Practice-based research has the potential to dramatically improve the speed, efficiency, relevance, and impact of mental health clinical and services research. Realizing those gains will require a practice-based research network capable of anticipating and adapting to changes in mental health care delivery, including:

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

In pursuit of those goals, the NIMH-funded Mental Health Research Network (MHRN), has developed a robust national research infrastructure and implemented a diverse program of mental health research aligned with each of these requirements. The MHRN portfolio now includes over 20 research projects, many led by external investigators, encompassing a wide range of clinical topics (suicide prevention, first-episode psychosis, depression in primary care, antipsychotic use in youth, co-occurring conditions) and a wide range of research methods (observational epidemiology, qualitative research, pragmatic trials, machine learning, implementation science).

With this application, we propose to expand MHRN to include 14 research centers embedded in large integrated health systems serving a combined member/patient population of over 25 million in 16 states. MHRN infrastructure will be enhanced to support a next-generation practice-based network, including:

- Expansion of data resources regarding patient-reported outcomes from real-world practice
- Development of new data resources in high-priority areas (e.g. perinatal exposures)
- A Scientific Analysis interest group to increase the rigor of analytic methods across MHRN projects
- Methods development focused on evaluation of adaptive treatment strategies for people with more severe mental health conditions and on predictive analytic tools designed to address stakeholder priorities

This overall application requests support for an Administrative Core, a Methods core, two Signature research projects and two Pilot research projects.

The Methods Core will include an Informatics Unit, led by Drs. Gregory Simon and Christine Stewart, and a Scientific Analysis Unit, led by Drs. Susan Shortreed and Patrick Heagerty. The Informatics Unit will continue highly successful work over the past 5 years, supporting routine data quality assessment and descriptive analyses of diagnosis and treatment patterns across all participating health systems. New work will include development of tools and resources to assess and minimize privacy risks when sharing sensitive health data for research and development of specific new data areas (perinatal mental health and prenatal exposures, expanded list of patient-reported outcomes, and assessments of social determinants of health). The Informatics Unit will provide consultation to all MHRN core and affiliated projects and share all resources with other researchers and health systems via MHRN's public repository of specifications, code lists, and analytic code. The Scientific Analysis Unit will support to all MHRN core and affiliated projects via project-specific consultation and development of a learning community of analysts and biostatisticians across MHRN research centers. This Unit will also focus on development and dissemination of analytic methods in two areas directly relevant to MHRN research. Work on *evaluating adaptive treatment strategies* will build on Dr. Shortreed's recently funded methods grant to evaluate and disseminate methods for using health system data to tailor treatments for individuals with more chronic or severe mental health conditions, focusing on assessing treatment effects when treatments are adjusted or switched according to previous treatment failures or adverse effects. Work on *stakeholder-driven predictive analytics* will build on MHRN's development of accurate suicide risk prediction models, focusing on matching specific study designs and model development methods with stakeholder priorities and implementation constraints.

All technical resources developed by the Methods Core will be freely shared, consistent with our aim that MHRN become a highly collaborative national laboratory to accelerate mental health research.