ADMINISTRATIVE CORE BACKGROUND AND PRELIMINARY STUDIES

As we describe in the associated Overall application, development of a learning mental health system will require a robust and efficient national infrastructure for practice-based mental health research, including:

- Research fully embedded in real-world practice[1]
- Alignment of research goals with priorities of patient and health system stakeholders[2]
- Large-scale data infrastructure available for rapid analysis[3]
- A culture of trust and transparency to facilitate collaborative learning and improvement

In pursuit of those goals, the Mental Health Research Network (MHRN) has developed a robust national research infrastructure and implemented a diverse program of clinical and health services research. We propose to expand MHRN to include 14 research centers embedded in large health systems serving a patient population of over 25 million in 16 states. Each health system provides mental health and general medical care to a defined patient population, including substantial numbers from all racial and ethnic groups and substantial numbers insured by Medicaid and other low-income insurance. Each health system has organized longitudinal records into compatible research data warehouses. The MHRN portfolio now includes over 20 projects, spanning a range of methods (qualitative research, observational studies, pragmatic clinical trials).

We describe below how this infrastructure will be enhanced to support a next-generation network, including:

- Increased engagement of patients and other stakeholders in network planning and governance
- An expanded public, open-source library of software tools and other technical resources
- More formal processes for feasibility analyses and rapid response to stakeholder queries
- Expanded outreach to external stakeholders and research partners

ADMINISTRATIVE CORE RESEARCH STRATEGY

1) Overview - The Administrative Core will include:
   - An Organizational Unit responsible for governance, strategic planning, fiscal management, and compliance
   - An Outreach and External Collaboration Unit responsible for communications, resource sharing, promoting new collaborations, and rapid response to stakeholder queries and requests for pilot/feasibility data
   - An Emerging Issues Unit to rapidly identify and help address emerging public health questions.
2) Organizational Unit – Leadership and management resources, based at the KP Washington lead site, will support MHRN infrastructure, core-funded research projects, and affiliated research projects.
   - Executive Leadership – Gregory Simon will continue as network Principal Investigator. Dr. Simon has led this network since 2010. He has extensive experience with management of large, multi-site research programs and engagement with health system leaders. He currently holds leadership roles in the broader Health Care Systems Research Network and the NIH Health Systems Research Collaboratory. Belinda Operskalski will continue as Project Director. Ms. Operskalski has extensive experience with the management of multi-site, multi-component research networks – including strategic planning, financial oversight, regulatory compliance, and coordination across network activities.
   - Site Leadership and Staffing – In general, Administrative Core resources will support effort by a site lead investigator (responsible for supervising local data infrastructure activities and health system engagement), a programmer/analyst (responsible for data infrastructure quality control, routine descriptive analyses, and analyses regarding emerging issues), and a project manager (responsible for local financial management and regulatory compliance). Staffing plans vary according to research center organization and contribution of in-kind resources (see Budget justification narrative for each site).
   - Steering Committee – The network Steering Committee will remain the primary vehicle for strategic planning, monitoring progress of network projects, and allocation of network resources. Voting members will continue to include the lead investigator in each member research center and principal investigator of each project supported by the core cooperative agreement. As described below, patient/consumer partners will join as voting members. The Steering Committee will continue to meet monthly by teleconference and twice-yearly in person – with a Spring in-person meeting alongside the Health Care Systems Research Network annual conference and a Fall in-person meeting in the Bethesda, MD area to facilitate engagement with NIMH leadership and program staff. As always, every Steering Committee

meeting (teleconference and in-person) will be open to any interested researcher (in our outside of MHRN member research centers), health system leader (in our outside of MHRN member health systems), patient/consumer stakeholder, or member of the general public. We also hope to explore opportunities for shared meetings with other network(s) funded under this announcement.

- External Advisory Committee - An External Advisory Committee will include 1 – 2 members from the following areas: 1) leaders in "big data" and implementation science methods; 2) organizations developing practice guidelines and quality metrics; 3) private and/or public payers; 4) national consumer and advocacy groups; and 5) leaders in promoting health equity. Members will be identified by NIMH and the MHRN Steering Committee through a formal nomination process led by Karen Coleman, who leads the stakeholder engagement process for the MHRN. This committee will be engaged in quarterly virtual meetings led by Drs. Coleman, Simon, and NIMH partners as appropriate. Meetings will be audio-recorded and meeting notes will be publicly available and discussed in the MHRN Steering Committee meetings. Recommendations from the External Advisory Committee will be considered by the Steering Committee and by relevant project leadership who will make specific responses (including action plans) prior to the next quarterly Advisory Committee meeting. We hope to explore sharing Advisory Committee processes with other practice-based research network(s) funded under this announcement.
- Fiscal Management – The current MHRN cooperative agreement includes 29 distinct budget components (13 site infrastructure budgets, 9 project budgets at 7 sites, and 12 administrative supplement budgets at 7 sites). To manage this portfolio, Ms. Operskalski and her colleagues have developed a robust system for monitoring spending rates, monitoring timeliness of invoicing, and projecting year-end financial status. We will continue to use these tools to monitor and assure prudent use of limited taxpayer dollars. To illustrate the effectiveness of MHRN fiscal management:
  - The MHRN-based Suicide Prevention Outreach Trial[4], a patient-level randomized trial of outreach to prevent suicide attempt in high-risk outpatients, enrolled and randomized 18,889 participants at a total cost (including indirect cost) of approximately $460 per participant randomized.
  - The MHRN CV Wizard Trial, a cluster-randomized trial of decision support to reduce cardiovascular risk in people with severe mental illness has now enrolled and randomized over 11,177 participants at a total cost of approximately $250 per participant randomized.
  - The MHRN Suicide Risk Calculator project[5] has extracted and organized data for approximately 20 million outpatient visits in 7 health systems to develop and validate best-in-class machine learning models to predict suicide attempt and suicide death, at a total cost of approximately $650,000.
- Regulatory Compliance –
  - 45 CFR 46 Compliance and IRB Review –We will continue and expand use of IRB reliance and expedited review procedures that have significantly improved the efficiency of current projects. Ms. Operskalski, in collaboration with site project managers, has developed efficient and transparent processes for sharing IRB materials across sites and tracking status of IRB initial approval and continuing review across sites, and monitoring site adherence to approved procedures.
  - HIPAA Compliance – The same tools described above facilitate tracking the need for and execution of data use agreements or data transfer agreements (DUA/DTA) across multi-site projects. During the proposed new funding cycle, we will continue to expect use of standard DUA/DTA templates for all multi-site projects to reduce delays in execution of multi-site analyses.

3) Outreach and External Collaboration Unit – MHRN's communications, knowledge management, and stakeholder engagement resources will support MHRN infrastructure and research projects, disseminate MHRN resources to the research community, and facilitate new research partnerships. For example:

- Publications and Dissemination – We will continue to support high-quality peer-reviewed publications by MHRN-based and external investigators, emphasizing publication opportunities and analytic support for early- and mid-career investigators. We will encourage rapid publication of all results, and we do not propose any central publications committee to control or restrict MHRN manuscripts.
- Other Communications – We propose to continue each of the public communications programs described in the associated Overall application, with each focused on a different audience and/or purpose:
  - Researcher newsletter – This quarterly newsletter for mental health and health services researchers informs current and potential research partners of MHRN resources and collaboration opportunities.

- Health system leader newsletter – This quarterly newsletter for leaders within and beyond MHRN promotes collaborations with system leaders and elicits suggestions regarding research priorities
- Website – This public resource (http://mhresearchnetwork.org) informs potential collaborators about MHRN technical and other research resources, interest groups, and active projects.
- MHRN Blog – This monthly posting (http://hcsrn.org/mhrn/en/Blog/) , publicized by email and social media, engages research leaders, health system leaders, and policy-makers in discussions regarding the ethical and social aspects of health system-based mental health research.

- Resource Sharing – We will continue to share all MHRN technical resources with other researchers and health systems (including our direct competitors) via our online repository. Resources will include:
  - EHR computable phenotypes – These will include already developed specifications (e.g. diagnosis groups, self-harm events)[6-15] as well as new phenotypes developed by MHRN core and affiliated projects (e.g. predictors of suicide risk, opioid-related exposures and outcomes).
  - Analytic code – This will include code for completed analyses (e.g. variable selection models for suicide risk prediction[5], multi-level models evaluating provider variation[16]) as well as code developed by new projects (see description of Scientific Analysis Unit in the Methods Core application).
  - Assessment tools – These will include self-report or interviewer-administered measures (e.g. Columbia Suicide Severity Rating Scale) and assessments based on electronic health records data elements.
  - Intervention tools – These will include conventional intervention materials (e.g. therapist manuals, patient workbooks) as well as technical materials supporting online interventions and decision support.
  - Resources for protection of human subjects – We will continue sharing all resources for protection of human subjects (e.g. invitation messages, consent forms and scripts) via our online repository.
- Health System Engagement – We will continue our comprehensive efforts to engage with leaders of MHRN health systems, other mental health care systems and provider organizations, including:
  - Participation of MHRN health system leaders in Steering Committee meetings (teleconference and in-person), interest group meetings, and project meetings
  - Periodic surveys of MHRN health system mental health leaders regarding research priorities
  - Targeted engagement regarding specific research opportunities (e.g. engagement regarding priorities for the pilot projects included in this application)
  - Engagement with a wider range of health systems via involvement in the NIH Healthcare Systems Research Collaboratory and the National Academy of Medicine Real-World Evidence Workshop series
  - Regular newsletters for health system leaders within and outside of MHRN (described above)
- External Investigator Engagement – We will continue our vigorous efforts to engage with external investigators and identify new opportunities for collaboration, including:
  - Regular investigator newsletters (described above)
  - Participation in a range of relevant regional and national clinical and policy forums, such as the National Action Alliance for Suicide Prevention, SAMHSA Technical Expert panels, AHRQ Evidence-Based Practice Center panels, and National Academy of Medicine panels.
  - Presentations at relevant national research conferences (e.g. NIMH MHSR Conference, AFSP/IASR summit, Academy Health, HCSRN annual conference, American Psychiatric Association annual meeting, AMIA annual symposium, Epic users annual meeting)
  - Individual outreach to potential partners in high-priority research areas
- Academic partnerships – We will maintain the partnerships described in the associated Overall application and actively pursue additional collaborations through the communication channels and engagement processes described above. External university-affiliated investigators will collaborate in the Methods Core and two of the proposed research projects. MHRN participation in the AHRQ Learning Health System K12 training grant program will create new opportunities for academic partnerships.
- External health system partnerships – We will maintain the partnerships with the Veterans Health Administration and other large integrated care systems described above and will pursue additional collaborations through the communication channels and engagement processes described above.
- Patient/Consumer Engagement – In 2018, supported by an Engagement Award from the Patient-Centered Outcomes Research Institute to Dr. Coleman, MHRN began integrating patients and consumer

advocates to the Steering Committee as voting members. The current patient and consumer advocacy group members represent broad interests including mood disorders, suicide prevention, serious mental illness, and under-served populations such as racial/ethnic and gender minorities. We will also form a separate Patient/Consumer Engagement Workgroup as part of the PCORI award. This will include 1 – 2 patients/caregivers from each of the 14 participating MHRN healthcare systems and members from other national advocacy groups. This committee will be engaged in 1 hour monthly virtual meetings led by Dr. Coleman. Meetings will be audio-recorded and meeting notes will be publicly available and discussed in the MHRN Steering Committee meetings. This group will assist with and monitor meaningful engagement of stakeholders in all MHRN-affiliated projects, from design to dissemination. This work will be coordinated by Dr. Coleman and her research team.

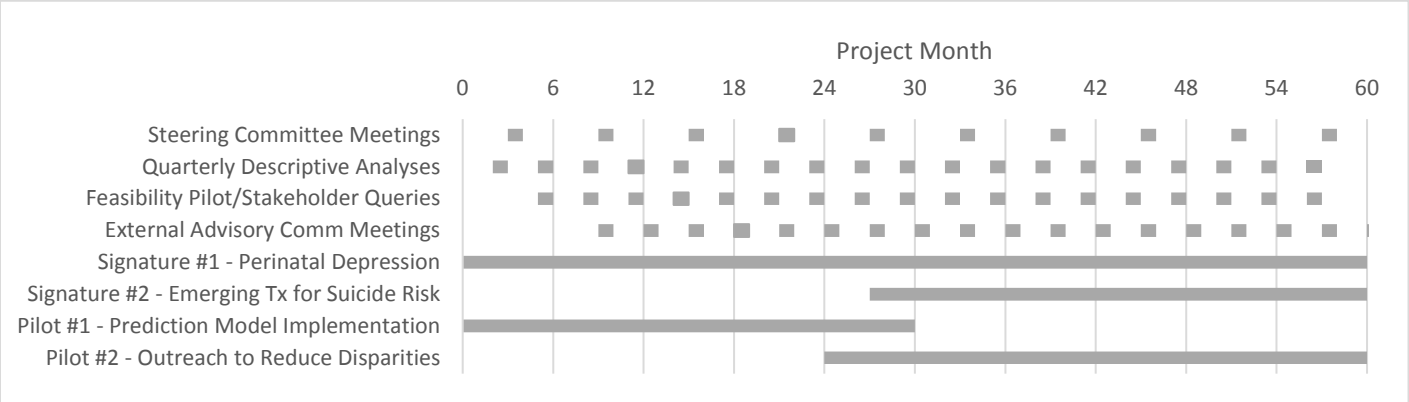
- Feasibility Pilot Projects – MHRN infrastructure resources have frequently supported the development of feasibility or pilot data for new projects led by MHRN-affiliated and external investigators. We propose to formalize and scale up this existing process. Most feasibility pilot projects will involve analysis of existing records data, but some could involve surveys, qualitative data collection, or feasibility testing of interventions. We will adapt and enhance processes created by the NCI-funded Cancer Research Network (CRN) to respond to preparatory-to-research queries[17] and support trainees and early-career investigators[18]. Rebecca Ziebell, technical lead for that CRN work, will join our team for that purpose.
  - Flexible initiation – Feasibility or pilot questions regarding future research may be raised by a wide range of users, including existing MHRN research teams or interest groups and external investigators. Any user (internal or external) will complete a brief intake document (available via the MHRN website or on request) describing the potential future research project, the feasibility or pilot question(s) to be addressed, and the general methods anticipated (e.g. analyses of records data, provider survey).
  - Stakeholder engagement in planning and prioritization – Any investigator proposing a feasibility pilot will be encouraged to consult with relevant stakeholder representatives (patients, families, clinicians, health system leaders) prior to completing an intake document. As described below, formal stakeholder endorsement will be required for projects including direct interaction with clinicians or patients.
  - As-needed mentoring and technical assistance – Investigators not affiliated with an MHRN health system will be offered appropriate mentoring and/or technical support by core-supported MHRN personnel. Depending on the pilot work proposed, this consultation could cover MHRN data resources, regulatory compliance, survey methods, clinic procedures, and/or analytic methods.
  - Scoping and budgeting – Following the stakeholder input and mentoring/technical assistance processes described above, investigators will complete a full application detailing necessary resources (e.g. programmer effort, analyst and/or biostatistician effort, project manager effort, research interviewer effort, etc.). Requests for analyses of existing records data will include a structured query-building tool developed by Drs. Stewart and Simon. Feasibility projects that can be integrated with routine descriptive analyses (described above) will not require specific additional budget. No single feasibility pilot is expected to require more than $40,000 of direct cost over no more than 12 months.
  - Transparent evaluation and resource allocation process – Matching the quarterly cycle for routine descriptive analyses, the MHRN Steering Committee will review new feasibility pilot proposals each quarter to approve, disapprove, or recommend revision or change in scope. As described above, patient stakeholders will be full participants in this process. Criteria for approval will include:
    o Scientific validity and methodologic rigor
    o Potential to inform future high-impact research
    o Value of pilot work and potential future research to patient, health system, and external stakeholders
    o Efficient use of network resources
    o Potential conflict with other research activities or health system initiatives
    The number of proposals approved in any year will depend on funds in the Administrative Core budget.
  - Data sharing and privacy protection – Users will be strongly encouraged to use privacy-preserving approaches[19], sharing minimum necessary information to address specific scientific questions.
  - Open library of technical resources – Investigators proposing feasibility pilots will be strongly encouraged to use existing MHRN technical resources, including EHR computable phenotypes, prototype data extraction code, standard analytic processes, survey instruments, and IRB materials.

- Dissemination of findings – Investigators will be encouraged to publish feasibility pilot results as appropriate. Results not published may be made available via MHRN's website or GitHub repository.
- Accountability – Status of all queries will be reported in the annual evaluation described below.

4) Emerging Issues Unit – Technical, knowledge management, communication, and stakeholder engagement resources will support rapid identification of emerging public health questions, rapid organization and analyses of relevant population-based data, and rapid communication of results and recommendations to a range of clinical, health system, and policy stakeholders – both inside and outside of MHRN health systems.
   - Routine Descriptive Analyses – Routine analyses (described under the Methods Core) describing patterns of mental health diagnoses and treatments across MHRN health systems (including stratification or subgroup analyses by age, sex, race, and ethnicity) serve as an ongoing and public health monitoring system. These analyses will both examine anticipated changes in diagnosis or treatment rates (e.g. changes in procedure coding, adoption of new medications) and identify any unexpected changes or discontinuities (e.g. sudden changes in self-harm diagnoses due to changes in EHR coding logic).
   - Stakeholder Engagement – The processes for engaging with external investigators, health system leaders, patients, and families described above will also be used to identify emerging issues for additional investigation using MHRN data resources. In addition, our regular communications with NIMH program staff will continue to be an important source of emerging questions requiring timely response.
   - Library of Tools and Methods – A described in the Methods Core application, MHRN's large and growing library of specification/phenotypes, data extraction routines, and analytic code have and will continue to facilitate rapid assessment of changes in practice or responses to regulatory or policy changes.
   - Rapid Response Capability – Taken together, the resources and expertise described above create a continuous capability to identify emerging clinical or public health questions, rapidly assemble relevant data, rapidly deploy appropriate methods, and address stakeholders' decisional needs.
   - Process for Responding to Stakeholder Queries – During the current funding cycle, MHRN infrastructure resources have frequently supported timely responses to specific queries from NIMH and other federal partners, health system partners, and other national stakeholders (e.g. NCQA, AHRQ Evidence-Based Practice Centers). We now propose to organize and scale up this existing informal process. In some cases, stakeholder queries can be immediately addressed using routine descriptive analyses described above. Some queries will require additions/modifications to those routine analyses or require extracting and organizing additional specific data elements from health system records. This work will adapt and enhance the successful CRN-developed processes described above. Specific work to respond to stakeholder queries will be similar to those described above for feasibility pilot projects, including:
     - Stakeholder initiation – Queries may arise through established MHRN components (Steering Committee, External Advisory Committee) or from participating health systems, NIMH partners, other federal stakeholders (CDC, FDA, SAMHSA), or other national stakeholders (Joint Commission, NCQA).
     - Structured intake process – A standard intake document (similar to that for feasibility pilots described above) will record the specific question and (if known) the relevant data elements and analytic methods.
     - As-needed technical assistance – Administrative and Methods Core personnel (e.g. Christine Stewart, Gregory Simon) will provide technical assistance regarding mapping of queries to specific data elements and analytic methods. Whenever possible, queries will be mapped to processes for routine descriptive analyses or to existing MHRN data extraction and analytic tools (described above).
     - Structured query-building tools – This structured process will enable non-technical users to completely specify queries using standard menus and existing code sets.
     - Transparent evaluation and resource allocation process – Corresponding to the cycle of routine descriptive analyses, the MHRN steering committee will review all query proposals once per quarter, anticipating that many queries can be addressed by minor modifications to existing processes. Proposals will be evaluated based on:
       o Scientific validity and methodologic rigor
       o Value to patient, health system, and external stakeholders
       o Efficient use of network resources

- Data sharing and privacy protection – In general, queries will be addressed using privacy-preserving distributed analytic approaches[19], with no sharing of individual-level data. Any sharing of individual-level data will require explicit approval by the Steering Committee and by relevant health system IRBs.
- Dissemination of findings – When appropriate, findings may be disseminated via traditional academic publication or presentation. All newly-created technical resources will also be shared.
- Accountability – Status of all queries will be reported in the annual evaluation described below.

5) Network Timeline – Timing of specific activities planned for the 60-month project period is shown below:



Specific milestones for Administrative Core Activities include:

- In-person Steering Committee meetings will continue at the current 6-month intervals
- Quarterly descriptive analyses will be established by month 3 and continue at 3-month intervals
- Feasibility/pilot and stakeholder queries will be established by month 6 and continue at 3-month intervals
- External advisory committee meetings will be established by month 9 and continue at 3-month intervals

Detailed timelines for Signature and Pilot projects are included in Research Plans for those components.

6) Network Evaluation – Following the measures of success listed in RFA-MH-19-225, annual reports to the Steering Committee, External Advisory Committee, and NIMH will include these progress indicators:

- Status for all new research proposals submitted by MHRN-affiliated and external investigators
- Status for all publications supported by the core MHRN cooperative agreement
- Status and time to final disposition for all Feasibility Pilot and Stakeholder Query requests
- Timeliness and completeness of routine data quality and descriptive analyses
- New resources added to the MHRN online Github repository
- Recruitment and participation rates for signature and pilot clinical trials
- Dissemination activities in MHRN and external health systems
- Support for trainees and early-career investigators
- Expenditures and projected expenditures compared to budget

Formative evaluation recommendations by the External Advisory Committee will include both suggestions for process improvements and strategic priorities for new research. The Steering Committee, in consultation with NIMH colleagues, will have the authority to discontinue funding for any site failing to fulfill Administrative Core responsibilities or failing to fulfill responsibilities to any specific project.