UPMC Center for High-Value Health Care

Study Title: Specialty Medical Homes to Improve Outcomes for Patients with Inflammatory Bowel Disease and Behavioral Health Conditions

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List of Common Abbreviations in Protocol:

- BH: Behavioral health
- IBD: Inflammatory bowel disease
- SMH: Specialty medical home
- UPMC ISD: UPMC Insurance Services Division

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Research Synopsis

Study Population: This research study will examine the impact of two existing approaches for delivering care within a specialty medical home (SMH) clinical model for patients with inflammatory bowel disease (IBD) and behavioral health (BH) conditions. Care approaches available to patients include traditional high-touch care delivered by a multidisciplinary team of IBD and BH clinicians (TEAM) and a health technology-based (TECH) approach that uses telemedicine and other evidence-based digital tools designed to deliver accessible, convenient care. This study seeks to understand the differential impact of TEAM and TECH on important health outcomes such as IBD and BH symptom severity, functional impairment, health care service utilization and costs, patient quality of life, and patient disease self-management.

Study Design: A comparative effectiveness study using an individual-level randomized design along with a pragmatic, mixed-methods approach to compare two evidence -based SMH care strategies (e.g. high-touch multidisciplinary care and low-human touch technology-enhanced care). Quantitative (e.g. self-report, electronic health record, process) and qualitative (e.g. interviews) data will be collected across multiple time points during the study period.

Sample Size: We expect to enroll 675 individuals.

Study Duration: The contract period begins February 1, 2019 and concludes September 30, 2026. Participants were actively enrolled in the study between July 1, 2019 and February 28, 2024.

Primary Aim 1: Examine the impact of TEAM vs. TECH on two main patient-centered outcomes of IBD and BH symptom severity and secondary outcomes of functional impairment, healthcare utilization, quality of life, and self-efficacy.

> **Hypothesis 1:** Both TEAM and TECH approaches will result in clinically meaningful improvement across all outcomes.

Primary Aim 2: Examine the impact of patient characteristics on clinical response to TEAM or TECH approaches and establish subgroups of patients who will benefit most from each approach. The study focused on baseline IBD activity and age as primary moderators but secondarily explored site, IBD diagnosis, and health literacy.

> **Hypothesis 2a:** The TEAM approach will show greater effects in those with active IBD, while TECH will show greater effects in those with inactive IBD.
> **Hypothesis 2b:** The TECH approach will improve outcomes more in younger patients.

Primary Aim 3: Examine IBD patient and provider perspectives on facilitators and barriers to efficient and effective implementation of TEAM and TECH and the potential for scaling the interventions and SMH model to other common chronic diseases and community care settings to inform high-quality, efficient ongoing implementation and dissemination.

Background and Significance

Inflammatory bowel diseases, including Crohn's disease (CD) and ulcerative colitis (UC), are among the most costly gastrointestinal (GI) conditions in the United States (US) and are life-long chronic diseases that, if not well managed, can significantly disrupt the lives of individuals. IBD afflicts three million U.S. patients and families with incidence rising globally, especially among younger age groups, during a critical social and career development period.[1,2] IBD is a relapsing and remitting condition associated with varying degrees of GI inflammation (disease activity) and related symptoms of abdominal pain, diarrhea, nutritional deficits and fatigue. In the presence of anxiety and depression, IBD symptom load is even higher, even when inflammation is mild or absent.[3] IBD carries a financial burden between $14-31 billion annually in the U.S.,[4,5] with about 30% of adult IBD patients accounting for more than 80% of IBD-related healthcare spend; the largest drivers of cost are surgeries and hospitalizations, many of which are preventable.[6,7] Prior studies have shown that medical utilization (both emergency department (ED) visits and unplanned hospitalizations) is driven by serious disease and IBD activity requiring steroids, biologics, or surgery, chronic unexplained pain and related opioid use, and unaddressed or undertreated behavioral health (BH) problems.[8-13]

IBD patients exhibit higher rates of comorbid BH conditions, especially anxiety and depression, than healthy counterparts – these further compound disease complexity.[14] Indeed, when present, BH issues directly and negatively impact medical/surgical treatment response, adherence to treatment regimens, care utilization including surgeries, and disease-related quality of life and functioning.[15-19] Emerging adults with IBD are a large and uniquely vulnerable subpopulation who, if not effectively integrated into an adult-centered healthcare system, are at significantly higher risk for poor disease outcomes,[20] including high rates of anxiety and depression. Beginning in 2020, BH symptoms were further exacerbated by the COVID-19 pandemic, particularly for IBD patients who reported elevated levels of anxiety surrounding their vulnerability and concerns about securing needed care.[21-23]

Unfortunately, BH care has been siloed, falling short of the seamless, integrated health care necessary for complex patient populations. Most existing models of chronic, lifelong disease management do not adequately address psychosocial issues, nor necessarily address the individualized, whole health needs of patients at different stages of their lives, despite the recognized importance of these issues and their impact on health outcomes.[24-26] Healthcare systems have not found optimal ways to provide integrated behavioral support in routine care, leading to unidentified or undermanaged psychological issues, impaired disease self-management, and poor healthcare access and coordination.[27-33]

In recent years, there has been transformative and widely accepted change around how care is organized and delivered with emphasis on meeting patients where they are.[34-37] In primary care, medical home models have growing evidence for clinical efficacy, improved care quality,

and reduction in medical utilization and costs.[37-42] Published studies show that these results are also attainable in specialty medical homes (SMH)[43-48] including those focused on IBD.[17,33,49] Despite proven success, such intensive, highly staffed and resourced models are expensive to implement and may not be necessary for all chronically ill patients.[50] Workforce limitations and patient concerns related to time, distance, and cost suggest that on-site multidisciplinary teams alone may not be sufficient to provide effective and efficient patient-centered care for the growing number of individuals with chronic diseases like IBD. Health technology, including digital interventions, remote monitoring of health outcomes, and telemedicine visits, is one way to address this gap with growing evidence linking its use to improved access and adherence to BH care and better outcomes.[51-55] Patient preference results already support team-based care and health technology within SMHs,[38,45,56,57] but less is known about how these models impact the outcomes that patients care about most and how to efficiently and effectively implement, maintain, and disseminate these approaches.

Objectives

The goal of this collaborative study is to provide evidence on the impact of two-evidence based SMH approaches on patient-centered disease and healthcare utilization outcomes at three academic medical centers in the northeastern US – UPMC in Pittsburgh, PA, Mount Sinai Hospital (MSH) in New York, NY, and the Cleveland Clinic Foundation (CCF) in Cleveland OH.

To ensure our study's focus was patient-centered, the study team worked closely with patient-, provider-, and system-level stakeholders to develop all aspects of this study protocol, including the early development efforts of in-person and technology-supported care approaches, the research questions, the study outcomes, the evaluation procedures, and the dissemination strategies included in this protocol.

Aims

This study aimed to compare the effectiveness of two evidence-based, patient-centered behavioral approaches implemented within three existing medical homes: **TEAM**, a high-human touch multidisciplinary team-based approach delivered at point-of-care, and **TECH**, a low-human touch technology-based approach delivered at the patient's convenience with the guidance of health coaches. The study focused on patient-centered outcomes, impact on healthcare utilization, determining which intervention worked best for whom, and potential scalability of the model to other healthcare environments and for other chronic conditions.

Primary Aim 1: Examine the impact of TEAM vs. TECH on two main patient-centered outcomes of IBD and BH symptom severity and secondary outcomes of functional impairment, healthcare utilization, quality of life, and self-efficacy.

> **Hypothesis 1:** Both TEAM and TECH approaches will result in clinically meaningful improvement across all outcomes.

Primary Aim 2: Examine the impact of patient characteristics on clinical response to TEAM or TECH approaches and establish subgroups of patients who will benefit most from each approach. The study focused on baseline IBD activity and age as primary moderators but secondarily explored site, IBD diagnosis, and health literacy.

Hypothesis 2a: The TEAM approach will show greater effects in those with active IBD, while TECH will show greater effects in those with inactive IBD.
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Interventions Compared

TEAM is a high-human touch, multidisciplinary SMH approach that connects participants with a personalized care team including gastroenterologists, advanced practice providers (APP)s, BH specialists, dietitians, registered nurses, pharmacists, and health coordinators who provide intensive support and resources for patients.

TECH is a low-human touch approach leveraging behavioral digital tools – primarily a digital cognitive behavioral therapy-focused mobile application with embedded health coaches – to deliver BH care at the patient's convenience.

Study Design/Methodology

This multi-center study will involve an individual-level randomized design along with a pragmatic, mixed-methods approach to compare two existing care approaches, TEAM (high-human touch) and TECH (technology-supported care), for delivering IBD and behavioral health services to individuals with IBD within and SMH model. Participants will be actively enrolled in the study for 12 months. Study participants will receive care from the IBD SMH clinical team per usual care delivery processes established for TEAM and TECH for the duration of the study.

Randomization Procedure

Eligible participants who consent to participate in the study will be stratified by age (18-30, 31+), IBD disease activity (active/inactive), and IBD type (UC or Crohn's) which will be assessed at enrollment and before randomization to ensure that intervention arms are balanced with respect to these variables. The age cut-off of 30 was chosen because it includes the age-range patients are most often transitioned from pediatric to adult care; 18 is the age patients have the right to make their own health choices, and age 30 is usually when patients transition off their parents' health insurance. Within each stratum, random block sizes of two and four will be used to maximize balance between groups while minimizing the ability to unmask investigators to next treatment assignment, triggering an automated alert to staff on which approach to use.

We will monitor the randomization process throughout the study period to ensure there are no systematic differences between study arms and selection or assignment biases.

Measures

Primary outcomes

IBD symptom severity will be captured from the IBD Complexity Composite Score[58,59] which is a disease complexity grid developed for primary care patients that is used with IBD patients in order to quantify biological, psychosocial, and health system access domains of IBD, considering both history and current status so that integrated treatment can be personalized. It includes PROMIS GI symptoms scale[60], a self-report of breadth and depth of GI symptoms and Harvey Bradshaw Index (HBI)[61] and Ulcerative Colitis Activity Index (UCAI),[62] provider-rated scales for IBD disease activity. IBD disease activity will also be assessed using the PRO-2 disease severity index, which is a brief, recently validated patient-reported assessment for individuals with Chron's disease and ulcerative colitis.[63,64]

Behavioral health symptom severity will be measured using scores from IBD Complexity Grid which uses the Patient Health Questionnaire Anxiety-Depression Scale (PHQ-ADS)[65] – which combines the PHQ-8 and GAD-7 scales – as a composite measure of depression and anxiety. The Patient Health Questionnaire 8-item depression scale (PHQ-8)[66] and 7-item Generalized Anxiety Disorder scale (GAD-7)[67] are among the best validated and most commonly used depression and anxiety measures, respectively. The PHQ-ADS is the sum of the PHQ-8 and GAD-7.

Secondary outcomes

Functional impairment will be measured using the Short Form 12 Health Survey Version 2 (SF-12v2)[68] which includes 12 items from the Short-Form 36 Health Survey and yields a physical and mental composite score as well as 8 subscale values: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Lower scores correspond with poorer health-related functioning/quality of life.

IBD-IBS Symptom Severity. The Irritable Bowel Syndrome Symptoms Severity Scale (IBS-SSS)[69] more accurately captures IBD symptom severity for many individuals with IBD, particularly those with inactive IBD but persistent functional GI symptoms (e.g., IBD-IBS). The IBS-SSS scores pain severity, pain frequency, abdominal bloating, bowel satisfaction and interference with life on a 0-100 scale with a total score of 500. A 50-point or more reduction in this score is considered clinically meaningful.

Health care utilization will be captured categorically via medical record data including ED visits and hospitalizations.

Patient engagement will be measured using the IBD Self-efficacy Scale[70] which assesses one's confidence level in managing stress and emotions, managing medical care, managing symptoms and disease, and maintaining remission.

Quality of life will be measured using the Short Quality of Life in Inflammatory Bowel Disease Questionnaire (SIBDQ)[71].

Covariates

Patient demographic and clinical characteristics will be obtained through existing clinical and administrative data on age, gender, race/ethnicity, insurance type, IBD age of onset, surgical history, and presence of ostomy.

e-health literacy will be measured using the eHealth Literacy Scale (eHEALS),[72] which is an 8-item measure of eHealth literacy developed to measure consumers' combined knowledge, comfort, and perceived skills at finding, evaluating, and applying electronic health information to health problems.

Engagement in interventions will be assessed using automatically generated usage statistics, administrative/utilization data routinely collected for in-person visits, remote monitoring activity, and other intervention technologies. The integrity of care delivery for both approaches will be evaluated with existing checklists as part of weekly team huddles.

Resiliency will be measured using the Connor-Davidson Resilience Scale (CD-RISC 10),[73] a validated, clinician-administered, EHR-integrated tool that quantifies, on a 100-point scale, an individual's personal strengths (high resiliency) vs. complexity (low resiliency).

Physical and behavioral health comorbidity will be assessed using the DSM-5 Cross-Cutting Symptom Measure[74] which is an informant-rated measure that assesses current mental health domains across psychiatric diagnoses. ICD 10 codes will be used for current and past psychiatric diagnoses from initial SMH visit and past year ICD 10 codes for medical diagnoses.

Medications will include the use of psychotropic, opioid, and IBD medications.

Transition Readiness will be measured using the Transition Readiness Assessment Questionnaire[75] (TRAQ), a self-reported assessment of health and skills needed for management of chronic disease and will evaluate patient readiness to change from traditional care to patient-centered care where patients and a provider team collaborate on treatment decisions.

Clinic/clinician characteristics will be assessed using clinician self-report years of experience and site-level patient load data. This information will be coupled with the "Engagement in interventions" variables described above.

Process measures

Patient participant and ICT staff perceptions/experience will be assessed via telephonic qualitative interviews with a sample of patient participants and SMH clinical staff to examine perceived barriers and facilitators to efficient and effective implementation of TEAM and TECH and to identify strategies for improvement and scalability of SMH to other chronic diseases.

Integrity of care/fidelity: For both interventions, we will track usage information such as time spent on each session in each arm, techniques covered in practice, techniques practiced, and total number of sessions and techniques completed. For the TEAM arm, the social workers will track if other types of therapy modalities were included from a comprehensive list that can be quantified. For the TECH arm, text messaging from the behavioral coaches will be reviewed for fidelity as part of routine care. Prescription of adjunctive psychotropic medications as part of stepped behavioral care will be tracked in both arms.

Study Population

Our study population will comprise IBD patients receiving care at one of the three included SMHs with a confirmed diagnosis of Crohn's or UC, age 18 to 60 with BH symptom severity in the mild to severe range, defined as a score of >=6 on either depressive or anxiety severity scales (PHQ-4).

Inclusion/Exclusion Criteria

Inclusion Criteria

Individuals who (1) are age 18-60; (2) have a diagnosis of Crohn's or UC; (3) have mild-to-severe behavioral health symptoms, defined as >=6 on either depressive or anxiety severity scales (PHQ-4); (4) consent to be randomized; (5) must have a smartphone; and (6) speak English.

Exclusion Criteria

Individuals who are (1) not able to speak English; (2) do not have a smartphone; and/or (3) exhibiting acute BH symptoms that require a higher level of treatment (e.g., suicidality, active eating disorder).

Study Duration/Study Timeline

February 1, 2019 – June 30, 2019: Pre-Implementation Period
July 1, 2019 – March 28, 2025: Implementation Period
March 29, 2025 – September 30, 2026: Post-Implementation Period

Statistical Analysis Plan

Sample Size and Power Calculations

The bundles of TEAM and TECH services have been tested as packages. For the TEAM approach, we evaluated the feasibility, durability, and impact of the IBD specialty medical home for 346 IBD patients after one year of enrollment.[58] In the year following enrollment, there was a significant reduction in IBD disease activity for both UC (p=.0003) and CD (p=.002), unplanned care (both ER visits (p<.0001) and hospitalizations (p=.008), while there was an observed improvement in health-related quality of life (p<.0001), depression (p<.0001) and anxiety (p=.02). For the TECH approach, a combination of digital tools- an app based cognitive behavioral program, remote monitoring and telepsychiatry (TECH) was compared to behavioral treatment as usual (control) using a randomized trial prospective design for patients with IBD with anxiety and/or depression. There was a significantly greater reduction in anxiety in the TECH group over 3 months (delta 5.6); CI (3.9, 7.6); p<.0001; n=34) than in the control group (delta 2.5; CI (0.5, 4.6); p=.02; n=35. There was also a greater reduction in depression (delta 2.6 CI (0.6, 4.6); p=.01 in the active versus control group (delta=.0.4; CI (-2.2, 3.1); NS).[76] Ninety-six percent of patients in TECH group engaged with the digital CBT program and participated in remote monitoring with 69% completing a clinically meaningful number of sessions. Both studies were conducted in "real world" clinical setting and powerfully show how both approaches can provide powerful solutions in improving health care delivery in sustainable ways.

Aim 1: We calculated statistical power for the target sample size of 675, with approximately 337 participants enrolled into both TEAM and TECH. After adjusting for the multiple testing in Aim 1 (2 tests) and considering 25% attrition, a sample size of 505 (approximately 252 per treatment group) will provide over 99.9% power for the hypothesis test for Aim 1. Among patients enrolled in the specialty medical home at that time who met active behavioral criteria (PHQ-4 >= 6), there was a significantly greater change in TECH (n=73; ES .49) versus TEAM (n=106; ES .36) for the behavioral composite but both approaches were associated with significant change over time (p=.005). Both approaches were also associated with significant improvement in the biological composite for both TEAM (ES .22) and TECH (ES .16). With the IBD SMH models of care being clinically operational at all three sites, we are collecting ongoing useful and robust information that has been published. In our most recent analyses of our clinical research registry tracking our TEAM approach (n=280), our most recent analyses show effect sizes comparable to these initial findings for both approaches.

Aim 2: We considered both subgroup analyses and formal tests of moderation. *Subgroup analyses* – Based on current data, our subgroups are relatively evenly proportioned. We expect that the smallest subgroup will be 42% of the sample and the largest will be 58% of the sample. Thus, our expected subgroup sizes after 25% attrition are between 212 and 293 for projected enrollment. For this range of subgroup Ns, we expect 0.80 power to detect small treatment effects ranging between 0.26 and 0.30. *Moderation* – We used Monte Carlo methods (100 runs) to simulate the binary moderator (M) and treatment (X) (both p=0.5), assuming M independent of X as expected in a randomized trial. Considering a range of effect sizes for B1, B2, and B3, we estimated the outcome Y as $Y=B1*X+B2*M+B3*X*M+ \varepsilon$, where $\varepsilon \sim N(0,1)$. We averaged across

scenarios to determine the typical effect of B3 that can be detected with our current and projected sample sizes after 25% attrition. B3 can be interpreted as the difference between the treatment effect size among those with M=0 (D0=B1). With our projected sample sizes (N=505 after 25% attrition), we expect 0.80 power to detect a significant interaction when the magnitude of B3 is at least 0.50. To provide context for these effect sizes, we note that a B3 of 0.50 could correspond, for example, to a moderate effect of X in one subgroup (e.g., D1=0.60) and a small effect of X in the other subgroup (e.g., D0=0.10).

Our sample size calculations are consistent with the literature for both TEAM and TECH for behavioral and physical disease severity outcomes[77-82] and there is literature supporting engagement and better outcomes with TECH approach with the younger cohort and those with higher eHealth-literacy.[62] However, the research proposed will be beneficial even if we do not prove our hypotheses. For example, even if TEAM and TECH do not differ in Aim 1, the results can still suggest that TECH is feasible and allows TEAM to be utilized more efficiently. In Aim 2, even if we do not show a strong differential impact of the interventions based on IBD activity, we will still learn valuable information about which subgroups of behaviorally complex IBD patients have highest engagement and impact with each approach.

Quantitative Analysis

We will conduct descriptive analyses and multivariate modeling of data to examine changes in outcomes over time and explore moderating variables. All analyses will be intent to treat and conducted as described in our analytic plan and associated protocol. If diagnostic or sensitivity analyses dictate changes to those plans, we will clearly identify subsequent analyses as ad hoc or otherwise deviating from an a priori plan, including labeling subgroup and interaction analyses as confirmatory, exploratory, or post hoc. Our statistician will remain masked to study arm to reduce bias.

Prior to hypothesis testing for Aims 1 and 2, data will be explored by **descriptive data analysis**. Summary statistics including means, standard deviations, medians, and ranges for continuous variables, or frequencies and percentages for categorical variables, will be presented for the entire sample and stratified by approach at each time point. We will assess the balance of key covariates by visually assessing the standardized differences. We will conduct baseline data analysis for each outcome to explore any pre-intervention differences in outcomes between TEAM and TECH at baseline. Two-sided Wald T-test or Wald F-test using the generalized linear mixed models (GLMMs) with normally distributed random effects for three sites will be used. This estimating method using GLMMs will produce consistent estimations of the regression parameters under the missing at random (MAR) or missing completely at random (MCAR) mechanism. The MAR assumption will be verified in the sensitivity analysis (see handling missing data in quantitative analyses). Distributions of outcomes and key covariates over time will also be visually examined to identify systematic departures from normality and overall pattern over time, assisting us in evaluating the distribution of data and determining if assumptions are met for subsequent modeling approaches. We will conduct statistical analysis on transformed outcomes using Box Cox- or log-transformation to address any asymmetry.

Aim 1 will examine the impact of TEAM vs. TECH on the primary and secondary outcomes and will determine if changes in outcomes over time are different between the two groups. We will fit the GLMMs to associate each outcome with the intervention (TEAM vs. TECH) and other covariates of interest. To account for the within-patient correlation in longitudinal data and to reflect potential differences among three sites, we will add normally distributed random effects for patients and sites in addition to the fixed effects for intervention and covariates of interest. An inference of the intervention effects for each outcome will be carried out using Wald test based on the either F-distribution or Chi-square distribution as appropriate. For each outcome, the null hypothesis of homogeneous change in outcomes overtime between TEAM and TECH will be examined by testing the treatment-by-time interaction effect on each outcome. In the absence of significant interaction effects, the marginal difference in outcomes between TEAM and TECH will be examined using the same GLMMs without the interaction effect. All hypothesis tests for Aim 1 will be conducted at the overall significance level of 0.05. The score changes from baseline to each time point and their difference between TEAM and TECH will be estimated with 95% confidence intervals.

Given our study **Aim 2** to understand how TEAM and TECH provide different benefits to individuals with different characteristics, we will explore potential heterogeneity of treatment effects in clinical response between subgroups of patients defined using patients' baseline characteristics. All co-variates will be identified a-priori. For **Aim 2.a**, we will examine whether and how the effect of TEAM and TECH approaches on BH symptom severity varies between patients with a high level of IBD disease activity (HBI or UCAI score > 4) and patients with low disease activity (HBI or UCAI score <=4) at baseline. IBD disease activity and effect of TEAM and TECH approach will also be assessed using a recently developed, validated, and preferred measure of disease activity for Crohn's disease and UC (PRO-2).[63,64] For statistical inference, we will fit the same GLMMs as described in Aim 1 and will include the higher order interaction terms with subgroups of patients defined by IBD activity. The null hypothesis of homogenous treatment effect between patients with high and low IBD activity in each outcome will be examined via interaction analysis (three-way interaction of time, treatment, and subgroup of IBD severity; two-way interaction of treatment and subgroup of IBD severity in the absence of a significant three-way interaction effect) using Wald test based on either F-distribution or Chi-square distribution as appropriate at the significance level of 0.05. In the presence of statistically significant treatment heterogeneity, the score change in BH symptom severity from baseline to each time point and their difference between TEAM and TECH will be estimated with 95% confidence intervals for subgroup of patients defined by IBD severity. For **Aim 2.b**, we will explore whether and how the effect of TEAM and TECH approaches on primary outcomes varies between young (age<=30) and older (age>30) patients. We will also examine the impact of TEAM and TECH on patients with differing IBD diagnoses, namely ulcerative colitis and Crohn's disease. Further, we will explore the effect of site differences, behavioral health history, insurance type (public vs. not), e-health literacy, and medications on response to TEAM or TECH intervention as secondary and exploratory analyses. For statistical inference, the same hypothesis test and statistical model described in Aim 2.a will be used. We will make a Bonferroni correction for multiple testing in order to conduct subgroup analyses at the overall significance level of 0.05. In the presence of statistically significant treatment heterogeneity,

estimation of score changes in each outcome and their difference between TEAM and TECH will be presented with 95% confidence intervals for each subgroup of patients.

In **handling missing data in quantitative analyses**, we will attempt to determine the reasons for missing data and dropouts. The MAR assumption will be examined by comparing baseline characteristics between participants with and without missing data and conducting sensitivity analysis by repeating the main analyses without participants with missing data. If we observe statistical evidence that data are not MAR, we will stratify the participants into subgroups that share the same missing data pattern and estimate the statistical model separately for each missing data pattern. The results of all missing data analyses will be presented, and the sensitivity of our inference to the assumptions and approaches will be included in the interpretation of results.

COVID Considerations for Aims 1-2: Of our 675 projected participants, 32 were enrolled and completed their 6-month/primary outcomes surveys before the beginning of the COVID-19 (i.e., prior to March 12, 2020); 211 are potentially COVID-confounded (i.e., enrolled prior to or during the acute phase of the pandemic and were followed during it), and 432 were enrolled in the post-COVID phase of the study (after June 2021). Primary analyses will focus on the full sample of N=675, controlling for whether the participant was COVID-confounded. In sensitivity analyses, we will include only participants enrolled during the post-COVID phase. Effect sizes from sensitivity analyses will be assessed to evaluate whether findings are similar to those from the primary analyses.

Qualitative Analysis

For **Aim 3**, qualitative interviews will be transcribed verbatim to support the analytic process. Separate codebooks for patients and provider interviews will be constructed and follow standard editing methods,[83] including audit trails to document creation of codes during the iterative process. Two trained independent analysts will code the interviews in Dedoose, an qualitative analysis software. After each transcript is coded, coders will meet to process and adjudicate differences until agreement is achieved. Codes determined through this process will be recorded in a master file to be used in final analysis. For each qualitative cohort and wave of data, we will examine key topics to better understand barriers and facilitators to intervention implementation and how SMHs impact patients' ability to manage IBD and behavioral health conditions. In addition, for each subsequent wave of data collection, we will examine changes and consistency across the data waves.

Informed Consent Process

If a patient is eligible and is interested in participating in the study, the research assistants/research staff will provide the patient with a copy of the consent form to review and obtain informed consent during a clinic visit. Patients will be given the opportunity to take the consent form home to further consider participation in the study. Participants may return the signed consent form by using a prepaid envelope provided by the study team or in-person at later clinic visit.

Study participants will be given a copy of the informed consent to read and research staff will be available to describe its content and answer any questions about the study. Any questions that cannot be answered by research staff will be referred to the PI prior to proceeding with the consent process. All participants will be given an opportunity to take the informed consent document home for further consideration before consenting. Research staff will provide participants with contact information for research staff and the PI so that any questions they may have can be answered before providing consent. Research staff will make it clear to participants that their decision to participate or not in the study will have no impact on the medical care they receive and will stress to the participant that participation in the study is voluntary (their choice). Research staff will also make it clear to participants that they may withdraw their consent at any time during the course of the study.

Privacy and Confidentiality

Self-report and qualitative data collected for this study will be used for research purposes only. Access to the data will be restricted to the PI, Co-Is, and other Research Team members trained in UPMC and University of Pittsburgh HRPO Human Subject Research Training requirements. Research staff will sign confidentiality agreements as required. Identifying links to all data will be maintained at baseline and other data collection time points using a secure password-protected server, accessible only by authorized members of the study team. Once the data is collected, the file containing the link between identifying information and the participant's data will be destroyed.

Qualitative data will be audio recorded using digital recording devices, transferred to a secure server immediately following recording and deleted as soon as it is fully transcribed. Interviews will be audio recorded, transcribed, and scrubbed of identifying information. Participants will be asked not to include any identifying information in their responses, and coders will not code any identifying information that may be provided inadvertently.

All data obtained over the course of the study will be confidential and secure. Paper study records will be secured using the “double-lock” method (i.e., in a locked cabinet within a locked office). Data stored on computers will be password protected and stored on a secure server behind the organization’s firewall. Each Research Team member has a unique network account and a secure password that complies with existing institutional policies and procedures. Only members of the team who are authorized by the PI will have access to the secured files. Identities of participants will not be revealed in the publication or presentation of any results from this study.

Risk/Benefit

Risk to Participants

<u>Infrequent (Rare) Risks:</u>

- The risks associated with this study include the potential for a breach of confidentiality for both groups in the study. To reduce the risk of that happening, we will protect the confidentiality of this information by giving all participants a unique study ID that will be kept separate from any identifying information. The final data set will be de-identified prior to analysis and done so according to HIPAA standards.

- Participants will be asked questions about private, personal matters and information related to their health. They may feel uncomfortable answering questionnaires or assessments or discussing their health with the research team. They may also feel tired from answering questionnaires or having discussions with the research team. There are no known psychological or physical risks associated with the questionnaires and assessments that will be used for this study. Participants will be given the option to stop the assessments or take a break at any time.
- Participants will be monitored by the PI and other members of the research team throughout the duration of the research study. If a participant reports clinical distress to a member of the research team (via study assessment or other form of communication), then the research team will immediately contact the PI. The PI will contact the participant personally to ensure their immediate safety and offer referral for appropriate care. If a clinically significant, unexpected disease or condition is identified during the conduct of the study, members of the IBD SMH will systematically monitor the physical health status of all participating patients through routine care management and patient-level interactions. The assessment of adverse medical sequelae will be managed through a participant's existing and routine care. If during research assessments a high level of medical risk is identified, the research team will attempt to ascertain the nature and level of risk and immediately contact IBD SMH clinical staff for direct follow-up with the participant. The IBD SMH clinical staff will directly contact the participant and refer them to the appropriate level of care in accordance with established protocols
- Electronic or smartphone communications (e.g., text messages, emails, video visits) or internet communication that may happen as part of normal IBD care cannot be guaranteed as confidential. It is possible that confidential information may be collected and used by individuals who do not have permission to do so. All study sites take precautions to prevent this from happening, but there is still a risk that confidentiality may be breached. All electronic study records will be password protected and stored on secure institutional networks or REDCap Cloud, a HIPAA-compliant and secure web-based data collection platform. Paper-based records will be stored in locked filing cabinets and only accessible to members of the research team.

<u>Unknown Risks:</u>

- In addition to the risks listed above, there may be other risks to participant health or well-being that are unknown at this time. They study team proactively monitors participant safety during participation in this research study.

Benefits to Participants

Participants may not directly benefit from research procedures but may benefit from the clinical care approaches being studied in terms of improved physical and behavioral health symptoms, quality of life, and satisfaction with their care.

Compensation for Participation

Total possible compensation for the entire study: $140

Timepoint 1: $20 for baseline self-report measures
Timepoint 3: $20 for 6-month self-report measures
Timepoint 4: $40 for 12-month self-report measures

Timepoint 1: $30 for baseline interview
Timepoint 2: $30 for 6-month interview

Data Safety Monitoring

Dr. Szigethy (Co-PI) will be responsible for data and safety monitoring. She will meet with the study team to review all data protocols and policies, including informed consent and data confidentiality procedures. Co-investigator leads at each participating research site will likewise regularly meet with their respective research teams to review all data protocols and policies. All key personnel will adhere to the National Institutes of Health (NIH) policy on education in the protection of human subject participants in the conduct of research. Additionally, we will convene biannual Data Safety and Monitoring Board (DSMB) meetings to ensure any issues related to participant or data safety are fully addressed.

Conflict of Interest

Drs. Laurie Keefer (Co-PI) and Marla Dubinsky (Co-I) are named inventors on the patented technology entitled "GRITTIBD" (the technology being investigated in this study). The GRITT-IBD technology has been licensed to Trellus Health by the Icahn School of Medicine at Mount Sinai. Trellus Health is a public, for-profit company that develops digital health solutions to manage chronic conditions such as Inflammatory Bowel Disease (IBD). Dr. Keefer is a co-founder, equity owner, consultant, and scientific advisory board member of Trellus Health. Dr. Dubinsky is CEO, a co-founder, equity owner of Trellus Health. Dr. Dubinsky is also co-founder, scientific advisor, and equity owner at MiTest Health. In addition, the Icahn School of Medicine at Mount Sinai has equity ownership in Trellus Health. A Data Management Plan was developed to ensure appropriate management.

Publication and Presentation Plans

We will form a Stakeholder Dissemination Committee in Year 5 of the study. The committee will be comprised of members from the Stakeholder Advisory Board, the Site Working Groups, and additional stakeholders with interest/expertise in SMH models. Collaborators include the Crohn's and Colitis Foundation, the Pediatric IBD Foundation, Connecting to Cure Crohn's and Colitis, and UPMC Health Plan.

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