Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH)

Components of Participating Organizations

National Institute of Mental Health (NIMH)

Funding Opportunity Title

A Practice-Based Research to Transform Mental Health Care: Science, Service Delivery & Sustainability (U19 Clinical Trial Required)

Activity Code

U19 Research Program – Cooperative Agreements

Announcement Type

New

Related Notices

None

Funding Opportunity Announcement (FOA) Number

RFA-MH-19-225

Companion Funding Opportunity

None

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Catalog of Federal Domestic Assistance (CFDA) Number(s)

93.242

Funding Opportunity Purpose

The purpose of this Funding Opportunity Announcement (FOA) is to support a practice-based research Network in the United States to transform the development, delivery, and sustainability of evidence-based mental health practices and services. Through a research consortium embedded within large and integrated healthcare delivery systems (public and/or commercial systems) that serve representative populations, this Network would constitute a continuously learning healthcare system, as defined by the Institute of Medicine, to enable “a continuous cycle or feedback loop in which scientific evidence informs clinical practice while data gathered from clinical practice and administrative sources inform scientific investigation.”

The practice-based research Network is intended to provide infrastructures that can be leveraged to: efficiently and rapidly identify, recruit and enroll large and diverse patient populations into effectiveness trials; harmonize electronic health record (EHR) data across multiple integrated systems for common analyses; build capacity for the collection, storage, and analysis of biologic and/or genetic material; study low base-rate events (e.g., suicide, autism spectrum disorders, first episode psychosis) by using and advancing innovative methodologies (e.g., predictive analytics); develop, test, and deploy large-scale mental health information technology (IT) interventions, workflows, and decision support systems; develop and test strategies to address health disparities; and generate data that will fuel the transformation of mental health care.

The Network will support a wide range of practice-based research, including pragmatic and comparative effectiveness trials, focused on optimizing and testing scalable preventive and therapeutic interventions, and services research focused on identifying and intervening on mutable factors to increase access, engagement, continuity, equity, efficiency/value, and quality of mental health care.

Key Dates

Posted Date

November 29, 2018

Open Date (Earliest Submission Date)

January 28, 2019

Letter of Intent Due Date(s)

30 days prior to the application due date

Application Due Date(s)

February 28, 2019, by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on this date.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

AIDS Application Due Date(s)

Not Applicable

Scientific Merit Review

May 2019

Advisory Council Review

August 2019

Earliest Start Date

September 2019)

Expiration Date

March 1, 2019

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the Multi-Project (M) Instructions in the SF424 (R&R) Application Guide, except where instructed to do otherwise (in this FOA or in a Notice from the *NIH Guide for Grants and Contracts*). Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions. **Applications that do not comply with these instructions may be delayed or not accepted for review.**

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.
   Apply Online Using ASSIST
2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons to track your application. Check with your institutional officials regarding availability.

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Purpose

This Funding Opportunity Announcement (FOA) seeks applications to develop and leverage a practice-based research network (Network) in the United States central to a continuously learning healthcare system and to serve as a national research laboratory to improve mental health outcomes by generating the evidence base that healthcare system decision-makers need. In turn, the healthcare system will drive the research questions based on urgent practice priorities. Studies conducted through this Network will be pragmatic and deployment-focused, incorporating stakeholder perspectives and criteria used for decision making. The goal is to inform, develop, and test interventions and service delivery strategies that are feasible, scalable, and sustainable, and will ultimately improve routine mental health services.

Rationale

The healthcare landscape in the United States is constantly changing, creating new challenges to the delivery of high-quality treatments and services to children, youth, adults, and older adults with unmet or under-met mental health needs. Epidemiological findings suggest that approximately one-half of the United States population meets lifetime criteria for a mental disorder, and approximately one-quarter of the population meets criteria in any given year. However, only one-half of people with any mental health disorder and only two-thirds of people with a serious mental health disorder received mental health services in the previous year. Of those that find their way into mental health care, many fall out of care and/or do not receive guideline-concordant treatment. Documented disparities in access, quality, and outcomes of treatment and services (e.g., in racial, ethnic, sexual, and gender minority communities, and/or rural populations), a fragmented healthcare system, provider shortages, healthcare affordability, and other factors moderate these findings.

While investments in research have generated potential solutions to many of these challenges, that research has little public health impact if findings do not influence actual healthcare practice. This outcome is especially common when research questions, strategies for addressing those questions, and methods for disseminating and implementing research findings are not embedded in healthcare practice. Moreover, the cost of individually conducting large-scale pragmatic and/or comparative effectiveness trials and other research can be prohibitive without a common infrastructure that can be leveraged.

Practice-based research networks have robust infrastructures that can be leveraged to (1) efficiently and rapidly identify, recruit and enroll large and diverse patient populations into effectiveness trials; (2) harmonize electronic health record (EHR) data across multiple integrated systems for common analyses; (3) build capacity for the collection, storage, and analysis of biologic and/or genetic material; (4) study low base-rate events (e.g., suicide, autism spectrum disorders, first episode psychosis) by using and advancing innovative methodologies (e.g., predictive analytics); (5) develop, test, and deploy large-scale mental health information technology (IT) interventions, workflows, and decision support systems; (6) develop and test strategies to address health disparities; and (7) generate data that will fuel the transformation of mental health care.

NIMH recognizes the importance of such networks and directly calls for researchers to leverage such partnerships when designing high impact studies. See https://www.nimh.nih.gov/about/strategic-planning-reports/strategic-research-priorities/srp-objective-4/index.shtml for details.

An innovative and robust research infrastructure within large, representative healthcare settings may facilitate capacity for pragmatic, generalizable research that yields effective and efficient strategies for care. As NIMH's prototype of a continuously learning healthcare system, the practice-based research Network will be embedded within one or more integrated (public and/or commercial) healthcare settings serving large and representative patient populations, including people with severe mental illness, and including settings offering evidence-supported integrated care (e.g., collaborative care and/or coordinated specialty care) across the United States. The Network will leverage and enhance a sophisticated infrastructure for research to be prioritized, conducted, and utilized by the affiliated healthcare system(s). Research on topics with relatively low incident cases (e.g., suicide, first episode psychosis, and autism spectrum disorder) and research which takes advantage of and improves upon (1) harmonization of common data elements, (2) EHR phenotyping, and (3) systematic procedures for rapid case finding, participant recruitment, eligibility determination, and assessment can be more easily conducted on such a Network.

General Requirements

The Network is expected to function as a resource to the broad mental health research community, and its impact will be assessed through achievement of the following activities:

- Maintaining accessibility to relevant patient, provider, and health system data;
- Facilitating and coordinating access to these data for research conducted by Network-affiliated and non-affiliated investigators using approaches and solutions that optimize the use of the Network and are conducive to collaborative efforts;
- Maintaining high levels of expertise and competency in scientific areas relevant to the Network, US healthcare system stakeholders, and federal, state, and other key stakeholders;
- Facilitating interactions and research collaborations among (non-Network affiliated) mental health researchers who might benefit from these data;
- Increasing participation of Network-affiliated and non-affiliated investigators in independently funded research, including efforts to increase the number, scope, and scientific impact of research projects conducted by external investigators in collaboration with the Network;
- Building from established relationships with relevant constituent groups (e.g., patients, providers, administrators, payors, relevant federal and state agencies) to inform research questions, and attending to front-end infrastructure to secure stakeholder commitment to adopt, implement and sustain successful practices and products developed within this Network;
- Developing and testing strategies (using implementation science) to encourage adoption, quality, scale-up, and sustainability of new innovations and existing best practices;
- Developing and maintaining capacity to rapidly respond to and address urgent questions from Network-affiliated healthcare system partners, as well as federal, state, and other key stakeholders;
- Advancing expertise in research methodology and "big data" science, with attention to implementing findings from these advances into routine practice;
- Conducting two (2) well-powered Signature Projects (described below), one of which must be a large-scale pragmatic trial to definitively answer a research question of high importance and impact and whose findings, whether positive or negative, will be used by the Network's healthcare system(s) to improve practice in an identifiable and measurable way;
- Conducting two (2) Pilot Projects (described below) of high importance to Network stakeholders that will allow Network and external investigators to develop competitive applications to support larger-scale research projects;

- Conducting clinical trials of interventions that include therapeutic (pharmacotherapies or psychosocial interventions), preventive, or services interventions;
- Ensuring that one (1) of the four (4) projects (i.e., either one of the two required Signature Projects or one of the two required Pilot Projects) is specifically designed to reduce racial, ethnic, sexual, and/or gender minority disparities in mental health status, service utilization, and/or treatment outcomes;
- Facilitating additional pilot feasibility research through a process for soliciting, reviewing, selecting, and supporting the conduct of promising pilot feasibility projects that can be completed within the project period.
- Including mid-career investigators in positions of leadership and fostering the careers of young investigators;
- Creating and demonstrating efficiencies in the Network business processes and in the Signature Projects (described below) compared to conducting studies de novo.
- Developing and utilizing simulation approaches to model the potential public health impact of implementing research informed approaches and guide decision making; and
- Harnessing perspectives from end-user stakeholders and from new and emerging fields (e.g., health information and communications technology, health systems engineering, decision science, behavioral economics) to transform clinical research and practice.

It is expected that by the end of the proposed funding period, investigators involved in the Network-sponsored research (including outside collaborators) will have collectively submitted a minimum of five (5) investigator-initiated research project applications, to include R01, R34, R21, and/or R03 applications.

This practice-based research Network for mental health will capitalize on the successes of and lessons learned from other such networks in mental health and other disease areas.

Overall Structure of the Network

To ensure efficient conduct of the activities outlined above, the proposed practice-based research network structure will be comprised of an Administrative Core and a Methods Core, as follows:

The *Administrative* Core will have three functional Units:

1) The *Organizational Unit* will coordinate the Network's administrative functions including, but not limited to, coordinating and implementing administrative functions, including interactions among Network members and providing organizational support for joint Network activities (e.g., organizing meetings, teleconferences, etc.). The Organizational Unit (with input from the other Administrative Core Units and the Methods Core) will also coordinate the evaluation of the Network's research activities, efficiencies created by the Network infrastructure, and the public health impact of the Network's activities. This formative evaluation data will be utilized to iteratively refine the Network's ongoing quality improvement activities and inform plans for future collaborative research.

2) The *Outreach and External Collaboration Unit* is expected to promote the Network as a resource to external investigators and to healthcare systems by cultivating new collaborations, facilitating access to Network resources by external investigators, and by supporting the implementation of Network findings within partnering and other health systems. Importantly, this Unit must serve a liaison function to help connect non-Network-affiliated investigators with Network investigators who would be most appropriate as potential consultants and/or collaborators. This Unit must also establish an efficient system and operating procedures for receiving, vetting, and managing requests for access to data, ideas for collaborations, and applications for research projects from the scientific community, and for supporting training experiences for junior investigators. Finally, this Unit must promote outreach to and communication with member and external health system operations, to facilitate the identification of new research topics for study and to promote the integration of findings and research-generated products into health system operations. This final function will

include dissemination of research products, including assessment/intervention approaches and materials, methodological/analytic approaches, common source programming for technology-assisted approaches, and de-identified data for integration/re-analysis.

3) *The Emerging Issues Unit* will develop a rapid and systematic capability for response to real-time inquiries to policy and practice relevant requests from Network leaders, as well as federal, state, and other stakeholders. These rapid responses will include data pulls and data analyses from Network healthcare systems. This capacity will include a transparent process to vet and prioritize requests, clarify the key question(s) being asked, determine requirements needed to fulfill the request, and develop the format and timeline for a response.

The Emerging Issues Unit will provide a rapid evidence brief that is responsive to the stakeholder inquiry. The application should include the capacity for vetting and prioritizing research topics, consistent with the following criteria:

- Topic nominated by system-level leadership: the proposed rapid response will be incorporated into health system decision-making and is likely to make a significant impact (e.g., clinical guidelines, formulary guidance, resource allocation, or research agenda development).
- Significant issue for Network leadership or key federal or state stakeholders: the topic represents important uncertainty for decision makers (e.g., benefits/harms, variation in care, new emerging technology, or controversy) and will help resolve health care dilemmas.
- Not duplicative: the topic is not already covered by an available or soon-to-be available high-quality review by VA, AHRQ, or other organization.
- Feasible: data to inform the review should be available within the Network's data infrastructure and the published literature.
- Engaged operational partner: nominator of the proposed review has been responsive and engaged during the topic development phase and has provided timely input regarding the proposed scope.

The Methods Core will have two functional Units:

1) *The Informatics Unit* comprises the Network resource function. This Unit should be organized to support the Network informatics infrastructure, including a data warehouse, and to develop and implement improvements in data collection methods and capacity, informatics tools, etc. The Informatics Unit should coordinate informatics-related efforts at individual Network member sites as well as interact with other Units and Projects (see below) to support their functions.

2) The *Scientific Analysis Unit* should be organized to generate new methodology and analytic/computational approaches and to apply state-of-the-art approaches from the fields of big data science, health services research, and implementation science. The Unit should facilitate the development and implementation of the Network's Signature and Pilot Projects, and the Network-affiliated research, in general.

Overall Scope of Research Activities

Signature Projects (2)

The Signature Projects should address a significant problem in the prevention, treatment, management, and/or the delivery of services to people with mental disorders served by the health systems affiliated with the Network.

Signature Projects might involve effectiveness research aimed at refining and optimizing preventive and therapeutic interventions; effectiveness research testing services interventions that target patient-, provider-, or systems-level factors in order to improve service use, care delivery, and/or outcomes; or mental health services research that is consistent with NIMH's Strategic Plan, but is not immediately focused on development and testing of services interventions, including studies to identify and elucidate mutable factors

that impact access, utilization, quality, financing, outcomes such as disparities in outcomes, or scalability of mental health services.

At least one (1) of the two (2) Signature Projects must be a clinical trial. The projects should align closely with NIMH Strategic Research Priorities, and the topic should be demonstrated to be of such value to the affiliated healthcare system(s), such that, a priori, there is a well-developed plan for how definitive findings (whether they are positive or negative) will inform practice. For example, if the findings are positive, how will the intervention be adopted, sustained, and/or scaled once the project period ends? Conversely, what practices will be changed or de-implemented should findings be negative? Projects should be designed such that whether findings are positive or negative, the findings will also inform future research directions (e.g., intervention optimization, empirically informed adaptations for refractory groups, refinements to facilitate implementation).

To be responsive, any projects that involve a clinical trial must follow the NIMH experimental therapeutics approach and applicants are strongly encouraged to review related information about this approach (http://www.nimh.nih.gov/about/director/2012/experimental-medicine.shtml and https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-17-608.html). Consistent with the NIMH experimental therapeutics approach, tests of intervention effectiveness or service delivery approaches should explicitly address whether the intervention engages the proximal target(s)/mechanism(s) presumed to underlie the intervention effects (the mechanism that accounts for changes in clinical/functional outcomes, changes in provider behavior, etc.) and explicitly examine whether intervention-induced changes in the presumed targets are associated with clinical benefit. In this manner, the results of the effectiveness trial will advance knowledge regarding therapeutic change mechanisms and inform decisions about whether further testing or implementation is warranted (see NIMH web page on Clinical Trials).

Signature Projects that involve a pragmatic clinical trial should be designed as a hybrid effectiveness-implementation clinical trial Type I, II, or III, depending on the level of pre-existing effectiveness evidence and implementation readiness. A comparison group (or groups) should be chosen so that findings will be interpretable in terms of public health impact, clinical significance, and/or readiness for intervention implementation within the Network and in the general community practice setting.

One of the two Signature Projects *or* one of the two Pilot Projects (described below) should be designed to reduce disparities in mental health status, services utilization and/or treatment outcomes.

The Scope of research for Signature Projects should be as follows:

- The research question(s) should be of major importance to people with mental disorders, and the interventions/approaches that are proposed for testing should have the potential to result in substantial functional and/or systemic improvements.
- The projects should exploit efficiencies made available by the practice-based research Network (e.g., potential trial participants can be identified and enrolled via EHR; primary endpoint events can be easily and objectively operationalized using routinely collected data (e.g., hospitalization, emergency department visits)). As such, there should be dramatic and demonstrable efficiencies created, which will be reported in the evaluation coordinated by the Administrative Core, compared to if the study was conducted de novo, without leveraging Network infrastructure.
- The projects should be adequately powered to definitively answer primary research questions and detect strong signals (even if not definitive) related to treatment optimization for a variety of selected subpopulations (e.g., populations at risk for suicide, of different ages; of different racial-ethnic backgrounds; with different health literacy levels; with medical, mental health, or substance use comorbidities; and/or with expected challenges related to engagement, adherence and continuity of care).

Project designs should maximize external validity of the study by testing the generalizability of findings across distinct health care settings and diverse staff and patient populations, with explicit a priori hypotheses about disparity populations and disparity settings.

For Projects that involve Clinical Trials:

- The clinical trial should test and compare interventions (which can involve service delivery approaches, therapeutic or preventive interventions (e.g., pharmacotherapies, psychosocial interventions), or policy or organizational changes) that apply broadly to patient populations and are suitable for use in multiple health systems, with the broad goal of determining whether the intervention improves health outcomes and adds value to the use of the nation's health care resources.
- The intervention(s) should be scalable, such that they could be implemented with fidelity by clinical providers or other staff typically found in the health care setting (not just those with exceptional levels of training or competence) or could be self-administered through computer-based technology with appropriate assessments of quality and utilization.
- As appropriate, project designs will incorporate rigorous and robust comparison conditions, with trial participants prospectively assigned to study conditions within the health care systems.
- The clinical trial must adhere to NIMH's experimental therapeutics paradigm. The clinical trial will be considered especially innovative if measurements of targets (i.e., mechanisms) can occur in an automated manner or with minimal burden to research participants.

Pilot Projects (2)

The two (2) Pilot Projects should propose innovative approaches consistent with the goals of this current announcement and the NIMH Strategic Research Priorities. The Pilots should seek to optimize and improve care for a diverse population of patients within defined healthcare systems of the Network; develop and/or test new IT platforms, risk algorithms, decision support systems, and preventive, therapeutic (to include pharmacotherapies), or services interventions; create efficiencies in all aspects of the conduct of research, dissemination of findings, and produce study results that can directly inform practice change; reduce health disparities by engaging intervention targets; and/or improve methodologies in systems research, and/or seek strategies to continuously improve the accessibility, quality, continuity, equity and value of services delivered within the Network. The general scope of research and the questions addressed by these Pilots should be modeled on the NIMH R34 mechanism for clinical trials (https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-18-706.html) and/or non-trial services research (https://grants.nih.gov/grants/guide/pa-files/PAR-18-267.html).

At least one Pilot must be a clinical trial. For any Pilot that is a clinical trial, the NIMH experimental therapeutics paradigm must be followed and research questions should be similar in type and scope to those supported by the NIMH R34 mechanism.

One of the two Pilot Projects *or* one of the two Signature Projects (described above) should be designed to reduce disparities in mental health status, services utilization and/or treatment outcomes.

Additional pilot feasibility research: In addition to the Signature and Pilot Projects, the Network is intended to facilitate emerging opportunities for additional pilot feasibility research through a process for soliciting, reviewing, selecting, and supporting the conduct of promising pilot feasibility projects of 1-2 years duration, similar in scope to an NIH R03 grant mechanism, that can be completed within the project period. Accordingly, the scope of science should include such pilot feasibility projects that can be proposed by new or established investigators to address innovative, interdisciplinary research that is consistent the Network's focus, in order to position the investigator(s) for subsequent research that aligns with the Network's program of research. Pilot feasibility projects should involve Network-affiliated as well as non-affiliated investigators, wherever possible.

It is expected that by leveraging the infrastructure of the Network and the healthcare systems, dramatic and demonstrable efficiencies will be created compared to similar studies conducted de novo.

Markers of Successful Practice-Based Research Network

A successful Network will accomplish the following tasks within the period of the award:

- Build and extend the capacity of the Network to conduct prospective trials via the successful completion of pilot studies of interventions not yet studied in such networks.
- Enhance the quality, type, and analysis of data within the EHR (to include biologic and/or genetic data) which will ultimately improve the delivery of mental health services in routine practice.
- Successfully complete: two (2) Signature Projects of high impact on the mental health and functioning of a large population, where positive or negative findings will lead to measurable improvements in practice across the Network sites; two (2) Pilot Projects; and, additional pilot feasibility studies that position the investigator(s) for subsequent research that aligns with the Network's program of research.
- Develop and submit at least five (5) investigator-initiated applications for research that will leverage Network infrastructure. Involving outside investigators in these applications is strongly encouraged.
- Expand tools to create efficiency in the rapid conduct and replication of effectiveness, services, and implementation research studies on the Network.
- Use business models which foster data sharing and collaboration with non-Network researchers and strengthen the self-sustainability of the Network.
- Benchmark the costs and document efficiencies associated with conducting a range of studies on the Network, as compared to traditional approaches to launching and conducting research.
- Successfully disseminate trial results to health system partners resulting in significant change of policy and/or practice as a direct result of study findings.
- Expeditiously disseminate primary and secondary outcomes in high-quality journals consistent with NOT-OD-16-149 and NOT-OD-18-011.
- Disseminate Network generated research products, including methodological/analytic approaches, assessment and intervention approaches and materials, sharable programing (e.g., for technology-based applications), and de-identified data.
- Reduce disparities in mental health status, service utilization, and treatment outcomes in the health of people with mental illness, including disparities in medical comorbidities among adults with serious mental illness and youth with serious emotional disturbance.
- Harmonize data systems with commercial and/or public healthcare systems that are providing services to diverse populations for the purposes of research and continuous quality improvement associated with a learning mental health healthcare system.
- Include individuals who are insured through commercial plans, Medicaid, and who are uninsured but are treated in commercial and/or public healthcare systems. Networks that include public healthcare systems are strongly encouraged."

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

Application Types Allowed

New

The OER Glossary and the SF424 (R&R) Application Guide provide details on these application types.

Clinical Trial?

Required: Only accepting applications that propose clinical trial(s)

Need help determining whether you are doing a clinical trial?

Funds Available and Anticipated Number of Awards

NIMH intends to commit $2.6M in FY 2019 to fund 2 awards.

Award Budget

Direct Costs are limited to no more than $1.3M in any year.

Award Project Period

The maximum project period is 5 years.

NIH grants policies as described in the *NIH Grants Policy Statement* will apply to the applications submitted and awards made from this FOA.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations

Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are not** eligible to apply.
Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement*, **are** allowed.

Required Registrations

Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- eRA Commons - Applicants must have an active DUNS number to register in eRA Commons. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program

Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

2. Cost Sharing

This FOA does not require cost sharing as defined in the *NIH Grants Policy Statement*.

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST or an institutional system-to-system solution. A button to apply using ASSIST is available in Part 1 of this FOA. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the Multi-Project (M) Instructions in the SF424 (R&R) Application Guide, except where instructed in this funding opportunity announcement to do otherwise and where instructions in the Application Guide are directly related to the Grants.gov downloadable forms currently used with most NIH opportunities. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Letter of Intent

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

By the date listed in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

The letter of intent should be sent to:

Email: nimhpeerreview@mail.nih.gov

Page Limitations

Available Component Types	Research Strategy/Program Plan Page Limits
Overall	12
Admin Core (use for Administrative Core)	6
Core (use for Methods Core)	6
Project (use for each Signature Project and each Pilot Project)	6

Additional page limits described in the SF424 Application Guide and the Table of Page Limits must be followed.

Instructions for the Submission of Multi-Component Applications

The following section supplements the instructions found in the SF424 (R&R) Application Guide, and should be used for preparing a multi-component application.

The application should consist of the following components:

- Overall: required; maximum one
- Administrative Core (including Units): required; maximum one
- Methods Cores (including Units): required; minimum two; maximum two
- Signature Projects (clinical trial required): required; minimum two; maximum two
- Pilot Project (clinical trial optional): required; minimum two; maximum two

Overall Component

When preparing your application, use Component Type ‘Overall’.

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions, as noted.

SF424 (R&R) Cover (Overall)

Complete entire form.

PHS 398 Cover Page Supplement (Overall)

Note: Human Embryonic Stem Cell lines from other components should be repeated in cell line table in Overall component.

Research & Related Other Project Information (Overall)

Follow standard instructions.

Project/Performance Site Location(s) (Overall)

Enter primary site only.

A summary of Project/Performance Sites in the Overall section of the assembled application image in eRA Commons compiled from data collected in the other components will be generated upon submission.

Research & Related Senior/Key Person Profile (Overall)

Include only the Project Director/Principal Investigator (PD/PI) and any multi-PDs/PIs (if applicable to this FOA) for the entire application.

It is expected that the Network (PD(s)/PI(s)) will have a demonstrated capability to organize, administer, and direct the Network. The director(s) must demonstrate leadership in the area of science proposed and have a strong record of high impact scientific achievements.

A summary of Senior/Key Persons followed by their Biographical Sketches in the Overall section of the assembled application image in eRA Commons will be generated upon submission.

Budget (Overall)

The only budget information included in the Overall component is the Estimated Project Funding section of the SF424 (R&R) Cover.

A budget summary in the Overall section of the assembled application image in eRA Commons compiled from detailed budget data collected in the other components will be generated upon submission.

PHS 398 Research Plan (Overall)

Specific Aims: Provide a concise description of the overall Network focus and aims. Outline how the Administrative Core, Methods Core, Signature Projects, Pilot Projects, and other Network-generated research will contribute to attaining the Network's objectives.

Research Strategy: The Research Strategy should begin with an overview of the Network that describes the healthcare systems to be part of the Network, the target populations for whom existing interventions or services do not adequately address mental health needs, the services, therapeutic or preventive interventions or implementation strategies to be studied and optimized, the service settings intended to implement optimized interventions and/or services, the integration of the Network components, the practice-based research priority setting that is central to a learning healthcare system, and why these components are essential for accomplishing the goals of the overall Network. The overview should be targeted to a broad audience and be concise.

The Overview section should include:

1. Goals, relevant background, significance and a description of the impact of the proposed research in relation to the state-of-the-art of the field. This section should also include an explanation of how the proposed work is both innovative and potentially impactful for advancing clinical practice and clinical outcomes with members of the target population and the Network stakeholders. The focus of the Network should be justified in terms of the potential impact of research, vis-à-vis the ability to accomplish the following:

Efficiently and rapidly identify, recruit and enroll large and diverse patient populations into clinical trials (including but not limited to pharmacotherapy, pragmatic, comparative effectiveness and/or hybrid effectiveness-implementation trials) that align with NIMH Strategic Research Priorities;

- Harmonize electronic health record (EHR) data across multiple integrated systems for research use, to include the potential for EHR phenotyping;
- Build capacity for the collection, storage, and analysis of biologic and/or genetic material;
- Develop, deploy, and test large-scale mental health information technology (IT) interventions, workflows, and decision support systems; and
- Generate data that will fuel the transformation of mental health care service delivery.

In addition, the Overview section should describe how the Network will:

- Provide rapid responses to address urgent questions from federal, state, and other key stakeholders (e.g., questions related to the clinical epidemiology of mental disorders and/or questions related to the uptake of and outcomes associated with mental health interventions and best practices);
- Maintain high levels of expertise and competency in scientific areas relevant to the Network, US healthcare system stakeholders, and federal, state, and other key stakeholders;
- Study low base-rate events (e.g., suicide, autism spectrum disorders, first episode psychosis, or other mental health conditions which are difficult to identify, predict, treat, or manage) by using and advancing innovative methodologies (e.g., predictive analytics) or resources which capitalize on the Network's unique sophistication in health information technology, overall size, or research efficiencies;
- Reduce disparities in mental health status, service utilization, and treatment outcomes in the health of people with mental illness, including disparities in medical comorbidities among adults with serious mental illness and youth with serious emotional disturbance;
- Facilitate and coordinate access to Network data for research conducted by Network-affiliated and non-affiliated investigators using approaches and solutions that optimize the use of the Network and are conducive to collaborative efforts;
- Increase participation of Network-affiliated and non-affiliated investigators in independently funded research, including efforts to increase the number, scope, and scientific impact of research projects conducted by external investigators in collaboration with the Network;
- Build from established relationships with relevant constituent groups (e.g., patients, providers, administrators, payors, relevant federal and state agencies) to inform research questions, and to secure stakeholder commitment to adopt, implement and sustain successful practices and products developed within this Network;
- Harness perspectives from new and emerging fields (e.g., health information and communications technology, health systems engineering, decision science, behavioral economics) to transform clinical research and practice;
- Demonstrate cost savings business processes among the Network members (to include public and/or commercial systems), relative to establishing these business processes de novo;
- Demonstrate and document substantial efficiencies (time and costs) in conducting the Pilot and Signature projects by leveraging the Network infrastructure, as compared to similar studies conducted de novo;
- Advance expertise in research methodology and "big data" science, with attention to implementing findings from these advances into routine practice;
- Conduct two (2) Signature Projects (one of which must be a large-scale pragmatic trial) to definitively answer research questions of high importance and impact and whose findings, whether positive or negative, will be used by the Network's healthcare system(s) to improve practice in an identifiable and measurable way;
- Conduct two (2) Pilot Projects (one of which must be a clinical trial) that will allow Network and external investigators to conduct research on emerging high priority topics that will lead to competitive

applications for funding large-scale research projects;
- Include and conduct research in one or more integrated (public and/or commercial) healthcare settings serving people with severe mental illness, and including settings already offering evidence-based integrated care (e.g., collaborative care and/or coordinated specialty care);
- Include representative sample sizes of people who are covered by commercial insurance, covered by Medicaid, and who are uninsured but who are treated through the Network's commercial and/or public healthcare systems; and,
- Include mid-career investigators in positions of leadership and foster opportunities for early-career investigators.

2. The Overview section should briefly but specifically address the efficiencies created by leveraging existing infrastructure, and how any newly developed infrastructure will measure proposed efficiencies. A description of the business model should be provided along with demonstrable efficiencies in cost sharing among Network sites. This section should also describe how findings will have public health impact within Network sites but also describe simulation approaches to model the potential public health and decision making beyond the Network sites. Essentially, this section summarizes how the Network's goals cannot be achieved by a cluster of individual research project grants (e.g., R01s) and justifies why the Network as a whole is greater than the sum of its parts.

The Research Strategy should also include:

1. Preliminary Data: This section should include evidence supporting the feasibility of conducting the proposed activities and preliminary findings. This section should also present very clear evidence that the research team has been/will be able to work together effectively to accomplish the research proposed in the projects.

2. Network Approach: This section should describe the working scientific and logistical design, as well as the resource support necessary to implement the research. Because multiple institutional sites are inherently involved, a detailed description of the cooperative administrative arrangements should be included. (Documentation of these arrangements should be included in the Letters of Support section.) Cost sharing or institutional support, if any, should be described in this section. Attention should be paid to areas of efficiency created because of shared and harmonized resources across healthcare systems.

Letters of Support:

Include letters of support relevant to the overall Network here. Letters detailing contributions to individual components (e.g., Cores, Signature or Pilot Projects) are to be placed in their respective individual components. It is strongly encouraged that letters of support from stakeholders (with at least partial decision authority to implement best practices) detail how seminal findings will be used to inform practice. For example, how will positive findings be used to implement best practices? Conversely, how will negative findings change how current services are delivered?

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. To advance the goal of facilitating research through widespread data sharing among researchers, investigators funded under this FOA are expected to share those data via the NIMH Data Archive (NDA) (https://ndar.nih.gov/; see NOT-MH-09-005, NOT-MH-14-015 and NOT-MH-15-012). Established by the NIH, the NDA is a secure informatics platform for scientific collaboration and data-sharing that enables the effective communication of detailed research results, tools, and supporting documentation.

Investigators funded under this FOA are expected to use NDA technologies to submit data in accordance with the NDA Data Sharing Terms and Conditions, incorporated by reference, which can be found at https://ndar.nih.gov/contribute_data_sharing_regimen.html. The resource sharing plan should be formulated in accordance with the NDA Data Sharing Terms and Conditions.

Appendix:

Only limited items are allowed in the Appendix. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide; any instructions provided here are in addition to the SF424 (R&R) Application Guide instructions.

PHS Human Subjects and Clinical Trials Information (Overall)

When involving NIH-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, there must be at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or a **Delayed Onset Study** record within the application. The study record(s) must be included in the component(s) where the work is being done, unless the same study spans multiple components. To avoid the creation of duplicate study records, a single study record with sufficient information for all involved components must be included in the Overall component when the same study spans multiple components.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed

Delayed Onset Study

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).

All instructions in the SF424 (R&R) Application Guide must be followed

PHS Assignment Request Form (Overall)

All instructions in the SF424 (R&R) Application Guide must be followed.

Administrative Core

When preparing your application, use Component Type ‘Administrative Core.’

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions, as noted.

SF424 (R&R) Cover (Administrative Core)

Complete only the following fields:

- Applicant Information
- Type of Applicant (optional)
- Descriptive Title of Applicant’s Project
- Proposed Project Start/Ending Dates

PHS 398 Cover Page Supplement (Administrative Core)

Enter Human Embryonic Stem Cells in each relevant component.

Research & Related Other Project Information (Administrative Core)

Human Subjects: Answer only the 'Are Human Subjects Involved?' and 'Is the Project Exempt from Federal regulations?' questions.

Vertebrate Animals: Answer only the 'Are Vertebrate Animals Used?' question.

Project Narrative: Do not complete. Note: ASSIST screens will show an asterisk for this attachment indicating it is required. However, eRA systems only enforce this requirement in the Overall component and applications will not receive an error if omitted in other components.

Project /Performance Site Location(s) (Administrative Core)

List all performance sites that apply to the specific component.

Note: The Project Performance Site form allows up to 300 sites, prior to using additional attachment for additional entries.

Research & Related Senior/Key Person Profile (Administrative Core)

- In the Project Director/Principal Investigator section of the form, use Project Role of 'Other' with Category of 'Administrative Core Lead' and provide a valid eRA Commons ID in the Credential field.
- In the additional Senior/Key Profiles section, list Senior/Key persons that are working in the component.
- Include a single Biographical Sketch for each Senior/Key person listed in the application regardless of the number of components in which they participate. When a Senior/Key person is listed in multiple components, the Biographical Sketch can be included in any one component.
- If more than 100 Senior/Key persons are included in a component, the Additional Senior Key Person attachments should be used.

Budget (Administrative Core)

Budget forms appropriate for the specific component will be included in the application package.

The Network PD/PI must commit a minimum effort of 3 person months per year overall to the Network and be a leader of one of the signature projects and of the Administrative Core. The three (3) person months should be a total of the Network Director's efforts on his/her project(s) and Core(s). The 3-person month requirement also applies to any individual listed as a PD/PI in a multiple PD/PI Network.

The Leadership of the Administrative Core must commit a cumulative minimum effort of one (1) person month per year to the Administrative Core. Multiple leaders are allowed for the Administrative Core. If there are multiple leaders for this Core, the combined effort of the identified Administrative Core Leaders must total at least one (1) person month per year.

The Administrative Core budget should include costs for:

- Network PD/PI salaries: Any Network PD/PI must commit a minimum effort of 3 person months per year serving as the overall Network PD/PI as well as the leader of one research project and the Administrative Core.
- Annual support for soliciting, reviewing, selecting, and executing two (2) or more pilot feasibility projects of 1-2 years duration, proposed by new or established investigators, that will inform the development of larger, peer-reviewed research applications that can compete successfully for NIH or other funding.
- Data and resource sharing (e.g., personnel, assessment and intervention protocols, software and/or programming for technology-assisted approaches, data analytic strategies, etc.), as appropriate. For data sharing, the NIMH Data Archive (NDA) website provides a customizable Excel worksheet that includes tasks and hours for the Program Director/Principal Investigator and Data Manager to budget for data sharing (https://data-archive.nimh.nih.gov/s/sharedcontent/plan/plan.html).
- Investigator and advisory board travel.
- Website and Training.

Note: The R&R Budget form included in many of the component types allows for up to 100 Senior/Key

Persons in section A and 100 Equipment Items in section C prior to using attachments for additional entries. All other SF424 (R&R) instructions apply.

PHS 398 Research Plan (Administrative Core)

Specific Aims: Provide a concise description of the Administrative Core including the Organizational Unit, Outreach and Engagement Unit, and Emerging Issues Unit.

Research Strategy:

In this section, highlight features of the Administrative Core that will enhance the collaborative effort, including optimizing communication, decision-making and sharing between the Research Projects and the Methods Core.

Describe how each Research Project and Methods Core (as applicable) will draw upon the Administrative Core and how it, in turn, will respond to Research Project or Methods Core needs. The description of the Administrative Core should clearly indicate the facilities, resources, services and professional skills that the Core will provide. Moreover, information must be provided about how the collective operation of the Core will be affected in a coherent manner.

For each year of the award, the Administrative Core should include provisions for two (2) or more pilot feasibility studies. These feasibility studies are different from the Pilot Project (described elsewhere). They should be of 1-2 years duration that can be proposed by new or established investigators, including projects that are proposed by or involve trainees preparing for independent research careers. These feasibility projects should be similar in purpose and scope to small research project grants (R03), and address innovative, interdisciplinary research consistent with the Network's focus. Feasibility studies should serve as a mechanism for conducting nimble proof-of-concept studies (e.g., to rapidly refine/optimize intervention and service delivery approaches) that will position the investigator(s) for subsequent research that aligns with the Network's scientific goals. The application should detail a systematic approach for soliciting, reviewing, selecting, and monitoring the progress of the feasibility studies. All feasibility projects must comply with applicable NIH policies and the evidence that proposed plans for protection of human subjects; inclusion of women, minorities, and children; and assurance of animal welfare must be submitted to the NIMH Program Official prior to study initiation.

Describe the Structure and functional Units of the Administrative Core, as follows:

1) Organizational Unit.

Describe how the Organizational Unit will coordinate the Network’s administrative functions, including, but not limited to, mediating and coordinating administrative interactions among Network members and providing organizational support for joint Network activities (e.g., organizing meetings, teleconferences, etc.).

Describe how the Organizational Unit (with input from the other Administrative Core Units and the Methods Core) will coordinate the evaluation of the Network’s research activities, efficiencies created by the Network infrastructure, and public health impact of the Network’s activities. Describe how the evaluation plan will be used to iteratively refine the Network's ongoing activities and inform plans for future collaborative research. And, describe how this evaluation will provide data to demonstrate the significant efficiencies created in the conduct of research, compared to conducting studies *de novo*. Describe plans for evaluation of the Network's:

- *Research progress, impact, and efficiencies* (e.g., progress on the research projects and other studies that may be proposed during the project period as well as success at disseminating research results; developing and disseminating technological, methodological, and analytic innovations; cost and

other resource-related efficiencies created through use of the Network; identifying, integrating, and mentoring junior investigators; and, generating new interdisciplinary collaborations and new R01 research projects and grant applications).

- *Public health benefit* (e.g., modeling the incremental benefit and potential public health impact of optimized interventions and service delivery approaches; quantifying the uptake of Network-generated prevention, treatment, and service delivery approaches; and, engaging new end-users and forming academic-stakeholder partnerships to implement research-supported strategies in clinical and community practice settings).

2) Outreach and External Collaboration Unit.

Describe how the Outreach and External Collaboration Unit will work to increase the usage of the Network by external investigators, as well as to support the implementation of Network findings within the partnering health systems (whether findings are positive or negative). Discuss how the Unit will promote the Network as a resource and facilitate access to external, non-Network-affiliated investigators. Importantly, this Unit must provide a liaison function to help connect non-Network-affiliated investigators with those Network investigators who would be most appropriate as experts and/or potential collaborators.

Describe how this Unit will establish an efficient system and operating procedures for:

- Soliciting and vetting requests for access to data, ideas for collaborations, and applications for research projects from the scientific community and for processing inquiries/requests (i.e., assignment to relevant Network components, leaders, or researchers);
- Establishing and implementing procedures for training and supporting trainees and early-career investigators interested in conducting research within Network sites;
- Establishing partnerships with key mental health stakeholders – e.g., service users, family members, clinicians, payers, system leaders – who will help identify unmet mental health needs within the target population, develop and refine strategies for optimizing interventions and services, inform research topics, maximize the external validity of Network research findings and ensure findings (positive or negative) inform practice within Network sites;
- Developing and implementing procedures to improve the connectivity of Network findings to member and external health system operations, both in identifying new research topics for study and to foster population impact of scientific findings. This final function will include dissemination of research products like assessment/intervention approaches and materials, methodological/analytic approaches, common source programming for technology-assisted approaches, and de-identified data for integration/re-analysis. It must also include development of a website and other dissemination strategies; and,
- Measuring progress and success at achieving the goals of this Unit in a demonstrable way.

3) Emerging Issues Unit.

Describe the rapid and systematic capability for response to real-time inquiries to policy and practice relevant requests from Network and address urgent questions from the Network-affiliated healthcare system partners, as well as federal, state, and other key stakeholders. These rapid responses will include data pulls and data analysis from Network healthcare systems and will also require some synthesis of available literature. Operationalize the process that will be used to vet and prioritize requests, clarify the key question(s) being asked, determine resources required to fulfill the request, and develop the format and timeline for a response. Describe how requests will be prioritized and clarified (to minimize overlap with other evidence syntheses), and how responses will be disseminated.

Additional information required in the Administrative Core Research Strategy:

Timeline, Milestones, and Steering Committee: A graphic Timeline and a descriptive Milestones section must be included in the Research Strategy section for the Administrative Core. Milestones should be identified along the timeline. Milestones should be well described, quantifiable, and scientifically justified benchmarks at critical junctures as well as annual indicators of progress. This section should also include alternative strategies should any component efforts fail to perform as expected.

Steering Committee: Describe the process for establishing and convening a Steering Committee that will govern the Network. Describe the composition, roles/responsibilities, and schedule for convening regular and ad hoc steering committee meetings, including at least one in-person meeting at NIMH annually.

External Advisory Committee: Describe the composition, roles/responsibilities, and schedule for soliciting input from a standing, External Advisory Committee that will provide appropriate and objective advice and evaluation regularly to the Administrative Core Director. Describe the process for responding to recommendations from the Committee. Potential advisory committee members should not be contacted or recruited prior to review of the application and should not be proposed as part of the application.

Letters of Support: Include letters of support relevant to the Administrative Core here.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

To advance research through widespread data sharing among researchers, investigators funded under this FOA are expected to share human subjects data via the NIMH Data Archive (NDA) (http://data-archive.nimh.nih.gov/; see NOT-MH-09-005, NOT-MH-14-015 and NOT-MH-15-012). Established by the NIMH, and supported by other NIH Institutes, the NDA is a secure informatics platform for scientific collaboration and data-sharing that enables the effective communication of detailed research data, results, tools, and supporting documentation. All human subjects data collected and/or derived for a project funded under this FOA are expected to be submitted to the NDA. Data resulting from existing samples, cells, or sequences previously collected are also expected to be submitted to the NDA. Products such as tools, pipelines, and algorithms that will not result in a commercial product are expected to be shared via the NDA Study.

Investigators funded under this FOA are expected to use NDA technologies to submit data in accordance with the NDA Data Sharing Terms and Conditions, incorporated by reference, which can be found at https://ndar.nih.gov/contribute_data_sharing_regimen.html. A resource sharing plan, formulated in accordance with these NDA Data Sharing Terms and Conditions, should be included in the grant application. The NDA links data across research projects through its Global Unique Identifier (GUID) and Data Dictionary technologies. Investigators funded under this FOA are expected to use these technologies to submit and share their research data and results at the appropriate times. To accomplish this objective, it will be important to formulate a) an enrollment and consent strategy that will obtain the information necessary to generate a GUID for each research participant; and, b) a budget strategy that will cover the costs of data sharing. The NDA Cost Estimation Tool is a customizable Excel worksheet that can be used to calculate an estimate of the resources needed to submit and share data with the NDA. This resource estimate should be submitted as part of the application budget (http://ndar.nih.gov/contribute_cost_estimation.html).

Appendix:

Only limited items are allowed in the Appendix.Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide; any instructions provided here are in addition to the SF424 (R&R)

Application Guide instructions.

PHS Human Subjects and Clinical Trials Information (Administrative Core)

When involving NIH-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or a **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed.

Delayed Onset Study

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

Methods Core

When preparing your application in ASSIST, use Component Type 'Methods Core.'

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions, as noted.

SF424 (R&R) Cover (Methods Core)

Complete only the following fields:

- Applicant Information
- Type of Applicant (optional)
- Descriptive Title of Applicant's Project
- Proposed Project Start/Ending Dates

PHS 398 Cover Page Supplement (Methods Core)

Enter Human Embryonic Stem Cells in each relevant component.

Research & Related Other Project Information(Methods Core)

Human Subjects: Answer only the 'Are Human Subjects Involved?' and 'Is the Project Exempt from Federal regulations?' questions.

Vertebrate Animals: Answer only the 'Are Vertebrate Animals Used?' question.

Project Narrative: Do not complete. Note: ASSIST screens will show an asterisk for this attachment indicating it is required. However, eRA systems only enforce this requirement in the Overall component and applications will not receive an error if omitted in other components.

Project /Performance Site Location(s) (Methods Core)

List all performance sites that apply to the specific component.

Note: The Project Performance Site form allows up to 300 sites, prior to using additional attachment for additional entries.

Research & Related Senior/Key Person Profile (Methods Core)

- In the Project Director/Principal Investigator section of the form, use Project Role of 'Other' with Category of 'Methods Core Lead' and provide a valid eRA Commons ID in the Credential field.
- In the additional Senior/Key Profiles section, list Senior/Key persons that are working in the component.
- Include a single Biographical Sketch for each Senior/Key person listed in the application regardless of the number of components in which they participate. When a Senior/Key person is listed in multiple components, the Biographical Sketch can be included in any one component.
- If more than 100 Senior/Key persons are included in a component, the Additional Senior Key Person attachments should be used.

Budget (Methods Core)

Budget forms appropriate for the specific component will be included in the application package.

Note: The R&R Budget form included in many of the component types allows for up to 100 Senior/Key Persons in section A and 100 Equipment Items in section C prior to using attachments for additional entries. All other SF424 (R&R) instructions apply.

The Leadership of the Methods Core must commit a cumulative minimum effort of 3 person months per year to the Methods Core. Multiple leaders are allowed for the Methods Core. If there are multiple leaders for this Core, the combined effort of the identified Methods Core Leaders must total at least 3 person months per year.

PHS 398 Research Plan (Methods Core)

Specific Aims: Provide a concise description of the goals of the Methods Core including the Informatics and Scientific Analysis Units. Explain how the Methods Core will contribute to the Administrative Core, and the individual research projects, and to attaining the Network's objectives.

Research Strategy: Organize the Methods Core's descriptions along the two functional Units: 1) Informatics Unit and 2) Scientific Analysis Unit.

1) Describe how the Informatics Unit will be the key component for the Network resource function. Describe how the Unit will support Network informatics infrastructure, notably including a data warehouse, and how the Unit will facilitate improvements in data collection and capacity, informatics tools, etc. Address how the Unit will coordinate informatics-related efforts at individual Network member sites as well as interact with other Units, Projects, and the NIMH Data Archive (NDA) into which data resulting from the Signature and Pilot Projects will be deposited according to the NDA Terms and Conditions.

2) Describe how the Scientific Analysis Unit will be organized to generate new methodology and analytic/computational approaches and to apply state-of-the-art approaches and principles relevant to big data science, health services research, and implementation science. Discuss how the Unit will focus on the development, identification, and testing of putative change mechanisms that can drive improvements in health systems at this scale and with diverse populations and settings.

In general, describe how the Methods Core will function as an incubator for innovative approaches to optimizing and enhancing the effectiveness, adoption, scalability, and sustainability of interventions/service delivery models for target populations. Describe how the Methods Core will facilitate novel and convergent solutions to intractable mental health problems by integrating input from clinical and services researchers, insights from key mental health stakeholders and decision makers, and contributions from diverse experts in complementary fields, as relevant (e.g., behavioral and social science, health information and communications technology, health system engineering, decision science, bioinformatics, and/or data modeling). Describe how the Methods Core will stimulate additional research collaborations, identify future research directions, and ultimately boost the clinical impact, delivery, reach, and continuous improvement of mental health interventions. Detail how the Core's

collective expertise will function to facilitate each of the following:

Development of Research Projects: Detail how the Methods Core will facilitate the development and design of the Network's two Signature Projects, two Pilot Projects, and additional pilot feasibility studies (described in the Administrative Core Research Strategy section). Describe how the Core will identify and apply scientific, technological, and methodological innovations and tools to facilitate the research enterprise (e.g., identify opportunities to rapidly refine/optimize intervention content and delivery; apply innovative approaches to study design, participant selection/engagement, ecologically valid assessment, and monitoring of study progress). Describe how the Core's efforts will accelerate delivery of convergent interventions and services in healthcare systems (e.g., identify and test novel applications of emerging technologies, information science, systems engineering, and other approaches that can be used to seamlessly integrate research-supported strategies into routine practice).

Operational Support to Research Projects: Describe how the Methods Core will provide expert conceptual, methodological, technical, informatics, and analytic statistical support to the Network's investigators. Describe the facilities and resources that will be available for conducting research projects of the Network, including (a) laboratories, research clinics, and/or community practice settings, (b) a Central Institutional Review Board (IRB), and (c) centralized clinical assessment and data management services. Present the plan for data collection, data quality assurance, and data management for studies presented in the Research Projects section and for additional Network-based research, together with the plans for statistical analyses. Describe the operational structures that will ensure Good Clinical Practice as well as human subject protections for the Network's clinical research.

Generate Innovative Research Methods and Chart Future Directions: Describe the Core's role in generating new research opportunities that capitalize on the Network's transdisciplinary nature and practice infrastructure. Detail the Core's role in synthesizing findings from the proposed research projects to inform future research directions. Describe strategies that will be used to monitor and incorporate emerging scientific, technological, methodological, and analytic innovations and to identify and engage new collaborators working in allied areas, such as adult learning, machine learning, artificial intelligence, bioinformatics, etc. Describe how collaborative activities among Core investigators and stakeholders will culminate in future projects and grant applications that build off the Signature, Pilot, and feasibility projects.

Dissemination of Methodological Advances and other Network-generated Resources: Describe how the Core will function as a national consultation resource beyond the Network collaborations. Detail the Core's role in facilitating the development and dissemination of research resources (e.g., new data collection/assessment approaches and analytic methods); web/mobile platforms for identifying and recruiting participants and accelerating research; data sets that can be shared for re-analysis/meta-analysis; and, other common-source materials (e.g., new methods and analytic strategies for mining and analyzing 'big data' from large-scale data collection efforts, programming for technology-assisted approaches).

Letters of Support: Include letters of support relevant to the Research Methods Core.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.

To advance research through widespread data sharing among researchers, investigators funded under this FOA are expected to share human subjects data via the NIMH Data Archive (NDA) (http://data-archive.nimh.nih.gov/; see NOT-MH-09-005, NOT-MH-14-015 and NOT-MH-15-012). Established by the NIMH, and supported by other NIH Institutes, the NDA is a secure informatics platform for scientific collaboration and data-sharing that enables the effective communication of detailed research data,

results, tools, and supporting documentation. All human subjects data collected and/or derived for a project funded under this FOA are expected to be submitted to the NDA. Data resulting from existing samples, cells, or sequences previously collected are also expected to be submitted to the NDA. Products such as tools, pipelines, and algorithms that will not result in a commercial product are expected to be shared via the NDA Study.

Investigators funded under this FOA are expected to use NDA technologies to submit data in accordance with the NDA Data Sharing Terms and Conditions, incorporated by reference, which can be found at https://ndar.nih.gov/contribute_data_sharing_regimen.html. A resource sharing plan, formulated in accordance with these NDA Data Sharing Terms and Conditions, should be included in the grant application. The NDA links data across research projects through its Global Unique Identifier (GUID) and Data Dictionary technologies. Investigators funded under this FOA are expected to use these technologies to submit and share their research data and results at the appropriate times. To accomplish this objective, it will be important to formulate a) an enrollment and consent strategy that will obtain the information necessary to generate a GUID for each research participant; and, b) a budget strategy that will cover the costs of data sharing. The NDA Cost Estimation Tool is a customizable Excel worksheet that can be used to calculate an estimate of the resources needed to submit and share data with the NDA. This resource estimate should be submitted as part of the application budget (http://ndar.nih.gov/contribute_cost_estimation.html).

Generally, Resource Sharing Plans are expected, but they are not applicable for this Component.

Appendix: Only limited items are allowed in the Appendix. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Human Subjects and Clinical Trials Information (Methods Core)

When involving NIH-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or a **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Section 3 - Protection and Monitoring Plans

3.1 Protection of Human Subjects

Applications with data collection plans that involve multiple respondent groups (e.g., clients/patients, therapists/providers, supervisors, administrators) should address provisions for human subject protections and consenting procedures for all participant groups, accordingly.

The NIMH has published updated policies and guidance for investigators regarding human research protection and clinical research data and safety monitoring (NOT-MH-15-025). The application’s Protection of Human Subjects section should reflect the policies and guidance in this notice. Plans for the protection of research subjects and data and safety monitoring will be reviewed by the NIMH for consistency with NIMH and NIH policies and federal regulations.

Delayed Onset Study

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

Signature Projects

When preparing your application in ASSIST, use Component Type 'Signature Projects.'

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions, as noted.

SF424 (R&R) Cover (Signature Projects)

Complete only the following fields:

- Applicant Information
- Type of Applicant (optional)
- Descriptive Title of Applicant's Project
- Proposed Project Start/Ending Dates

PHS 398 Cover Page Supplement (Signature Projects)

Enter Human Embryonic Stem Cells in each relevant component.

Research & Related Other Project Information (Signature Projects)

Human Subjects: Answer only the 'Are Human Subjects Involved?' and 'Is the Project Exempt from Federal regulations?' questions.

Vertebrate Animals: Answer only the 'Are Vertebrate Animals Used?' question.

Project Narrative: Do not complete. Note: ASSIST screens will show an asterisk for this attachment indicating it is required. However, eRA systems only enforce this requirement in the Overall component and applications will not receive an error if omitted in other components.

Project /Performance Site Location(s) (Signature Projects)

List all performance sites that apply to the specific component.

Note: The Project Performance Site form allows up to 300 sites, prior to using additional attachment for additional entries.

Research & Related Senior/Key Person Profile (Signature Projects)

- In the Project Director/Principal Investigator section of the form, use Project Role of 'Other' with Category of 'Project Lead' and provide a valid eRA Commons ID in the Credential field.
- In the additional Senior/Key Profiles section, list Senior/Key persons that are working in the component.
- Include a single Biographical Sketch for each Senior/Key person listed in the application regardless of the number of components in which they participate. When a Senior/Key person is listed in multiple components, the Biographical Sketch can be included in any one component.
- If more than 100 Senior/Key persons are included in a component, the Additional Senior Key Person attachments should be used.

Budget (Signature Projects)

Budget forms appropriate for the specific component will be included in the application package.

Note: The R&R Budget form included in many of the component types allows for up to 100 Senior/Key Persons in section A and 100 Equipment Items in section C prior to using attachments for additional entries. All other SF424 (R&R) instructions apply.

PHS 398 Research Plan (Signature Projects)

Specific Aims: The specific aims should provide a concise description of the aims of the individual research project. Projects should align closely to NIMH's Strategic Research Priorities.

Research Strategy: This section should provide details about how the Network resources will be used to complete the project. The research should be consistent with the goals identified earlier in detail in this funding announcement. Describe the anticipated interactions between this project and other components of the Network, including the role of the Cores in facilitating participant enrollment, conduct of study, and analysis, interpretation, and dissemination of the results.

For ease and clarity of review, use the headers, below, in organizing each individual Project.

Significance: Describe overall goals and the impact of the science proposed in the project in relation to the state-of-the-art of the field. This section should also explain the contribution of the project to the overall goals of the Network, how the project will interact with and benefit from other components of the Network and the appropriateness of the Network approach and environment.

Innovation: Describe the unique and innovative contributions that will be made by the research project. Explain how these contributions will synergize with the rest of the Network to achieve more than what could be achieved through an independent research project. Research projects should propose novel, transdisciplinary, convergent solutions to intractable mental health problems by integrating input from the diverse experts brought together in the Network.

Approach: Describe how the Signature Project is designed to study a significant problem in the prevention, treatment, management, and/or the delivery of services to people with mental disorders served by the health systems affiliated with the Network. The study should be appropriately powered and of sufficient scope to definitively answer the primary research question(s). The application should explain how the proposed Signature Project will demonstrate the Network's capacity to conduct a highly efficient, large-scale study at a significantly lower cost than historical comparisons, in an area of high public health importance.

At least one (1) of the two (2) projects must be a clinical trial.

One of the two Signature Projects *or* one of the two Pilot Projects (described above) should be designed to reduce disparities in mental health status, services utilization and/or treatment outcomes.

For Projects that involve Clinical Trials, discuss the following (without duplicating information collected in the PHS Human Subjects and Clinical Trials Information Form):

- Justify the practical effect of the intervention or service approach in terms of the estimated hypothesized effect size (in terms of key outcomes, such as clinical benefit, safety/tolerability, value and efficiency, or scalability), compared with already available approaches. Address both (1) the empirical basis for the anticipated effect size (e.g., citing data regarding the magnitude of the association between the target and the clinical endpoint of interest and/or effect sizes obtained in prior efficacy studies), and (2) the clinical meaningfulness of the anticipated increment in effects compared to existing approaches.
- Provide the justification for the design (e.g., hybrid effectiveness-implementation clinical trial Type I, II, or III), in terms of the level of pre-existing effectiveness evidence and implementation readiness.
- Consistent with the experimental therapeutics approach, detail the plan for testing whether the intervention engages the mechanism that is presumed to underlie the intervention effects (the mechanism(s) that account(s) for changes in clinical/functional outcomes, changes in provider behavior, etc.). Include the following: (1) a conceptual framework that clearly identifies the

target(s)/mechanism(s) and the empirical evidence linking the target(s)/mechanism(s) to the clinical symptoms, functional deficits, or patient-, provider- or system-level behaviors/processes that the intervention seeks to improve; (2) plans for assessing engagement of the target(s)/mechanism(s) using valid measures that are as direct and objective as is feasible in the effectiveness context, including the specific measures, the assessment schedule, and the justification for the assessment strategy (e.g., evidence regarding the validity and feasibility of the proposed measures in the effectiveness context); and (3) a statistical analysis plan and corresponding power calculations for data analyses that will be used to examine whether the intervention engages the target(s)/mechanism(s) and whether intervention-induced changes in the target(s)/mechanism(s) are associated with clinical benefit (i.e., mediation). In the case of multi-component interventions, the application should specify the conceptual basis, assessment plan, and analytic strategy, as detailed above, for the target(s)/mechanism(s) corresponding to each intervention component, as appropriate in the effectiveness context (see NIMH web page on Clinical Trials).

- Detail plans for the assessment and monitoring of the fidelity of intervention delivery via procedures that are feasible and valid for use in community practice settings.
- Describe plans for including outcome measures validated and generally accepted by the field, including stakeholder-relevant outcomes, as appropriate (e.g., functioning, health services use).

Letters of Support:

Include letters of support from key stakeholders (e.g., to indicate willingness to collaborate/ participate in the research, to acknowledge relevance of the proposed research to clinical practice, to indicate readiness to implement research findings, as relevant).

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

Appendix:

Only limited items are allowed in the Appendix. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Human Subjects and Clinical Trials Information (Signature Projects)

When involving NIH-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or a **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information: All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Section 2 - Study Population Characteristics

2.5 Recruitment and Retention Plan

Applications involving clinical trials must include a single attachment, with no more than three (3) pages, that clearly describes the following information:

Participant Recruitment and Retention Procedures:

- Recruitment and Referral sources, including detailed descriptions of the census/rate of new cases and anticipated yield of eligible participants from each source;
- Procedures that will be used to monitor enrollment and track/retain participants for any proposed follow-up assessments;
- Strategies that will be used to ensure a diverse, representative sample beyond the information in plans for inclusion of women, minorities, and children;
- Potential recruitment/enrollment challenges and strategies that can be implemented in the event of enrollment shortfalls (e.g., additional outreach procedures, alternate/back-up referral sources);
- Evidence to support the feasibility of enrollment, including descriptions of prior experiences and yield from research efforts employing similar referral sources and/or strategies.

2.7 Study Timeline

Applicants must provide Signature Project milestones and timelines for each research project.

Delayed Onset Study:

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

Pilot Projects

When preparing your application in ASSIST, use Component Type 'Pilot Projects.'

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions, as noted.

SF424 (R&R) Cover (Pilot Projects)

Complete only the following fields:

- Applicant Information
- Type of Applicant (optional)
- Descriptive Title of Applicant's Project
- Proposed Project Start/Ending Dates

PHS 398 Cover Page Supplement (Pilot Projects)

Enter Human Embryonic Stem Cells in each relevant component.

Research & Related Other Project Information (Pilot Projects)

Human Subjects: Answer only the 'Are Human Subjects Involved?' and 'Is the Project Exempt from Federal regulations?' questions.

Vertebrate Animals: Answer only the 'Are Vertebrate Animals Used?' question.

Project Narrative: Do not complete. Note: ASSIST screens will show an asterisk for this attachment indicating it is required. However, eRA systems only enforce this requirement in the Overall component and applications will not receive an error if omitted in other components.

Project /Performance Site Location(s) (Pilot Projects)

List all performance sites that apply to the specific component.

Note: The Project Performance Site form allows up to 300 sites, prior to using additional attachment for additional entries.

Research & Related Senior/Key Person Profile (Pilot Projects)

- In the Project Director/Principal Investigator section of the form, use Project Role of 'Other' with Category of 'Project Lead' and provide a valid eRA Commons ID in the Credential field.
- In the additional Senior/Key Profiles section, list Senior/Key persons that are working in the component.
- Include a single Biographical Sketch for each Senior/Key person listed in the application regardless of the number of components in which they participate. When a Senior/Key person is listed in multiple components, the Biographical Sketch can be included in any one component.
- If more than 100 Senior/Key persons are included in a component, the Additional Senior Key Person attachments should be used.

Budget (Pilot Projects)

Budget forms appropriate for the specific component will be included in the application package.

Note: The R&R Budget form included in many of the component types allows for up to 100 Senior/Key Persons in section A and 100 Equipment Items in section C prior to using attachments for additional entries. All other SF424 (R&R) instructions apply.

PHS 398 Research Plan (Pilot Projects)

Specific Aims: The specific aims should provide a concise description of the aims of the individual research project. Projects should align closely to NIMH's Strategic Research Priorities.

Research Strategy: This section should provide details about how the Network resources will be used to complete the project. The research should be consistent with the goals identified earlier in detail in this funding announcement. Describe the anticipated interactions between this project and other components of the Network, including the role of the Cores in facilitating participant enrollment, conduct of study, and analysis, interpretation, and dissemination of the results.

For ease and clarity of review, use the headers, below, in organizing each individual Project.

Significance: Describe overall goals and the impact of the science proposed in the project in relation to the state-of-the-art of the field. This section should also explain the contribution of the project to the overall goals of the Network, how the project will interact with and benefit from other components of the Network and the appropriateness of the Network approach and environment.

Innovation: Describe the unique and innovative contributions that will be made by the research project. Explain how these contributions will synergize with the rest of the Network to achieve more than what could be achieved through an independent research project. Research projects should propose novel, transdisciplinary, convergent solutions to intractable mental health problems by integrating input from the diverse experts brought together in the Network.

Approach: Detail how the proposed Pilot Project will generate data that will lead to a firm conclusion about the feasibility of a regular research project grant or full-scale clinical trial and provide information about the anticipated scope and goals of intended future work. At least one of the Pilots must be a clinical trial.

Pilot Projects should propose innovative approaches consistent with the goals of this current announcement and the NIMH Strategic Research Priorities. The Pilots should seek to optimize and improve care for a diverse population of patients within defined healthcare systems of the Network; develop and/or test new IT platforms, risk algorithms, decision support systems, and preventive, therapeutic (to include pharmacotherapies), or services interventions; create efficiencies in all aspects of the conduct of research, dissemination of findings, and produce study results that can directly inform practice change; reduce health disparities by engaging intervention targets; improve methodologies in systems research; and/or, seek strategies to continuously improve the accessibility, quality, continuity,

equity and value of services delivered within the Network. The scope of research and research questions associated with these Pilots should be modeled on the NIMH R34 mechanism for clinical trials (https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-18-706.html) and/or non-trial services research (https://grants.nih.gov/grants/guide/pa-files/PAR-18-267.html).

One of the two Signature Pilots *or* one of the two Pilot Projects (described above) should be designed to reduce disparities in mental health status, services utilization and/or treatment outcomes.

For Projects that involve Clinical Trials, discuss the following (without duplicating information collected in the PHS Human Subjects and Clinical Trials Information Form):

- Justify the practical effect of the intervention or service approach in terms of the estimated hypothesized effect size (in terms of key outcomes, such as clinical benefit, safety/tolerability, value and efficiency, or scalability), compared with already available approaches. Address both (1) the empirical basis for the anticipated effect size (e.g., citing data regarding the magnitude of the association between the target and the clinical endpoint of interest and/or effect sizes obtained in prior efficacy studies), and (2) the clinical meaningfulness of the anticipated increment in effects compared to existing approaches.
- Provide the justification for the design (e.g., hybrid effectiveness-implementation clinical trial Type I, II, or III), in terms of the level of pre-existing effectiveness evidence and implementation readiness.
- Consistent with the experimental therapeutics approach, detail the plan to explicitly test whether the services/preventive/therapeutic intervention engages the target(s)/mechanism(s) presumed to underlie the intervention effects (i.e., the mechanism that accounts for changes in clinical/functional outcomes, changes in provider behavior, improved access or continuity of services, etc.). The application should include (1) a conceptual framework that clearly identifies the target(s)/mechanism(s) and the empirical evidence linking the target(s)/mechanism(s) to the clinical symptoms, functional deficits, or patient-, provider- or system-level behaviors/processes that the intervention seeks to improve; (2) plans for assessing engagement of the target(s)/mechanism(s) using valid measures that are as direct and objective as is feasible in the effectiveness context, including the specific measures, the assessment schedule, and the justification for the assessment strategy (e.g., evidence regarding the validity and feasibility of the proposed measures in the effectiveness context); and, (3) a statistical analysis plan for data analyses that will be used to examine whether the intervention engages the target(s)/mechanism(s) and to conduct a preliminary examination of whether intervention-induced changes in the target(s)/mechanism(s) are associated with clinical benefit, as appropriate in the Pilot study. In the case of multi-element interventions, the application should specify the conceptual basis, assessment plan, and analytic strategy, as detailed above, for the target(s)/mechanism(s) corresponding to each intervention element, as appropriate in the effectiveness context (see NIMH web page on Clinical Trials).
- Detail plans for the assessment and monitoring of the fidelity of intervention delivery via procedures that are feasible and valid for use in community practice settings.
- Describe plans for including outcome measures validated and generally accepted by the field, including stakeholder-relevant outcomes, as appropriate (e.g., functioning, health services use).

Letters of Support:

Include letters of support from key stakeholders (e.g., to indicate willingness to collaborate/ participate in the research, to acknowledge relevance of the proposed research to clinical practice, to indicate readiness to implement research findings, as relevant).

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

Appendix:

Only limited items are allowed in the Appendix. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Human Subjects and Clinical Trials Information (Pilot Projects)

When involving NIH-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or a **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information: All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Section 2 - Study Population Characteristics

2.5 Recruitment and Retention Plan

Applications involving clinical trials must include a single attachment, with no more than three (3) pages, that clearly describes the following information:

Participant Recruitment and Retention Procedures:

- Recruitment and Referral sources, including detailed descriptions of the census/rate of new cases and anticipated yield of eligible participants from each source;
- Procedures that will be used to monitor enrollment and track/retain participants for any proposed follow-up assessments;
- Strategies that will be used to ensure a diverse, representative sample beyond the information in plans for inclusion of women, minorities, and children;
- Potential recruitment/enrollment challenges and strategies that can be implemented in the event of enrollment shortfalls (e.g., additional outreach procedures, alternate/back-up referral sources);
- Evidence to support the feasibility of enrollment, including descriptions of prior experiences and yield from research efforts employing similar referral sources and/or strategies.

2.7 Study Timeline

Applicants must provide Signature Project milestones and timelines for each research project.

Delayed Onset Study: Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov.

4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday, the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (the online portal to find and apply for grants across all Federal agencies) using ASSIST or other electronic submission systems. Applicants must then complete the submission process by tracking the status of the application in the eRA Commons, NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review.

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the *NIH Grants Policy Statement*.

Pre-award costs are allowable only as described in the *NIH Grants Policy Statement*.

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

For information on how your application will be automatically assembled for review and funding consideration after submission go to: http://grants.nih.gov/grants/ElectronicReceipt/files/Electronic_Multi-project_Application_Image_Assembly.pdf.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit How to Apply – Application Guide. If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) and component Project Leads must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package**.** Failure to register in the

Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management (SAM). Additional information may be found in the SF424 (R&R) Application Guide.

See more tips for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

In order to expedite review, applicants are requested to notify the NIMH Referral Office by email at nimhreferral@mail.nih.gov when the application has been submitted. Please include the FOA number and title, PD/PI name, and title of the application.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy. Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the NIH mission are evaluated for scientific and technical merit through the NIH peer review system.

A proposed Clinical Trial application may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs. Additionally, the results of the clinical trial may indicate that further clinical development of the intervention is unwarranted or lead to new avenues of scientific investigation.

Overall Impact - Overall

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the Network to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the Network proposed).

Scored Review Criteria - Overall

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a Network that by its nature is not innovative may be essential to advance a field.

Significance

Does the Network address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the Network are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

How well does the Network support a wide range of practice-based research, including pragmatic and

comparative effectiveness trials focused on optimizing and testing scalable preventive and therapeutic interventions and services research focused on identifying and intervening on mutable factors to increase access, engagement, continuity, equity, efficiency/value, and quality of mental health care? To what extent will leveraging this practice-based Network to launch effectiveness studies yield efficiencies, compared to conducting studies de novo?

Are the scientific rationale and need for a clinical trial to test the proposed hypothesis or intervention well supported by preliminary data, clinical and/or preclinical studies, or information in the literature or knowledge of biological mechanisms? For trials focusing on clinical or public health endpoints, is this clinical trial necessary for testing the safety, efficacy or effectiveness of an intervention that could lead to a change in clinical practice, community behaviors or health care policy? For trials focusing on mechanistic, behavioral, physiological, biochemical, or other biomedical endpoints, is this trial needed to advance scientific understanding?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the Network? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

With regard to proposed leadership for the Network, do the PD/PI(s) and key personnel have the expertise, experience, and ability to organize, manage and implement the proposed clinical trial and meet milestones and timelines? Do they have appropriate expertise in study coordination, data management and statistics? For a multicenter trial, is the organizational structure appropriate and does the application identify a core of potential center investigators and staffing for a coordinating center?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Does the design/research plan include innovative elements, as appropriate, that enhance its sensitivity, potential for information or potential to advance scientific knowledge or clinical practice?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the Network? Have investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the Network involves human subjects and/or NIH-defined clinical research, are the plans to address:

1) the protection of human subjects from research risks, and

2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the

inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

Does the application adequately address the following, if applicable?

Study Design

Is the study design justified and appropriate to address primary and secondary outcome variable(s)/endpoints that will be clear, informative and relevant to the hypothesis being tested? Is the scientific rationale/premise of the study based on previously well-designed preclinical and/or clinical research? Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research question(s), test the proposed hypothesis/hypotheses, and provide interpretable results? Is the trial appropriately designed to conduct the research efficiently? Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, and duration of the trial, appropriate and well justified?

Are potential ethical issues adequately addressed? Is the process for obtaining informed consent or assent appropriate? Is the eligible population available? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed? Are differences addressed, if applicable, in the intervention effect due to sex/gender and race/ethnicity?

Are the plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Is there a plan to obtain required study agent(s)? Does the application propose to use existing available resources, as applicable?

Data Management and Statistical Analysis

Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Are the procedures for data management and quality control of data adequate at clinical site(s) or at center laboratories, as applicable? Have the methods for standardization of procedures for data management to assess the effect of the intervention and quality control been addressed? Is there a plan to complete data analysis within the proposed period of the award?

Evaluate the Network infrastructure in terms of its capacity to accomplish the following:

- Efficiently and rapidly identify, recruit and enroll large and diverse patient populations into effectiveness and pragmatic trials that align with NIMH priorities;
- Harmonize electronic health record (EHR) data across multiple integrated systems for research use, to include (EHR) phenotyping and the development of integrated tools to enhance workflows;
- Develop and implement a system to collect, store, and analyze biologic and/or genetic material;
- Provide rapid responses to address urgent questions from federal, state, and other key stakeholders (e.g., questions related to the clinical epidemiology of mental disorders and/or questions related to the uptake of and outcomes associated with mental health interventions and best practices);
- Study low base-rate events (e.g., suicide, autism spectrum disorders, first episode psychosis, or other mental health conditions which are difficult to identify, predict, treat, and/or manage) by using and advancing innovative methodologies (e.g., predictive analytics) or resources which capitalize on the Network's unique sophistication in health information technology, overall size, or research efficiencies;
- Identify and test strategies to reduce disparities in mental health status, service utilization, and treatment outcomes in the health of people with mental illness, including disparities in medical

comorbidities among adults with serious mental illness and youth with serious emotional disturbance;
- Secure stakeholder commitment to adopt, implement, scale-up, and sustain best practices at the patient, provider, and health system levels.

If all aims are met, how well will the Network accomplish the following:

- Build and extend the capacity of a Practice-Based Research Network to conduct prospective trials via the successful completion of Pilot Projects and additional pilot feasibility studies, including tests of interventions not yet studied in such networks.
- Successfully complete two Signature Projects (one of which must be a clinical trial) of high impact on the mental health and functioning of a large population, where positive or negative findings will lead to measurable improvements in practice across the Network sites.
- Benchmark the costs of conducting a range of studies on the Network compared to historical norms, and progress toward Network-involved trials to be completed with costs at an order of magnitude below prior norms.
- Expand tools to create efficiency in the rapid conduct of effectiveness, services, and implementation research studies on the Network.
- Use business models which foster data sharing, cost efficiencies, and strengthen the self-sustainability of the Network.
- Successfully disseminate trial results to health system partners resulting in significant change of policy and/or practice as a direct result of study findings.

Disseminate Network generated research products, including methodological/analytic approaches, assessment and intervention approaches and materials, sharable programing (e.g. for technology-based tools), and de-identified data.

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Do Network sites include representative samples in terms of coverage (e.g., individuals covered by commercial systems, Medicaid, and uninsured individuals served by the system)?

If proposed, are the administrative, data coordinating, enrollment and laboratory/testing centers appropriate for the trial proposed?

Does the application adequately address the capability and ability to conduct the research at the proposed site(s) or centers? Are the plans to add or drop enrollment centers, as needed, appropriate?

If multi-sites/centers, is there evidence of the ability of the individual site or center to: (1) enroll the proposed numbers; (2) adhere to the protocol; (3) collect and transmit data in an accurate and timely fashion; and, (4) operate within the proposed organizational structure?

Additional Review Criteria - Overall

As applicable for the Network proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Milestones

To what extent are the proposed milestones feasible, well developed, and quantifiable with regard to the specific aims for each Project and Core, and for the goals of the Network as a whole? Are there other intermediate and overall goals that should be monitored?

Administrative Core

Is the Administrative Core Director an accomplished administrator capable of leading a complex, interdisciplinary organization to achieve its key aims and objectives?

Does the proposed Administrative Core have an appropriate and adequate administrative structure with an internal organization capable of planning, conducting, and evaluating Network activities?

Does the Core clearly delineate procedures and plans for Network administration and data management, analysis, and sharing?

Is there an adequate mechanism for internal review, decision-making, and priority-setting processes appropriate to conduct the activities of the Network?

Is a standing External Advisory Committee proposed that can provide appropriate and objective advice and evaluation regularly to the Administrative Core Director, and is an appropriate process proposed for responding to recommendations of the Committee?

How well will the features of the Administrative Core enhance the collaborative effort, including optimizing communication, decision-making and sharing between the Research Projects and the Methods Core?

Evaluate the provisions for pilot feasibility studies of 1-2 years duration that can be proposed by new or established investigators and the strength of the plans for soliciting, reviewing, and selecting pilot feasibility projects. How likely is it that the proposed plan will yield pilot feasibility projects that will position the Network investigators for subsequent research that advances and extends the Network's overall program of research?

How well do the Research Projects and Methods Core (as applicable) draw upon the Administrative Core and its three Units and it, in turn, respond to Research Projects or Methods Core needs? Does the description of the Administrative Core clearly indicate the facilities, resources, services and professional skills that the Core will provide?

Evaluate the proposed structure and plans for the functional Units of the Administrative Core, as follows:

1) Organizational Unit:

How well does the Organizational Unit coordinate the Network's administrative functions, including, but not limited to mediating and coordinating interactions among Network members and providing organizational support for joint Network activities (e.g., organizing meetings, teleconferences, etc.)?

How well does the Unit (with input from the other Administrative Core Units and the Methods Core) coordinate the evaluation of the Network's activities, in terms of: a) Research progress and impact; b) Cost- and other resource-related efficiencies created through use of the Network, as compared to conducting research studies de novo, outside of the Network Infrastructure; and c) Public health benefit? To what extent will the evaluation plan be useful for iteratively refining the Network's ongoing activities and informing plans for future collaborative research?

2) Outreach and External Collaboration Unit:

How well does the Outreach and External Collaboration Unit work to increase the usage of the Network by external investigators, as well as to support the implementation of Network findings within the partnering health systems (whether findings are positive or negative)? Evaluate the plan to promote the Network as a resource and facilitate access to external, non-Network-affiliated investigators.

Evaluate how well this Unit will establish an efficient system and operating procedures for: receiving and

managing requests for access to data, ideas for collaborations, and applications for research projects from the scientific community; supporting training experiences for junior investigators; establishing partnerships with key mental health stakeholders (e.g., service users, family members, clinicians, payers, system leaders); and, disseminating research results and research products.

3) Emerging Issues Unit:

Evaluate the Unit's capacity for rapid and systematic responses to address practice-relevant inquiries and requests (requests for data, analyses, and evidence synthesis) from Network-affiliated healthcare system partners, as well as federal, state, and other key stakeholders. Evaluate plans for prioritizing, processing, and responding to requests.

Evaluate the timeline and milestones described in the Administrative Core. Does the application include a graphic Timeline with clearly defined milestones? To what extent does the plan include milestones that are quantifiable, that are scientifically justified, that are feasible, and that represent benchmarks at critical junctures? How well does the plan address annual indicators of progress and alternative strategies that can be invoked, should any component efforts fail to perform as expected?

Methods Core

To what extent will the qualifications, past performance (if applicable), and time commitments of the Methods Core Leader(s) contribute to the likely success of the Network? Evaluate the appropriateness of the expertise of the Methods Core Leader(s) for carrying out the functions proposed for the Core.

Evaluate the proposed structure and plans for the functional Units of the Methods Core, as follows:

1) Informatics Unit: How well will the structure of the Informatics Unit be able to act as a key component for the Network resource function? How well will the Unit, as described, be able to support a Network informatics infrastructure, notably including a data warehouse, and facilitate improvements in data development, informatics tools, etc.? How well with the Unit be able to coordinate informatics-related efforts at the individual Network member sites as well as interact with other Units and Projects?

2) Scientific Analysis Unit: How well will the Scientific Analysis Unit be organized to generate new methodology and apply state of the art principles to the fields of big data science, health services research, and implementation science?

Evaluate the Methods Core's overall potential to:

- Function as an incubator for innovative approaches and facilitate novel and convergent solutions to intractable mental health problems by integrating input from clinical and services researchers, insights from key mental health stakeholders, and contributions from diverse experts in complementary fields, as relevant (e.g., behavioral and social science, health information and communications technology, health system engineering, decision science, bioinformatics, data modeling, research design, and/or biostatistics);
- Facilitate development and design the Signature Projects, Pilot Projects, and other Network research, and to identify and apply scientific, technological, and methodological innovations and tools to facilitate both the research enterprise and accelerate delivery of interventions and services in clinical and community settings?
- Provide expert conceptual, methodological, technical, and analytic statistical support to the Network's investigators;
- Offer facilities and resources that are appropriate and optimal for conducting exploratory research projects, given the goals of the Network;
- Facilitate research via centralized functions (e.g., IRB, clinical assessment, data

collection/management, quality assurance, data analysis);
- Ensure Good Clinical Practice as well as human subject protections for clinical research;
- Help generate research methods and future directions, including pilot feasibility projects of 1-2 years duration proposed by Network collaborators;
- Monitor and incorporate emerging scientific, technological, methodological, and analytic innovations and identify and engage new collaborators working in allied areas;
- Function as a consultation resource beyond the Network collaborations in order to disseminate methodological advances and other Networks-generated resources;
- Contribute to the Administrative Core's efforts to evaluate Network's progress by providing methodological and analytic expertise that informs a more comprehensive and valid evaluation of the Network's research progress and public health impact.

Research Projects

How important is the project topic to Network stakeholders and the health and welfare of Network beneficiaries such that Network decision makers have committed to use research findings to improve practice?

To what extent does the project incorporate efficiencies by utilizing existing infrastructure in the Network (e.g., electronic medical records, administrative databases, patient registries, or other available resources)?

Evaluate the project PD(s)/PI(s)'s expertise, experience, and ability to organize, manage and implement the proposed clinical trial/services research studies and meet milestones and timelines.

To what extent does the project incorporate collaborations and/or input from community partners and other stakeholders?

How well does the application address the potential public health impact of the proposed work in terms of 1) reach and effect on the target population; 2) meaningfulness of the anticipated outcomes (e.g., compared to existing approaches and/or current state of science in the topic area); and adoptability, scalability, and sustainability using typically available resources, staff, and services structures, including financing structures?

For Signature Projects: Does the application include an appropriately detailed power analysis? Is the study powered to provide conclusive results? Does the application describe how the results could be integrated into practice?

For Pilot Projects: How likely is it that the proposed research will generate data that will lead to a firm conclusion about the feasibility of a regular research project grant or full-scale clinical trial?

For Projects that involve a Clinical Trial:

- How well does the application justify the practical effect of the intervention or service approach in terms of the estimated hypothesized effect size (in terms of key outcomes, such as clinical benefit, safety/tolerability, value and efficiency, or scalability), compared with already available approaches? Does the application adequately address both (1) the empirical basis for the anticipated effect size (e.g., citing data regarding the magnitude of the association between the target and the clinical endpoint of interest and/or effect sizes obtained in prior efficacy studies), and (2) the clinical meaningfulness of the anticipated increment in effects compared to existing approaches?
- If the approach is successful, will it be scalable, adoptable, and/or sustainable and could it be disseminated into practice given typically available resources (e.g., trained, skilled providers), typical service structures (including health care financing), and typical service use patterns?
- How well does the application justify the design (e.g., hybrid effectiveness Type I, II, or III) in terms of

the level of scientific evidence and the organization's implementation readiness?

- How well does the study design address whether the intervention engages the mechanism that is presumed to underlie the intervention effects (the mechanism that accounts for changes in clinical/functional outcomes, changes in provider behavior, etc.)? To what extent does the application include (1) a well-supported empirical framework that clearly identifies the target(s)/mechanism(s); (2) well justified plans for assessing engagement of the target(s)/mechanism(s), including valid measures and an appropriate assessment schedule; and, (3) an appropriate analytic strategy that will be used to examine whether the intervention engages the target(s)/mechanism(s) and whether intervention-induced changes in the target(s)/mechanism(s) are associated with clinical benefit?
- Evaluate the provisions for the assessment and monitoring of the fidelity of intervention delivery via procedures that are feasible and valid for use in community practice settings.
- Evaluate the extent to which the assessment plan includes valid outcome measures that are accepted by the field, including stakeholder-relevant outcomes (e.g., functioning, health services use), as appropriate.

Study Timeline-Overall

Is the study timeline described in detail and does it take into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is the projected timeline feasible and well justified? Does the project incorporate efficiencies and utilize existing resources (e.g., CTSAs, practice-based research networks, electronic medical records, administrative databases, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate?

Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects.

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed Network involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research.

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals

versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section.

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

Not Applicable

Renewals

Not Applicable

Revisions

Not Applicable

Additional Review Considerations - Overall

As applicable for the Network proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Applications from Foreign Organizations

Not Applicable

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan; 2) Sharing Model Organisms; and 3) Genomic Data Sharing Plan .

Authentication of Key Biological and/or Chemical Resources

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s), convened by NIMH in accordance with NIH peer review policy and procedures, using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications:

- May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.
- Will receive a written critique.

Appeals of initial peer review will not be accepted for applications submitted in response to this FOA.

Applications will be assigned to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer review, recommended applications will receive a second level of review by the National Advisory Mental Health Council. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons. Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

Information regarding the disposition of applications is available in the *NIH Grants Policy Statement*.

Section VI. Award Administration Information

1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the *NIH Grants Policy Statement*.

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the grants management officer is the authorizing document and will be sent via email to the grantee’s business official.

Awardees must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

Individual awards are based on the application submitted to, and as approved by, the NIH and are subject to the IC-specific terms and conditions identified in the Notice of Award (NoA).

ClinicalTrials.gov: If an award provides for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register and submit results information for certain “applicable clinical trials” on the ClinicalTrials.gov Protocol Registration and Results System Information Website (https://register.clinicaltrials.gov). NIH expects registration of all trials whether required under the law or not. For more information, see http://grants.nih.gov/ClinicalTrials_fdaaa/

Institutional Review Board or Independent Ethics Committee Approval: Grantee institutions must ensure that the application as well as all protocols are reviewed by their IRB or IEC. To help ensure the safety of

participants enrolled in NIH-funded studies, the awardee must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

Data and Safety Monitoring Requirements: The NIH policy for data and safety monitoring requires oversight and monitoring of all NIH-conducted or -supported human biomedical and behavioral intervention studies (clinical trials) to ensure the safety of participants and the validity and integrity of the data. Further information concerning these requirements is found at http://grants.nih.gov/grants/policy/hs/data_safety.htm and in the application instructions (SF424 (R&R) and PHS 398).

Investigational New Drug or Investigational Device Exemption Requirements: Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

Prior Approval of Pilot Projects

Awardee-selected projects that involve {clinical trials or studies involving greater than minimal risk to human subjects} require prior approval by NIH prior to initiation.

- The awardee institution will provide NIH with written study protocols that address risks and protections for human subjects in accordance with NIH's Instructions for Preparing the Human Subjects Section of the Research Plan.
- The awardee institution will provide NIH with specific plans for data and safety monitoring, and will notify the IRB and NIH of serious adverse events and unanticipated problems, consistent with NIH DSMP policies.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* as part of the NoA. For these terms of award, see the *NIH Grants Policy Statement* Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities. More information is provided at Award Conditions and Information for NIH Grants.

Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons with limited English proficiency. HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research.

For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA. HHS provides general guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/index.html. The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-individuals/section-1557/index.html; and https://www.hhs.gov/civil-rights/for-providers/laws-regulations-guidance/index.html. Recipients of FFA also have specific legal

obligations for serving qualified individuals with disabilities. Please see https://www.hhs.gov/civil-rights/for-individuals/disability/index.html. Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at https://www.hhs.gov/ocr/about-us/contact-us/index.html or call 1-800-368-1019 or TDD 1-800-537-7697. Also note it is an HHS Departmental goal to ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations. For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53.

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the purpose of the NIH is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility reside with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for the Network effort as a whole, including research design and the actual performance of the Projects, and preparation of publications.

The PD(s)/PI(s) will attend all Network Steering Committee meetings, annually document progress in written reports to the NIMH Program Director and provide periodic supplementary reports upon request.

To accommodate the changing environment resulting from improved technologies, the PD(s)/PI(s) is expected to make any necessary adjustments in the overall research strategies during the project period. Although joint research projects are strongly encouraged under this FOA, research projects within an application are also allowed to be conducted under the supervision of site-specific Project Leaders at individual Network member organizations otherwise contributing to meeting the goals and objectives of this FOA. Project Leaders of such single member organization studies within an application will have equivalent status with all other PD(s)/PI(s) in regard to participation on the Network Steering Committee and other

Network committees.

The awardee will retain custody of and have primary rights to the data developed under this award, subject to Government rights of access consistent with current HHS, PHS, and NIH policies. The awardee and NIMH will jointly develop appropriate confidentiality procedures for data collection, processing, storage and analysis to ensure the confidentiality of data on individual health care organization patients, health care providers and institutions involved in Network research projects. No identifying information of individual patients or providers should be available through aggregated Network research databases. Encrypted study identification numbers will be used for all aggregated Network studies. The NIMH expects that limited access data will be released under this study. Limited access data refers to study data, with certain deletions and recoding that are released to requesting institutions and investigators for specific purposes and with certain restrictions and conditions.

The PD(s)/PI(s) will be responsible for the timely submission for publication of manuscripts (co)authored by members of the grant and supported in part or in total under this Agreement. All publications and presentation abstracts resulting from work done will be submitted to the Program Officer at least one week prior to journal submission for review, and within two weeks of acceptance for publication so that an up-to-date summary of the cooperative program accomplishments can be maintained and NIMH press releases can be prepared, if applicable. Publications or oral presentations of work performed under this Agreement are the responsibility of the PD(s)/PI(s) and appropriate Project Leaders and require acknowledgement of NIMH support. Timely publication of major findings is encouraged.

NIMH staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- NIH/NIMH will assign one staff member to serve as the Science Officer, who will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:
- Substantial involvement in coordinating the activities of the awardee with the non-Network researchers, as necessary.
- Participation in the Steering Committee and subcommittees.
- Serving as a resource with respect to other ongoing NIMH/NIH activities that may be relevant to this effort and providing expert advice to the awardee on specific scientific and/or analytic issues.
- Assisting, with the agreement of the PD/PI, in the design, development, and coordination of the Network, its Cores, and its studies.
- Reviewing study design and protocols, data abstraction and survey instruments, and analysis plans to ensure that they are within the scope of this effort and consistent with the results of peer review.
- In addition to the Science Officer, an NIMH Program Officer will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.
- The NIMH reserves the right to terminate or curtail the Network (or an individual component of the award) in the event of inadequate progress, data reporting, insufficient use of this resource, or safety issues.
- The NIMH Program Officer will interact with the PD(s)/PI(s) on a regular basis to monitor progress. Monitoring may include: regular communication with the PI and his/her staff, periodic site visits for discussion with the awardee research team, observation of field data collection and management techniques, fiscal reviews, and other relevant stewardship matters.
- The NIMH Program Officer may also identify additional extramural staff from NIMH and other participating organizations that have appropriate experience and expertise to collaborate with the Network in the development of research concepts, review of study designs and methods, participation in study analyses, and review of scientific reports and articles. These additional staff may serve on

various Network committees.

Areas of Joint Responsibility include:

- During the award period, the awardee will be invited to meet with the NIMH, other PDs/PIs, and/or other uninvolved experts in Bethesda, MD, to review scientific progress.
- The Network Steering Committee will be the main oversight body for this cooperative agreement. The Steering Committee will coordinate the overall governance of the Network and establish and administer specific Network-wide policies. Membership of the Steering Committee will consist of the Network PD/PI, Project Leaders from each Network member organization, Project Leaders for each Network research project detailed in Research Plan Section E., and the Science Officer from NIMH. The chair of the Steering Committee will be selected by the Steering Committee members in consultation with the NIMH. Each full member, who will have one vote, will be expected to attend each meeting in full or will be replaced.
- The Steering Committee will periodically review the research agenda and specific research projects, review the evaluation of the overall operations of the Network, determine directions for future development and improvement, and share experiences in implementing the Network activities. It is expected that decisions made, or actions taken by the Steering Committee will be by consensus, or majority vote when needed, and all Network organizations will be expected to implement them. Meetings of the Steering Committee will frequently be held by teleconference calls with in-person meetings usually held three times each year (see Section IV.6). Financial support for these meetings should be included in the Network application budget.

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to dispute resolution. A Dispute Resolution Panel composed of three members will be convened. The three members will be: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

3. Reporting

When multiple years are involved, awardees will be required to submit the Research Performance Progress Report (RPPR) annually and financial statements as required in the *NIH Grants Policy Statement*.

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the *NIH Grants Policy Statement*.

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov on all subawards over $25,000. See the *NIH Grants Policy Statement* for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative

proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues)

Finding Help Online: http://grants.nih.gov/support/ (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

General Grants Information (Questions regarding application instructions, application processes, and NIH grant resources)
Email: GrantsInfo@nih.gov (preferred method of contact)
Telephone: 301-945-7573

Grants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov

Scientific/Research Contact(s)

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Peer Review Contact(s)

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Email: nick.gaiano@nih.gov

Financial/Grants Management Contact(s)

Tamara Kees
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Email: tkees@mail.nih.gov

Section VIII. Other Information

Recently issued trans-NIH policy notices may affect your application submission. A full list of policy notices published by NIH is provided in the *NIH Guide for Grants and Contracts*. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

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