RESEARCH STRATEGY

A. BACKGROUND AND SIGNIFICANCE

A.1. COVID-19, Social Isolation, Stress and Mental Health.

The COVID-19 pandemic has triggered unprecedented disruptions in people's daily lives and routines. Across the country, people are mandated to shelter in place to avoid spread of the virus when possible. Many workers are deemed essential and are unable to fully shelter in place to work, including healthcare, public safety, factory, and grocery workers. These workers often earn lower incomes and are at increased risk of COVID-19 infection. Many other workers are deemed unessential and are also unable to work from home, resulting in large numbers of people being furloughed or fired and record numbers of Americans applying for unemployment benefits.[13] Many now struggle to afford basic needs, including food and housing.

COVID-19 has triggered many symptoms of anxiety and depression for Americans across the country.[2] The pandemic is affecting black communities in particular, with higher rates of infection and of poorer outcomes, in part due to higher rates of poverty, food and housing insecurity and chronic medical conditions.[14] The widespread mandate to shelter in place runs counter to many treatments for anxiety and depression, which typically encourage social engagement and support. Of note, the secondary consequences of social distancing and the economic stress of the pandemic is likely to increase suicide rates.[5] Further increasing risk of suicide, in this context of increased stress, people who would otherwise seek care are reluctant because of fears of contracting Coronavirus, and outpatient, urgent and emergent healthcare use has plummeted.[3]

A.2. Telehealth and Access to Care.

With the growing understanding that in-person office visits may be unnecessarily putting patients at risk of contracting Coronavirus, the pandemic has greatly accelerated the previously slow-moving transition to telehealth.[1] Within one week at HealthPartners, one healthcare system in this proposed study, primary care visits dropped from 7,500 to 500 per day. Of those still occurring, approximately 90% or more are telehealth encounters. At Henry Ford, another healthcare system in this study, primary care clinicians completed more telehealth encounters in one week of March 2020 than in all of 2019. Even after the pandemic subsides, healthcare leaders expect many outpatient office visits will remain telehealth visits, a paradigm shift in care delivery, as telehealth services were previously considered an add-on to standard in-person visits.[11, 12]

Despite this rapid shift to telehealth, we do not yet know which patients are poorly served by telehealth services. Many patients may not have the means, resources, familiarity with technology or trust in the healthcare system to make this transition. Certain patient groups, including patients who identify as black or Hispanic[8] and older adults[9], previously indicated a reluctance to use telehealth services prior to the pandemic, and it is likely that some patients may be left with limited access to mental health care at this time of increased need. Patients of minority racial and ethnic groups and those with lower socioeconomic status may be disproportionally unable to access telehealth care.[6] Policies regarding reimbursement for telehealth have been relaxed during this crisis, but reimbursement is higher for video visits as opposed to phone-only visits, and video visits require patients to have smartphones or other similar technology. Many disadvantaged patients do not have this technology, and publicly available technology, such as computers in a public library, do not provide the needed privacy for telehealth encounters (and, for many, public libraries are currently closed). There are many reasons to think that care for disadvantaged patients may be considerably more disrupted than others in the shift to telehealth.

A.3. Potential Adverse Consequences of Disruptions in Mental Healthcare, including Depression, Anxiety, ED Visits, Hospitalizations, Suicidal Ideation, and Suicide Attempts and Deaths.

Depression and anxiety are closely associated with suicide risk. In prior MHRN work, we found depression severity to be a strong predictor of suicidal ideation[15], and suicidal ideation to be a strong predictor of suicide attempts and deaths across patients of all ages and racial/ethnic groups.[16-18] Meta-analyses of other studies have found similar relationships between anxiety and suicidal ideation, attempts and deaths.[19] The COVID-19 pandemic is increasing anxiety and depression for the general population[2], but it is less clear how it is affecting those with pre-existing mental health conditions. With increased levels of anxiety and depression, one might logically expect suicidal behavior to increase as well. However, access or willingness to access care, especially emergency care, appears to be dramatically lower across the country[20]. Given this, it may be that documented suicide attempts may be declining while suicide deaths may be increasing. With our timely access to comprehensive data on our patients, including EHR data for all visits (including ED visits), claims data and state mortality data (updated monthly at the included sites), the MHRN is uniquely positioned to study these complicated relationships and outcomes to inform telehealth care going forward.

A.4. The Proposed Study, and the Population Surveillance Work and Capabilities of the Mental Health Research Network (MHRN).

This proposed administrative supplement to our current NIMH-funded Mental Health Research Network III (Award U19MH121738) seeks to leverage the MHRN's infrastructure, strong partnerships and virtual data warehouse (VDW) data to examine the effect that the COVID-19 pandemic has had on populations of interest, including patients of racial and ethnic minority groups, children/adolescents, older adults, and socioeconomically disadvantaged patients. As part of our work under our Administrative Core, all sites harvest and provide EHR, administrative and state mortality data quarterly to the prime site of the parent award, Kaiser Permanente Washington. This work is conducted using distributed programmatic code and relies on common data definitions across sites.

The proposed study clearly fits within the scope of our currently funded award, by:

- Using data from the large patient population followed by the MHRN, utilizing the harmonization of EHR and administrative and insurance claims data into a federated data model across sites
- Leveraging programmatic code and development of mental health-related definitions and metrics from our ongoing MHRN Administrative Core work, supported by the MHRN Methods Core's Informatics Unit
- Leveraging ongoing measurement of depression and anxiety severity, suicidal ideation and suicide attempts and deaths across time
- Utilizing the Scientific Analysis Unit of the MHRN Methods Core to provide consultation during ongoing data analyses for this supplement

We will capitalize on previous MHRN work to measure severity of depression and anxiety using structured assessments saved in the EHR (see Section C.4), as well as standard data definitions to capture medication orders, medication fills, psychotherapy visits, medication and psychotherapy adherence, ED visits, hospitalizations, and suicide attempts and deaths. We will leverage all of this work to conduct this study, but will need to engage in new work to accurate identify telehealth visits, both phone-only and video-assisted visits, as these are not currently categorized and captured in our VDW. We also need these supplemental funds to support analyses of our primary and secondary outcomes.

The parent study was funded in September 2019 and is making progress and moving forward as expected. We have continued work via the Informatics Unit of the Methods Core to collect, clean, assemble and monitor data from our 14 healthcare systems quarterly. This ongoing work allows us to leverage these data for the proposed supplemental study, aided by new work in identifying and categorizing telehealth visits. In addition, our steering committee continues to meet monthly and our VDW workgroup meets biweekly.

B. INNOVATION

Our proposed work in innovative in that it takes advantage of timely available data to examine the spread and impact of telehealth visits on continuity of care and outcomes for vulnerable populations. The MHRN is one of the few networks with nearly immediate access to rich EHR data (including measures of depression and anxiety severity and suicidal ideation), claims and administrative data (important for measuring outcomes like suicide attempts, as people may seek care outside of participating care systems that would not be documented in the EHR), *and* state mortality data for a large and racially and ethnically diverse sample of patients. Our vast and rich data sources, which include data on telehealth visits and psychiatric medications and psychotherapy visits, let us examine outcomes associated with the transition to telehealth that would not be possible in many other settings, including disruptions in mental healthcare, including psychiatric medications and psychotherapy. The underlying support and structure of the MHRN Administrative Core and the VDW allow us to assess these predictors and outcomes rapidly and at relatively low cost. Our findings will inform future telehealth interventions and will help to determine whether additional outreach is indicated for at-risk populations.

C. APPROACH

C.1. Study Setting and Population. The proposed study includes data from three MHRN-affiliated health systems from January 2019 through September 2020. All participating healthcare systems provide both comprehensive health care (outpatient and inpatient, general medical and behavioral health) as well as insurance coverage (commercial, Medicaid, Medicare, and self-pay) to defined member/patient populations. Linkage of EHR and insurance claims data allows each system to accurately and completely ascertain all psychotherapy visits, prescription pharmacy fills (including date and amount of opioid analgesic with detailed dosing information) and suicide attempts across a defined population, including suicide attempts among individuals presenting at external facilities. Linkage of insurance coverage and state vital statistics data allows each system to accurately and completely ascertain suicide deaths for all member/patients, including those who have disengaged from care. The three healthcare systems in this supplemental application were selected because each has timely access to monthly state mortality data, including cause of death data.

HealthPartners (HP) serves a defined population of 1.4 million patients and 1.8 million insurance members. HP employs 850 primary care and 231 mental health clinicians who work in 77 clinics and 8 hospitals across Minnesota and western Wisconsin. HealthPartners uses the Epic electronic health record system with Google Duo software for telehealth visits.

Henry Ford Health System (HFHS) serves a defined population of 1.2 million patients and 350,000 insurance members. HFHS has a network of 300 primary care and 100 mental health providers across 50 facilities and 6 hospitals in Michigan. Henry Ford uses the Epic electronic health record system with Vidyo software for telehealth visits.

Kaiser Permanente Washington (KPWA) serves a defined population of 710,000 member/patients through a network of 280 primary care and 103 mental health providers across 27 facilities in Washington. KPWA uses the Epic electronic health record system with Vidyo software for telehealth visits.

C.2. Study Sample. For this study, we will leverage the observational data collected across our healthcare systems as part of the Administrative Core infrastructure activities for MHRN, which characterizes data from 14 healthcare systems that care for over 25 million patients in 16 states. Each health system provides mental health and general medical care to a defined patient population, including substantial numbers from all racial and ethnic groups and substantial numbers insured by Medicaid and other low-income insurance. Each health system has organized longitudinal records into compatible VDWs. We will establish an overall defined patient population denominator of individuals who are healthcare system patients and health plan insurance members. We will define our denominator in monthly periods, and each observation month at each site will include unique patients who were enrolled in the health plan for that month. The sample is anticipated to include over 2.6 million patients with comprehensive capture of electronic health records and insurance claims data across the three healthcare systems. In 2019, among individuals age 12 and older, the 3 participating systems had 160,126 patients with any psychiatric disorder, 85,039 patients with depressive disorder, 110,225 patients with anxiety disorder, and 3,874 with a psychotic disorder. Also, 203,707 were on psychiatric medications and 65,210 received psychotherapy. Additionally, we identified 1,161 medically-treated suicide attempts and over 100 suicide deaths. We anticipate substantially larger samples over the full 21-month observation period for this study (January 2019 through September 2020).

C.3. Data Collection. All participating sites have comprehensive EHR and insurance claims records, which includes extensive clinical and demographic information for all patients. Data on demographics, encounters, prescription fills, diagnoses and procedures are coded using the same standard, national coding schemes across sites.[21-23] Using data quality processes developed in the MHRN, data for this study will be quality checked locally before secure file transfer to Henry Ford, and then will be cross-validated between sites.

C.4. Measures.

- ***Sociodemographic characteristics***: Include age, sex, race, ethnicity, and estimated household income and education using geocoded census data.
- ***Mood, anxiety and psychosis diagnoses:*** Defined using ICD10 codes; list found at https://github.com/MHResearchNetwork/Diagnosis-Codes/blob/master/mhrn_icd10_shortlist.pdf.
- ***Depression/anxiety severity:*** Captured via PHQ9 and GAD7 scores, saved as discrete data elements in the EHR. Mild depression is indicated by a PHQ9 score of 5-9, moderate depression = 10-14, moderately severe depression = 15-19, and severe depression = 20-27.[24]

- ***Suicidal Ideation:*** Captured via item 9 of the PHQ9, a discrete data element documented in the EHR. Suicidal ideation is defined as a PHQ9 item 9 score >0.[24]
- ***Psychiatric medications:*** Identified using National Drug Code (NDC) numbers to identify psychiatric medication fills during the observation period both within and outside of the health system using our VDW data structure across participating health system sites. We will include categories of antidepressants, stimulants, and other medications for attention deficit disorder, anticonvulsants/mood stabilizers (including lithium), anxiolytics, hypnotics, and antipsychotics. The full list is available at https://github.com/MHResearchNetwork/MHRN-Central/blob/master/GenericDrugNames_2019.xls.
- ***Psychotherapy visits:*** Defined as any visit greater than 30 minutes to a specialty mental health provider with a Current Procedural Terminology (CPT) code of 90785-90862 indicating either initial evaluation or individual psychotherapy.
- ***Psychiatric medication disruption*:** Defined as a gap of at least 30 days (i.e., days' supply + 30 days) between fills for any prescription psychiatric medication during the observation period. In sensitivity analyses, we will also examine disruption for new psychiatric medication orders.
- ***Psychotherapy disruption:*** Defined as a gap of at least 45 days with no psychotherapy visit documents after a previous psychotherapy visit during the observation period.
- ***Disruptions in Mental Healthcare:*** Defined as (a) gaps in psychiatric medications (as above), (b) gaps in psychotherapy appointments (as above), or (c) gaps in any mental healthcare of over 30 days for patients whose EHR records indicate they need timely mental health services (elevated Patient Health Questionnaire (PHQ9) scores[24], PHQ9 item 9 scores (indicating suicidal ideation), Generalized Anxiety scale (GAD7) scores[25] or Columbia Suicide Severity Risk Scale (CSSRS)[26] scores; recent psychiatric hospitalization or suicide attempt).
- ***Telehealth visits:*** Includes both phone and video visits. Phone visits are not currently included in our VDW, and with this study we will add these visits (CPT codes 99441, 99442, 99443) to the VDW. Additionally, we will work to accurately distinguish video visits from in-person visits. Early on during the pandemic, our care systems were using the same billing and coding for video visits as for in-person visits. Around the week of April 6th, our care systems instructed clinicians to use CPT modifiers for video telehealth visits, and instructed coders to add these modifiers to some pre-existing visits that had not yet been billed. A GQ modifier is used for asynchronous telehealth video visits, while a GT modifier is used for synchronous/interactive telehealth video visits.[27] Once we have developed code to distinguish visit type, we will audit at least 25 visits at each site to verify that we are correctly classifying visit types, and modify our programming code and re-audit charts as needed. In secondary analyses, we will examine outcomes for people only able to continue care by phone versus those who were able to have video telehealth visits.
- ***ED visits:*** Defined as encounters with a VDW encounter type = ED associated with a mental health or substance use disorder diagnosis.
- ***Psychiatric hospitalizations:*** Defined as encounters with a VDW encounter type = IP or IS associated with a mental health or substance use disorder diagnosis.
- ***Suicide attempts***: Nonfatal medically attended suicide attempts will be identified using diagnosis or encounter codes from all inpatient, outpatient, and emergency department encounters recorded in the EHR (for services delivered by participating health systems) or insurance claims (for outside services). ICD-10 codes include T14.91; X71-83; T36–T50 (with the 6th character = 2 (except for T36.9, T37.9, T39.9, T41.4, T42.7, T43.9, T45.9, T47.9, and T49.9, which are included if the 5th character = 2)), T51–T65 (with the 6th character = 2 (except for T51.9, T52.9, T53.9, T54.9, T56.9, T57.9, T58.0, T58.1, T58.9, T59.9, T60.9, T61.0, T61.1, T61.9, T62.9, T63.9, T64.0, T64.8, and T65.9, which are included if the 5th character = 2)), and T71 with the 6th character=2.[18]
- ***Suicide deaths:*** All suicide deaths will be identified via linkage to regularly updated state mortality data and the National Death Index (NDI) using methods routinely used in our previous research. Suicide deaths will be identified using ICD-10 codes indicating definite (X60 to X84) or possible (Y10 to Y34) self-inflicted injury, or deaths identified as suicides in state mortality data (updated monthly in all sites) and/or the National Death Index.[28]

C.5. Analyses. Prior to analysis, we will divide the individual study participants from each site into two groups: 1) 2/3 of the participants will be randomized to a discovery group and 2) the remaining 1/3 will be assigned to a validation group. In this manner, we will be able to use the data that we have to evaluate the rigor of the discovery findings independently. Consistent with the parent award, after basic descriptive analyses, including the characteristics of the populations stratified by site, the main analyses for Aim 1 of this supplement will determine patient-level predictors of disruption in mental health care using both single and multiple predictor approaches. In these analyses, the outcome of disruption in mental healthcare will be defined based on the three component disruptions (gaps in psychiatric medication, psychotherapy, and any mental healthcare) as well as the composite (one or more instances of any of the three components), with the composite being the primary outcome of interest. To account for the cohort design and the expected relatively common frequency (≥10%) of the outcome of interest in this population, association between each individual predictor and the primary outcome will be calculated using Poisson regression with robust variance estimation to allow for unbiased rate ratio estimates of effect. These single predictor associations will be calculated in models both unadjusted and adjusted for potential confounders of study site and insurance coverage. Further, multiplicative interaction effects between sex/race-ethnicity and the individual predictors will be tested to evaluate potential biological context dependent effects of these two variables. In addition to single predictor models, we will also construct multi-predictor models of the composite disruption outcome using an elastic net penalized Poisson approach, as implemented in R statistical package “glmnet”. For this model, the penalization parameters α and λ will be estimated using 10-fold cross-validation, and each model will include forced adjustment for the site and insurance coverage. The validation sample will then be applied to the resulting models to assess accuracy of prediction assessed via the concordance index.

In addition to the multi-predictor penalized Poisson model, we will also use a latent class mixture model (LCMM) to determine unique grouping of individuals with specific profiles of predictors contributing to a lapse in care. Here, we will apply the LCMM in supervised fashion, utilizing the significant predictors from the univariate or multivariate models of the outcome after adjusting for site and insurance coverage as inputs for the LCMM. While the majority of the predictors considered are categorical, we will use the Mplus (Los Angeles, CA) software to fit these models as it includes a latent class analysis extension that can accommodate additional variable types as needed. LCMM offers more flexibility than traditional cluster analysis, as well as increased classification accuracy [29]. We expect that patients within the same predictor class are similar with regard to the predictors in that class but different from those in other classes. Estimation of mixture models is an iterative process whereby multiple models are considered, typically with increasing numbers of classes, until the model best representing the data is selected. We will use the bootstrap likelihood ratio test and the Bayesian Information Criteria to determine optimal number of LCMM classes. Additionally, we will perform confirmatory latent class analysis[30] using the validation sample to assess the replicability of the discovery LCMM.

To address Aim 2, we will use Cox proportional hazards models to assess the association between mental healthcare disruption and time to the adverse consequences. The disruption in mental healthcare will be treated as a time dependent covariate, with a period of disruption initiated by a 30-day lapse in either medication fills or prescribed psychotherapy/mental healthcare and ended after resumption of care. With the exception of suicide death, all other outcomes could occur more than once during the observation period. To account for the correlation between repeated events within a subject, we will specify the individual events using the counting process approach and utilize the robust sandwich estimator to account for the bias in the variance of the parameter estimates.[31] For all adverse consequences, censoring will occur at the end of the study period or if the participant is lost to follow-up. For non-suicide death adverse consequences, death of the participant will also serve as a condition for censoring. Statistical significance will be assessed using the modified score test accounting for the robust variance estimation. Each model will be adjusted for site and insurance type. We will also more broadly explore potential confounders using directed acyclic graphs (DAGs).[32, 33] Specifically, the DAG methodology implemented in the R package “ggdag” (https://ggdag.netlify.com/) will be used to differentiate between potential confounding variables and those that may be causally related to the adverse outcomes through a mediated effect of disruption in mental health care. Therefore, the primary variables to be considered would include those identified as predictors of disruption in mental health care in Aim 1. Potential confounders identified by DAGs (i.e. associated with both the disruption in care and an adverse outcome but determined not to be in the causal pathway) will be evaluated as such and included in the model if they impart a ≥20% change in a parameter estimate for the main effect of disruption in mental health care. To assess the reproducibility of the findings, we will re-evaluate statistically significant associations from the discovery sample in the validation sample adjusting for the same confounding variables identified in the discovery.

We estimated statistical power to detect effect estimates in the discovery group (2/3 of the sample) assuming two-tailed hypothesis tests and a type-1 error rate of 5%. Further, among the 160,126 patients with any psychiatric disorder across the three health systems (approximately 105,683 randomly allocated to the discovery group), we conservatively assume that 10% will have at least one period of disruption in the 21-month follow-up period. Under these assumptions, for Aim 1, we will have ≥ 80% power to detect a dichotomous predictor that increases the rate ratio of disruption in care by ≥ 1.30 (or ≤ 0.77) and ≥ 1.23 (≤ 0.81) if that predictor is present at respective percentages of 10% and 20% in the cohort. For Aim 2, based on data from 2019 (see section C.2), we further assume that there will be approximately 2,000 suicide attempts (1,320 in the discovery group) in the cohort over the 21-month observation period. For this adverse outcome, we will have ≥ 80% power to detect a hazard ratio of ≥ 1.28 (or ≤ 0.78) associated with disruption in mental health care. In addition to being well-powered to detect reasonable effects in the discovery group, we will also be able to independently assess the significant associations from the discovery group in the validation group.

C.6. Generalizability. The comprehensive data of participating health systems will permit a robust evaluation of disruptions in mental healthcare related to the COVID-19 pandemic and rapid transition to telehealth visits. As the healthcare systems in this study have diversity in race/ethnicity, geography and insurance type, we expect our findings to be broadly relevant and representative of US outpatient primary care and specialty mental health practices, as well as emergency department and inpatient care settings.

C.7. Potential limitations. Predictors are limited to those available in health system data, and as such do not include potentially important risk factors for mental health conditions or suicide, such as bereavement or changes in employment or relationship status. In addition, these EHR data do not include suicide attempts that do not receive medical attention. Additionally, this study includes healthcare systems that were at least able to offer video visits; problems with the transition to telehealth care may be even greater in care settings where video visits were unable to be offered. Despite these potential limitations, our work will be an important contribution that will advance the field in understanding the ramifications of a rapid shift to telehealth and the implications for various patient populations, informing future telehealth interventions.

C.8. Dissemination. As part of our ongoing suicide prevention work in our MHRN healthcare systems and our Patient-Centered Outcomes Research Institute (PCORI) stakeholder engagement project (https://www.pcori.org/research-results/2018/building-capacity-stakeholder-engagement-mental-health-research-network), we will engage patient stakeholders to help interpret findings and brainstorm dissemination opportunities. Additionally, we have established communication channels with key internal and external stakeholders, including the National Committee for Quality Assurance/Healthcare Effectiveness Data and Information Set (NCQA/HEDIS), the Substance Abuse and Mental Health Services Administration (SAMHSA) and the National Action Alliance for Suicide Prevention (NAASP) that we will leverage to disseminate and promote our findings. We will also disseminate our methods, findings, and associated resources through healthcare leader meetings, presentations at local and national meetings, our broadly distributed network quarterly newsletter, our GitHub repository of technical materials and tools, and our websites. Additionally, we will publish manuscripts in peer-reviewed journals and present our findings at national conferences.

C.9. Clinical Implications and Avenues for Future Research. With this work, we expect to identify subpopulations of people who are not well served by a transition to telehealth, allowing us to inform our care systems of these findings and work together to implement additional safeguards and resources for disadvantaged patients to improve their access to care. Our research findings will also inform future research studies to implement enhanced telehealth strategies, including using case managers or health coaches to help patients navigate telehealth obstacles and remain connected with their care teams, or advocating for in-person office visits (when safe and available) for patients for whom telehealth strategies are disadvantageous.

C.10. Timeline.

Task	**Year 1**			
Quarter	**1**	**2**	**3**	**4**
Define policies and timeline of implementation				
Develop programmatic code				
Complete Aim 1 Analyses				
Complete Aim 2 Analyses				
Dissemination activities, submit manuscript				