

INVESTIGATOR STUDY PLAN - REQUIRED 5/16/2013

1) Study Title

A Methodological Study to Assess Mental Disorders for NCS Birth Parents

2) IRB Review History*

NA-no external IRB

3) Principal Investigator

Thomas McLaughlin, ScD.

4) Objectives*

The Parental Mental Health Formative Research Project (LOI#9) plans to develop a brief questionnaire to assess parental mental health that is a major driver of their children's behavioral and mental health. The questionnaire developed by the NCS Mental Health Working Team will be administered by telephone with an expected duration of approximately 10 minutes. Questionnaire responses indicative of mental illness will be compared to a gold standard-the Composite International Diagnostic Interview (CIDI). The CIDI will also be administered by phone and is estimated to take 30 minutes to complete.

5) Background*

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.^{3,4} 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 population⁵. 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 National Children Study (NCS) baseline assessments. However, these disorders are usually assessed and diagnosed using very lengthy and complicated instruments.

6) Inclusion and Exclusion Criteria*

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 mothers and fathers will also be included. Postpartum is defined as four weeks following birth. The subjects must be English speaking to participate. No minors, adults unable to consent or prisoners will be included in the study.

7) Study-Wide Number of Subjects*

The total number of participants to be recruited is 1,200 with an expectation that the recruitment of mothers and fathers would be 2:1. We will use clinical sites, prenatal classes, 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.

Participants will have to understand English though it need not be their first language since there is no budget at present for other languages.

In practice, a larger sample size tends to obtain a better level of precision in making statistical inferences about the population. It also allows for oversampling of small subgroups of interest, such as race or ethnicity. For the second-stage clinical reappraisal 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.

The goal of the analyses is to assess the accuracy of mental disorder screens for pregnant women by comparing the screening responses to a gold standard-the CIDI. The methods of these activities rely upon the McNemar chi-square tests at the aggregate level and are under the receiver operating characteristic curve (AUC) and kappa approaches at the individual level. We will use stepwise logistic regression models to evaluate any significant differences in concordance between screening scales and clinical diagnoses based on respondents' socio-demographic characteristics. We can develop separate calibration rules to adjust the estimates of predicted probability of diagnosis from screen scale scores.

An estimated 1,200 participants will be utilized in the above analyses with 1,200 of the parents will receive one questionnaire 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, well within our targeted sample size.

Through oversampling, we will target the racial and ethnic makeup of the final study cohort as follows.

Race	<p>What is your race? (One or more categories may be selected)</p> <p>a. <u>933</u> White</p> <p>b. <u>133</u> Black or African American</p> <p>c. <u> </u> American Indian or Alaska Native</p> <p>d. <u>67</u> Asian Indian</p> <p>e. <u> </u> Chinese</p> <p>f. <u> </u> Filipino</p> <p>g. <u> </u> Japanese</p> <p>h. <u> </u> Korean</p> <p>i. <u> </u> Vietnamese</p> <p>j. <u>67</u> Other Asian</p> <p>k. <u> </u> Native Hawaiian</p> <p>l. <u> </u> Guamanian or Chamorro</p> <p>m. <u> </u> Samoan</p> <p>n. <u> </u> Other Pacific Islander</p>
Ethnicity	<p>Are you Hispanic, Latino/a, or Spanish origin (One or more categories may be selected)</p> <p>a. <u>750</u> No, not of Hispanic, Latino/a, or Spanish origin</p> <p>b. <u>12</u> Yes, Mexican, Mexican American, Chicano/a</p> <p>c. <u>386</u> Yes, Puerto Rican</p> <p>d. <u>5</u> Yes, Cuban</p> <p>e. <u>44</u> Yes, Another Hispanic, Latino/a or Spanish origin</p>

8) Study-Wide Recruitment Methods*

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 through the website. This information will be available through advertisements on message boards or materials (e.g. flyers, brochures), 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 will call the parent from a land-line telephone with headphones. The woman will be verbally re-consented prior to the administration of the survey. A scripted text for responding to women calling the study center will be used.

All recruitment (and data analysis) will occur at the NCS Study Center in Worcester Co. Key personnel for the team are already on board and these will be added to through the hire of per diem recruiters and

interviewers. Personnel for training and use of study instruments currently exists in-house. Analytic methods and programs are being adapted to the study instruments, most especially since we changed from the SCID to the CIDI as the gold standard instrument, thus requiring revision of the programs.

9) **Study Timelines***

The study duration is from January 2013 to the end of January 2014. Subject enrollment will begin in March 2013 and end by August 2013. Subjects will be enrolled in the study for the maximum of 3 weeks. Analyses will be on-going throughout the duration of the project. From August to September 2013, the analyses will be finalized and a report completed.

10) **Study Endpoints***

1. Test the feasibility of implementing a short, telephone mental health screen.
2. Test the validity of the PMH screen against the gold standard, the CIDI.

11) **Procedures Involved***

There are two parts to this study:

1. The Parental Mental Health Screen
 - a. All pregnant women and fathers of the babies who agree to participate in this study will provide a phone number to the research assistant and they will schedule a time for a telephone call.
 - b. At the agreed upon time, the research assistant will call the pregnant parent. The research assistant will ask the parent a series of questions from the PMH Screen. This call will last approximately 10 minutes.
2. The Composite International Diagnostic interview (CIDI)
 - a. Half of the parents in the study will be randomly chosen to participate in a second phone call. This time questions from a mental health screening instrument called the Composite International Diagnostic interview will be asked. This phone call will last approximately 30 minutes.

Worcester County Study Center will administer the Parental Mental Health Screen (PMH Screen) via REDCap. REDCap is a secure, web-based application 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 FISMA compliant laptops to enter the data into REDCap.

The PMH screen will be entered directly into the REDCap system as the interview is conducted by phone in real time (Computer assisted telephone interview).

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. Both of these activities will be conducted by the PMH interviewers and research assistants.

Once a week, diagnostic algorithms (developed in SAS) will be run at the UMass NCS 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-stage clinical reappraisal interview using the CIDI. The CIDI will be administered as a telephone interview.

Participants will receive a monetary token of appreciation of \$25 for completing the Parental Mental Health Screen. If chosen to participate in the CIDI, participants will receive an additional monetary token of appreciation of \$25.

12) Data and Specimen Banking*

Study data (questionnaire responses) will be entered and transmitted electronically using the secured encrypted internet-based REDCap data platform accessed on NCS approved computers. The UMASS NCS study center intends to keep the de-identified research data at a minimum until the analysis of the information is completed and for the minimum period of 3-7 years as required for NIH studies.

13) Data Management*

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 Research Electronic Data Capture (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 centers' 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. Data will be maintained for 7 years after the date of the last publication.

14) **Provisions to Monitor the Data to Ensure the Safety of Subjects***

There is a very rare likelihood of potential risks to subjects, which may include: 1) experiencing minor discomfort related to the standard procedures of responding to the potentially sensitive and personal questions included on the questionnaires, and 2) minor risk of potential breach of confidentiality. 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 that their responses to questions are voluntary and that they may choose to refuse to answer any of the questions. 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. Though danger to self or others is expected to be a very low risk in the study population, , interviewers trained in the use of a previously approved risk assessment protocol (used in the cop study, right?) will contact the Project Manager or the PI and discuss the safest course of action for emergent care if necessary. (Also, please see below.in the section **Access to Emergency Mental Health Specialty Care** for additional details.)Participants who ask for support for issues raise 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. The original application did not include UMass as a data collection site. As part of the application, the other study sites were required to have a safety plan in place for a mental health crisis. Below is the plan for UMass NCS.

Safety Plan: Access to Emergency Mental Health Specialty Care. A worrisome problem any mental health study is assuring immediate access to specialty mental health services for patients who might become dangerous to themselves or others, without any mental health care benefit. Fortunately, the study site at UMass Memorial is Central Massachusetts’ leading resource for providing vital mental health services in both outpatient and inpatient settings for adults as well as children. Emergency Mental Health Services (EMHS) are available to individuals regardless of their insurance or ability to pay. In the current year, more than 6,000 psychiatric evaluations will be handled by staff in the UMass Emergency Department. The EMHS team sees patients in crisis, such as those who may be planning to commit suicide or overdosed on drugs,

or patients who are feeling overwhelmed by events in their life. EMHS personnel can mobilize the mental health team to go to other hospitals or facilities in the Worcester area in the event a patient needs an emergency evaluation. When a patient comes or is sent to the emergency room, medical needs, if any, are met first. Once the patient's medical condition is stabilized, EMHS staff conduct a full mental health evaluation and develop a care plan for the patient that can involve discharge and arranging for outpatient services, being admitted for more intensive treatment, or being moved to a crisis stabilization unit. Patients in crisis stabilization units, located throughout the Central MA, stay for one to five days and receive intense, targeted treatments. A multidisciplinary team, including nurses, social workers, trained crisis counselors, psychiatric residents and attending psychiatrists operates EMHS 24/7. The goal of care is to stabilize the patient, identify the crisis and determine effective treatment, allowing the patient to return home.

15) Withdrawal of Subjects*

The study is voluntary. A subject can withdraw at any time without any impact upon her prenatal care.

16) Risks to Subjects*

To protect against potential breach of confidentiality, access and use of the participants' names and telephone numbers will be managed, accessed and stored on secure, encrypted computer data bases with any physical copy to be stored in a locked file by the local study manager in accordance with each participating centers' federally and locally approved security plan.

17) Potential Benefits to Subjects*

There are no benefits to the subjects as a result of participating in the study.

18) Vulnerable Populations*

Pregnant women are being recruited for this study.

No inducements, monetary or otherwise, will be offered to terminate a pregnancy. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. Individuals engaged in the research will have no part in determining the viability of a neonate.

19) Multi-Site Research*

UMMS is the only location of this study.

20) Community-Based Participatory Research*

N/A

21) Sharing of Results with Subjects*

The results of the tests will not be shared with the subjects or their medical/clinical providers with one exception: If a woman or man is experiencing significant, psychological distress, the results will be

shared directly with the person and the Emergency Mental Health Services (EMHS)

22) **Setting**

The recruitment will take place in the community at birth education, parenting and nutrition classes. The interviews will be conducted by phone. The NCS located at the Chang building has a designated call center where the interviews will be conducted. Data analyses will take place at the Chang or on the UMass Medical school campus.

23) **Resources Available**

This project is funded through a NICHD – NCS -Sub award. There are adequate resources and facilities to carry out this research, including staff, funding, space, recordkeeping capability, and resources to address serious adverse events

-Thomas McLaughlin ScD, Professor of Pediatrics and Psychiatry, and Co-Principal Investigator of the UMass NCS-Center, will serve as the Lead Investigator on this project and will be responsible for successful implementation and timely completion of all aspects of the proposed research. He is a mental health researcher who has conducted NIH and foundation research funded work in diverse populations: Medicaid patients with schizophrenia, bipolar disorders and since 1992 mental disorders in primary care. He has conducted randomized controlled trials, epidemiologic studies, clinical research and health services research. Presently he is focused on adolescent depression and leads the development of a mental health research program for the National Children's study. He is well experienced in information security training, operationalization and monitoring of sensitive data such as psychiatric information and sequestering of these data with access approved by the IRB and the PI. He is well versed in the development of safety nets especially suicide protocols aimed at reducing risk in study subjects. Typically his studies develop safety protocols that exceed federal standards. He has numerous publications in the area of mental health.

34- Project Manager, will have primary responsibility for overseeing proper implementation of the proposed work across the collaborating centers; with Dr. McLaughlin will be responsible for the specification of all the necessary explanatory statistical models and the interpretation of results. 5-Data Manager, TBH, will maintain the daily operations of the study; will enter data; will receive all data from the REDCap data platform and will check reliability of the data;

6- Informaticist/Programmer, will be responsible for developing and programming the web interface for the administration of the MH screening scales for the study in the REDCap system. The Informaticist/Programmer will provide ongoing trouble shooting through the duration of the project. The person will not access PHI of study subjects.

7-PMH Interviewer 1, T.B.H. will consent/conduct telephone PMH interviews with consented subjects

8-PMH Interviewer 2, T.B.H. will consent/conduct telephone PMH interviews with consented subjects

9. PMH Recruiter/Scheduler, T.B.H., will recruit/consent subjects to participate in the study.

10-PMH Recruiter/Scheduler, T.B.H. will recruit/consent subjects to participate in the study.

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. 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 and has been used extensively for decades in multiple international settings.

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 materials will be provided by Dr. Kessler. 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.

Recruiters and 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 that occurs.

24) Prior Approvals

This study has been previously approved by the UMass IRB.

25) Recruitment Methods

See Study-Wide Recruitment Methods

26) Local Number of Subjects

Up to 1,200 participants are planned to be recruited.

27) Confidentiality

See Data Management

28) Provisions to Protect the Privacy Interests of Subjects

NCS staff undergo training and certification in maintaining confidentiality and security of participants' data. NCS staff will only collect name and telephone numbers of those individuals interested in participating in the study. Subjects' names and telephone numbers will be stored on a separate log and secured according to IRB and NCS confidentiality requirements. Interviewers will make each phone call from an appropriate setting in accordance with institutional requirements and standards for maintaining patient confidentiality.

29) Compensation for Research-Related Injury

In the unlikely event of injury, UMMS is responsible for coverage.

30) Economic Burden to Subjects

None

31) Consent Process

The parent will sign an informed consent form prior to receiving a phone call from the PMH interviewer. At the time of the call, the PMH interviewer will verbally re-consent the parent prior to administering the PMH questionnaire. If a respondent is selected for the second-stage clinical reappraisal interview using the CIDI, the CIDI interviewer will verbally re-consent the parent prior to administering the CIDI.

32) Process to Document Consent in Writing

Eligible parents (1) can self-select into the study by calling the study phone number or through the website. This information will be available through advertisements on message boards or materials (e.g. flyers, brochures), or will be informed of the project by a brief presentation by a NCS staff person held at various community locations. If interested, the expectant parent(s) will be consented and their contact information will be obtained.

Consent process for (1): if the expectant parent self-selects into the study, a NCS staff member will arrange to meet with the parent for consent. (2) The NCS staff member will be present at various locations within the community, where they will give presentations about the study. This will take place at birth education or parenting classes. Parents who are interested in participating in the study can approach the NCS staff member, who will then begin the consent process. Parents will receive a copy of the informed consent.

33) Drugs or Devices

N/A