person held at various community locations. If interested, the parent will be consented by the NCS staff member and her contact information will be obtained. A trained PMH interviewer

NCS Formative Research Template for OIRA Clearance

will call the parent from a land-line telephone with headphone. The woman will be verbally re-consented prior to the administration of the PMH questionnaire. A scripted text for responding to women calling the study center will be used (Recruitment Script, Attach. 3).

All recruitment (and data analysis) will occur at the UMass Medical school campus in Worcester County. Key personnel for the team are already on board and will be added to the hire of per diem recruiters and interviewers. Personnel for training and use of study instruments currently exists in-house.

***Confidentiality:** Study Centers must abide by the terms of their Data Use Agreement, which should reference all formative research efforts involving the collection or management of NCS restricted-use data. All participating Study Centers will have approved Data Use Agreements and Security Plans prior to launch.

Each study subject will be assigned a subject identification code consisting of two elements to identify the interviewer and a subject number. The UMass Center will maintain a separate spreadsheet to link subject identification codes with each subject's name and telephone number.

Only NCS study staff will have access to the data (both electronic and paper). The CIDI interview will use a paper interview form and then entered into the REDCap system. The CIDI paper forms will be stored in a locked cabinet in a locked office and only accessed by study staff. The forms will be kept for a minimum of seven years after the date of the last publication.

Interviewers will enter a specified username and password provided by the UMass NCS center to gain access to the study survey, made available on the secured, encrypted web-based REDCap platform, developed by the UMass NCS center. Interviewers will then use the study survey to administer the interview questions, entering subjects' responses as each response is given where it is stored electronically on the secured, encrypted REDCap data platform.

Subjects' names and telephone numbers will be stored on a separate log and secured according to each data collection center's IRB and NCS confidentiality requirements. For security measures related to data, the baseline technical requirement per NCS is that laptops and other computing devices used in the data collection process should:

- Be equipped with FIPS 140-2 compliant full disk encryption
- Be hardened to the specifications set forth in the DISA STIGS <http://iase.dis.mil/stigs/index.html>

As of 1/10/2013, only 9 interviews are in the REDCap system. These data were collected as part of a pilot of the instrument. The 9 cases were collected from the South Dakota, State University.

***IRB Approval:** IRB clearance for this activity has been obtained by the participating field contractor. Please see the attached IRB protocol (Attach. 1) and the IRB approval letter (Attach. 2).

Incentives: As a token of appreciation for their participation, study participants will be offered a monetary incentive of \$25 for completing the Parental Mental Health Screen. If chosen to participate in the CIDI, participants will be offered an additional monetary incentive of \$25.

Sensitive Questions: The study involves an assessment of individuals' mental health. Therefore, respondents will be asked questions during the telephone interview(s) that may be regarded as sensitive, about emotional, behavioral, or substance abuse difficulties. To protect against the risk of discomfort, the informed consent process will prepare participants in advance as to the nature of the questions they will be asked. Participants will be advised 1) that their responses to questions are voluntary and that they may choose to refuse to answer any of the questions, 2) that many efforts will be made to maintain their confidentiality, and 3) that specific data about their individual responses will never be reported in any study report. Respondents will be provided with the phone number of a designated study staff person whom they can contact to report any suspected study-related adverse events; and the local study center is

* To be completed before project proposal is submitted for OIRA clearance.

NCS Formative Research Template for OIRA Clearance

prepared to refer and/or provide study participants with reasonable and necessary medical care resulting from study activities at no cost.

Interviewers will all be trained in conducting mental health interviews, and specific training will include how to alleviate participant discomfort and/or address any discomfort and how to respond to indications that subjects need mental health services. Participants who ask for support for issues raised during the screening interview will be directed to the local study manager for assistance seeking services. Following participation in the screening interview, all participants will be provided with a list of local resources, including mental health resources, should they desire to pursue support for any of the issues raised.

Proposed Project Schedule: We will begin this project upon receipt of all regulatory approvals.

Data Collection Burden:

Estimates of Annual Hour Burden – Parental Mental Health Formative Research Project (LOI3-MHLTH-09)

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Hours Per Response	Estimated Total Annual Burden Hours
Recruitment Script	Pregnant Women and Birth Fathers & Postpartum Parents	1200	1	5/60	100
Parental Mental Health Screen	Pregnant Women and Birth Fathers & Postpartum Parents	1200	1	10/60	200
Composite International Diagnostic Interview (CIDI)	Pregnant Women and Birth Fathers & Postpartum Parents	400	1	30/60	200
TOTAL		1200			500

Annualized Cost to Respondents – Parental Mental Health Formative Research Project (LOI#9)

Data Collection Activity	Type of Respondent	Estimated Total Annual Burden	Hourly Wage Rate	Respondent Cost
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NCS Formative Research Template for OIRA Clearance

Appendix 1. Maximum NCS Incentives, by Study Activity and Impact on Participants (Approved by OMB 1/5/12)

Data Collection Activity Characteristics	Initial NCS Vanguard Study	NCS Recruitment Substudy and Formative Research		
		Phase 1	Phase 2	Formative Research
Time for encounter	3 hours	0.5 to 1 hour	0.5 to 1 hour	0.5 to 1 hour
Sensitivity of questions	Sensitive, including sexual activity	Few sensitive questions	Few sensitive questions	Few sensitive questions
Physical measures	Yes	No	No	Yes*
Environmental specimens	Yes	No	Yes	Yes*
Biospecimens	Yes	No	Yes	Yes*
Participant observation	Yes	No	No	No
Monetary incentive, per visit	\$100	\$25	\$25 for the group of study questionnaires, plus \$25, in total, for any bio-specimens collected during a contact and, where appropriate for environmental specimens	\$25, in total, for any bio-specimens collected during a contact. For questionnaires, or any environmental specimens - up to \$25 when deemed necessary
Non-monetary incentives (tote bags, post its, key chains, etc.)	<u>In addition to the monetary incentive</u> , non-monetary incentives valued at \$25 or less may be offered to participants	<u>As an alternative to the monetary incentive</u> , NCS logo gifts valued at \$25 or less may be offered to the participants in lieu of cash or local incentives not exceeding \$25 in value and deemed non-coercive by local IRBs	<u>In addition to the monetary incentive</u> , NCS logo gifts valued at \$25 or less may be offered to the participants if these are deemed acceptable by local IRBs	<u>Instead of monetary incentives</u> , NCS logo gifts valued at \$25 or less may be offered to the participants if these are deemed acceptable by local IRBs