Records for Alcohol Care Enhancement (RACE) Study Protocol

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Summary of Changes:

Version	Date	Description of Change	Brief Rationale
1.3	11/3/2022	Change to section 14.2. Rather than require data from a hard-copy fidelity checklist be entered within 7 business to the electronic REDCap form, the information will be entered into REDCap within 30-days business days.	The change was made to provide flexibility for data entry procedures into REDCap as the data from fidelity checklists will not be used until the end of the study.
1.4	12/5/22	• Change to section 11 to include language regarding compensation for clinician participants, and expansion of the timeframe for participants to consider enrollment in the study. • Change to section 12 to allow for greater time for clinicians to complete the follow-up survey at the end of the study, and to increase the timeline from recruitment to randomization for the study team	• The change to add compensation was made to increase enrollment rates in the study. • The change to the timeframe participants have to decide to enter the study was made to provide the study team with more time to meet recruitment goals. • The change to increase the time clinician participants have to complete the follow-up survey was made to increase follow-up rates of the survey. • The increase in the timeline from recruitment to randomization was made to provide the study team with increased flexibility to randomize when recruitment goals have been met.

1.5	2/3/2023	• Change to sections 2, 11, and 15.2 is to modify the sample size of enrollment in RACE study, and clarify the total we intend to randomize. • Change to sections 5 and 12 is to allow for randomization to take place at more than one time point. A majority of the enrolled and consented clinicians will be randomized at one time point. Any remaining clinicians enrolled and consented on a rolling basis (until 128 participants have been randomized). With this change of randomization occurring at multiple time points, we also clarify that rather than having all clinicians participate for 18 months, participation in the RACE study may last up to 18 months • Change to section 8 is modify the method in which de-identified quarterly summary reports will be sent. Rather than sent via secure email, the de-identified quarterly reports will be sent via email. The list of identifiable high-risk patients will continue to be sent to clinicians via Epic or secure email. • Change to section 14.2 is to add a potential data source (user metrics from an email marketing campaign software (e.g., ActiveCampaign)) and document how the data collected would be stored securely. • Change to section 15.3 is to state we will do an additional analysis to adjust for the duration of time each clinician spent in the study to account for late entry or early withdrawal to see if they have an impact on treatment estimates. Additionally, upon reviewing the variation in clinician volume from updated CDW clinician volume and panel data, and clinician types (i.e., MD, NP, resident/intern) enrolled, we have modified the randomization stratification. • Change to section 18.1 it to update the schedule of events to note recruitment may take place in months 12-15.	• In our original application and protocol, we had used the number 128 to indicate our total enrollment, however, our intention was to randomize 128 clinicians. We intend to clarify that in order to randomize 128 clinician participants in the RACE study, we will need to consent and enroll more than 128 individuals to account for those who will be disqualified following consent because they did not meet the enrollment criteria to be randomized. • The change to section 5 and 12 is to allow for greater flexibility in the recruitment and randomization timeline. 95% of the needed sample has been enrolled in the RACE study, however, to appropriately reach our target randomization number, and to allow most clinician participants to engage in the intervention for approximately 18 months. With the change that randomization may occur at multiple time points, we clarify that the length of time associated with participation in the intervention to account for clinicians enrolled after the first randomization who may not participate in the intervention for the total 18 months. • The change to send de-identified quarterly summaries via email is to allow the study team flexibility to send the de-identified quarterly reports using email marketing campaign software such as ActiveCampaign to assist in collecting implementation and dose received data for the population health management (PHM) arm. • The change to add a potential data source, user metrics from email marketing campaign software, is to increase implementation data collected as part of the study that may help assess dose of the PHM intervention received by clinicians. Data collected may include number

			of clinicians who opened the email to view the deidentified quarterly report, time viewing the report, etc. Data pulled will be stored securely in HIPAA compliant storage software. • Change to section 15.3 is to state how we will account for and adjust for the time of the several clinician participants receiving the intervention for less than the full 18-months, as well as make a modification to randomization stratification to improve efficiency and effectiveness of randomization. • Change to section 18.1 was made to in response to the need to recruit several clinicians after the first initial randomization, and until 128 in total are randomized.
1.6	7/31/2023	Revise sections 2, 5, 11, 12, 15 to state that we intend to randomize at least 128 clinician participants.	Our power calculations estimated that with 128 clinicians randomized in the study, we would have reasonably high power to detect a difference between study arms for the primary endpoint of interest. Since 128 is our randomization goal, we are amending the protocol to clarify that at minimum we plan to randomize 128 clinicians; thus more than 128 clinicians may be randomized.
1.7	8/15/2024	Revise section 4.2.2 Secondary Outcome Measures to: • Remove Topiramate from the list of AUD medications in the outcome pertaining to patients prescribed AUD medications • Change “visits with a BMC integrated behavioral health social worker” to “visits with a BMC mental health clinician”	We have removed Topiramate from the list of AUD medications in our secondary outcome because, while occasionally prescribed to patients with AUD, Topiramate is not FDA approved for the treatment of AUD. Removing Topiramate from the AUD medications included in our secondary outcome will ensure our secondary outcome is aligned with AUD medications included in national quality of care measures, and limited to those FDA approved for the treatment of AUD. We have revised the language “integrated behavioral health social worker” to “mental health clinician” as the original language specific to integrated behavioral health social worker was unintentionally limiting and

			narrow and not reflective of the actual outcome the study intends to measure and capture. This outcome is meant to measure mental health treatment utilization (such as visits with a psychologist, etc, and not solely mental health treatment provided by integrated behavioral health social workers). As such, we've updated our language to more accurately align with the secondary outcome the study seeks to measure.

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1 List of Abbreviations

Abbreviation	Abbreviation definition
AA	Alcoholics Anonymous
ACO	Accountable Care Organization
AE	Adverse Events
ALT	Alanine Transaminase
AST	Aspartate Transaminase
AUDIT	Alcohol Use Disorder Identification Test
AUD	Alcohol Use Disorder
BEDAC	Biostatics Epidemiology and Data Analysis Center
BMC	Boston Medical Center
BMC ACO	BMC Medicaid Care Alliance Accountable Care Organization
BMCHNP	BMC Healthnet Plan
BPA	Best Practice Advisory
CCM	Clinical Care Manager
CDS	Clinical Decision Support
CDW	Clinical Data Warehouse
COVID-19	Novel Coronavirus Disease (SARS-CoV-2)
DSM	Diagnostic and Statistical Manual of Mental Disorders
ED	Emergency Department
EHR	Electronic Health Record
GEE	Generalized Estimating Equations
GIM	General Internal Medicine
HEDIS	The Healthcare Effectiveness Data and Information Set
HCU	Health Care Utilization
ICD	International Classification of Diseases
MASBIRT	Massachusetts Screening, Brief Intervention and Referral to Treatment
NIAAAA	National Institute on Alcohol Abuse and Alcoholism
NIH	National Institutes of Health
NCQA	National Committee for Quality Assurance
NP	Nurse Practitioner
OBAT	Office Based Addiction Treatment
PHM	Population Health Manager
PO-NTX	Oral Naltrexone
PPV	Positive Predictive Value
Principal Investigator	PI
Project Coordinator	PC
Project Manager	PM
RACE	Records for Alcohol Care Enhancement
SAE	Serious Adverse Events
SAS	Statistical Analysis System

SW	Social Worker
VIF	Variance Inflation Factor
XR-NTX	Injectable Naltrexone

2 Protocol Summary

Unhealthy alcohol use, (the spectrum from risky consumption through alcohol use disorder, **AUD**) is a leading cause of preventable death in the US (88,424 deaths annually[1]), costing $249 billion a year[2], and associated serious alcohol related health harms (e.g., AUD itself, cirrhosis) are increasing[3–6]. Though individuals with unhealthy alcohol use are frequently in contact with the medical system, most do not receive effective interventions to reduce alcohol-related harms[7], leaving them vulnerable to negative health consequences. Electronic health records (EHRs) are a tool that can be used to improve services and interventions for individuals with AUD. Integrated health systems[8–12] have the opportunity to leverage EHR systems to improve AUD care. However, it is not clear how settings that lack extensive infrastructure can utilize EHRs to improve population-based care outcomes beyond screening and prevention. The Records for Alcohol Care Enhancement (RACE) study will use data collected from routine clinical practices in EHRs along with population health management (PHM) and/or clinical care management (CCM) to improve the identification, management, and support for individuals with AUD in the Boston Medical Center (BMC) General Internal Medicine (GIM) primary care clinic, where a majority of patients are insured through an accountable care organization.

During the initial (R21) phase of the RACE grant (which is an R21/R33 mechanism), the study team updated an Epic-based best practice advisory (BPA) and clinical decision support (CDS) for patients with risky alcohol use or alcohol use disorder. The study team also created a usable live registry in Epic of BMC primary care patients with risky alcohol use and/or possible or confirmed alcohol use disorder. In this next phase of the project (the R33 phase for which this protocol is written), the research team will 1) maintain the BPA, CDS, and alcohol registry; 2) will re-introduce the features of the BPA/CDS and management of risky alcohol use/AUD to the BMC clinicians during study recruitment; and 3) test the feasibility and preliminary effectiveness of leveraging the electronic health record (EHR) for AUD care with or without population health management and/or clinical care management support. This R33 portion of the RACE study will implement a four-group randomized control trial whereby clinicians will be randomized to the BPA/CDS Epic tools only group (hereafter referred to as “BPA”), or one of three other intervention groups following a factorial design (BPA+CCM, BPA+PHM, or BPA+CCM+PHM) that provides targeted support to clinicians around identifying and treating their patients with alcohol use disorder. The trial will assess whether PHM and/or CCM enhancements improve and facilitate care for patients with AUD, and improve outcomes beyond EHR prompting (BPA) alone. We aim to enroll approximately 130 primary care clinicians (randomizing at least 128 clinicians), ages 18 years or older, and practice primary care at Boston Medical Center (BMC) in the General Internal Medicine (GIM) primary care clinic. Enrolled clinician participants will then be randomized to one of the following arms:

1. Clinician prompting and decision support best practice advisory alone (BPA)
2. BPA plus population health management (BPA+PHM)
3. BPA plus clinical care management (BPA+CCM)
4. BPA plus population health management plus clinical care management (BPA+PHM+ CCM)

The study is anticipated to last for a total of 3 years. The first year is used to design and prepare for the study, and recruit, enroll and randomize all participants. Following randomization, the active intervention with clinicians will last a total of 18 months. Data cleaning and analysis will be an ongoing process from the beginning of the intervention through study closure. Clinician participants will be involved in the study for up to 18 months regardless of the randomization group to which they are assigned. In the final year, there will be continued data collection from Medicaid claims data (the data source for the trial primary outcome), and from the BMC Clinical Data Warehouse (CDW), and data analysis, and reporting and dissemination of study results/findings.

The primary objective is to test the feasibility and obtain preliminary effectiveness estimates of the 4-arm randomized trial in increasing engagement in treatment for AUD, including AUD medication use, counseling, and specialty AUD care, to improve the identification and management of unhealthy alcohol use, particularly AUD, in a real-world urban accountable care organization (ACO) primary care setting. In achieving these aims, we will demonstrate the feasibility and potential ability of leveraging EHRs in an innovative way to improve AUD care. Results will inform improvements in clinical care, and systems of care to reduce alcohol-related morbidity and mortality.

3 Background/Rationale & Purpose

3.1 Background Information

Unhealthy alcohol use is very prevalent across the United States, contributing to many preventable deaths, and harms related to alcohol use are rising [1,3–6,13,14]. Despite high frequency of contacts with the medical system, most people with unhealthy alcohol use do not receive evidence-based interventions[7]. This may be due to a variety of factors such as stigma, lack of knowledge, challenges with implementing and maintaining tool-based screening, time or prioritization constraints in a busy clinical environment, and more[15–17].

EHRs are a useful and practical tool that may be utilized to improve care for individuals with AUD. Other integrated health systems have used EHRs (e.g., Veterans Health Administration, Kaiser Permanente, etc.) to improve health care in primary care settings[8–12], however there are limited examples that have not been supported by significant infrastructure. EHRs are also known to improve management of chronic disease (e.g., diabetes[18]) through BPAs, and registries by aggregating information about the target population, and by assisting the clinician in reminders, decision support, and disease-specific care management[19,20]. Particularly, EHRs may help clinicians identify, assess, treat and monitor care when assisted by targeted staff support such as a clinical care manager and population health manager (CCM and PHM)[21–25]. These support staff may help to track outcomes of care and treatments provided, allowing for increased engagement with the population, and facilitation of care that otherwise may not be prioritized.

In the R21 phase of the **RACE** (**R**ecords for **A**lcohol **C**are **E**nhancement) grant (2019-2021), the study team created a clinically useful live database/registry of patients with unhealthy alcohol use in BMC Epic, and updated Epic-based BPAs and clinical decision support (Epic Smart Set) for risky alcohol use and alcohol use disorder. Initial findings suggest that the changes made to the EHR were valuable, and that there is a need and opportunity to continue to improve screening, identification, diagnosis, and treatment for patients with an alcohol use disorder in the primary care setting. The current R33 phase aims to improve recognition, management, and overall services provided to patients with AUD by continuing to leverage the alcohol registry and changes made to the EHRs, and allocate targeted supports to primary care

clinicians – specifically a CCM and PHM, to further prompt screening/identification of AUD and support clinicians in engaging their patients with AUD in treatment. A four-group randomized control trial will be implemented to determine which of four interventions is most effective at increasing rates of initiation and engagement in AUD treatment, as well as other clinical processes and outcomes such as referral to AUD specialty care. The trial will compare the use of the 1) BPA alone (only Epic-based clinician prompting and clinical decision support), 2) BPA + PHM, 3) BPA + CCM, and 4) BPA + PHM + CCM, on the trials' primary, secondary, and exploratory outcomes. Trial results will be assessed by examining outcomes for patients on the clinician's panel.

The main risks of this research study include inconvenience (to clinicians) and potential loss of confidentiality (clinician and/or patient). The main benefits include the ability to improve patient health and outcomes, and inform health service organizations about pragmatic and useful innovations for improving care for vulnerable populations.

This study will be conducted in compliance with the protocol, applicable regulatory requirements, and policies and procedures of the Boston Medical Center and BU Medical Campus Human Research Protection Program.

3.2 Rationale and Purpose

Current recommended guidelines for alcohol screening and brief intervention have had little meaningful impact due to their modest efficacy[26], limited attention to treatment for AUD[27–29], and implementation failures[15,30–33]. Measurement-based care, the systematic use of patient-reported outcomes during clinical care to inform treatment decisions has been shown to improve outcomes in mental healthcare (example: depression), but has not been used consistently in SUD care, including AUD care[34]. Additionally, in primary care settings, the focus has been on intervening on individuals with risky alcohol use, rather than on patients with known or potential AUD. While continuing to intervene on individuals who have risky alcohol use, the RACE study will facilitate targeted interventions on patients with known or potential AUD through enhancement of tools in the EHR and through targeted clinician support. AUD is both an under-diagnosed and under-treated medical condition. EHRs are an existing mechanism and asset that can be used to improve identification and management of AUD. EHRs have previously been used to collect screening information, calculate and display results, prompt identification/diagnosis, and provide decision support for brief intervention, but they have not been leveraged for their potential to improve quality of AUD care[8,35–37]. Diverse populations in underserviced areas where the prevalence of AUD is high, are often not the environments where such technological advancements are applied.

The research team will work to expand the potential impact of the EHR tools for risky alcohol use and alcohol use disorder (the BPA, CDS, registry and registry-based reporting) by incorporating a PHM and CCM to augment reach and support to clinicians. This project has the potential to improve AUD care by implementing and maintaining an alcohol registry and the BPA/CDS, and by testing feasibility and effectiveness of targeted clinic personnel or roles. The combination of systems and service approaches employed in this study could be widely disseminated and implemented in many care settings. Though there are several barriers (e.g., stigma, lack of knowledge, lack of time, challenges with implementation of screening and recommendations for care[15–17]) to providing care for patients with an AUD, the EHR in combination with the PHM and CCM may serve as robust infrastructure for practical clinical approaches superior to the EHR alone. The four-group randomized trial will test the feasibility

and obtain preliminary effectiveness estimates. The primary hypotheses are that compared to arm 1 (BPA alone), the BPA combined with PHM (arm 2) and BPA combined with CCM (arm 3) separately, and the BPA combined with both CCM and PHM roles (arm 4) will improve engagement (a national quality of care measure), receipt of AUD care (e.g., medication, counseling), and reduce acute care utilization related to AUD.

The proposed project has several innovative elements: 1) Use of electronic records to support AUD management in an urban safety net ACO hospital-based primary care practice; 2) use of a widely implemented EHR to demonstrate feasibility and allow wider dissemination beyond large health systems that have substantial infrastructure support; 3) use of both health records and in-person screening to identify unhealthy alcohol use in a real world clinical care setting; 4) use of EHR and Medicaid claims data to capture clinical outcomes for clinical care and research; 5) and studying the incremental effect of PHM and CCM on EHR tools to improve AUD care.

4 Objectives

4.1 Study Objectives

The primary objective is to test the feasibility and obtain preliminary effectiveness estimates of a 4-arm randomized trial that provides targeted support for alcohol use disorder as a chronic disease by enhancing the utility of EHR tools to improve initiation and engagement in treatment for AUD (a national quality of care measure), as well as other outcomes such as rates of alcohol-related acute care utilization (emergency department visits and inpatient encounters). In achieving these aims, the research will demonstrate the feasibility and potential ability of leveraging EHRs to improve the identification and management of unhealthy alcohol use, particularly AUD, in a real-world urban ACO primary care setting. Preliminary testing will inform around effectiveness for improving care that could lead to better clinical outcomes including a reduction in heavy drinking, fewer alcohol-related emergency department visits, and less alcohol-related morbidity and mortality in the US.

4.2 Study Outcome Measures

Outcomes for the RACE trial include two outcomes that map onto the Healthcare Effectiveness Data and Information Set (HEDIS) initiation and engagement of Alcohol Abuse or Dependence Treatment, a national quality of care measure: initiation and engagement in AUD treatment (defined below)[38,39]. We will also measure alcohol attributable care such as acute (emergency department and inpatient) and outpatient healthcare utilization, and other AUD related health outcomes including AUD medication prescribing, AUD specialty care, and referrals to counseling. Outcome data will come from Medicaid claims data and BMC Epic data from the BMC CDW to assess the effect of the study intervention on outcomes. These data will be collected at multiple time points throughout the intervention period and after the intervention has concluded (due to lag times in processing Medicaid claims data and such data becoming available for researcher access and use).

4.2.1 Primary Outcome Measures

The primary outcome in the RACE study is engagement in AUD treatment. Engagement in AUD treatment was chosen as it is a national quality of care measure, and is feasible and generalizable to other settings[39,40]. Treatment engagement is associated with a reduction in mortality for individuals with

a substance use disorder, lower addiction severity especially for outpatients with AUD, improved employment and wages for individuals involved in the justice system, and fewer arrests for crimes[38,40,41]. Engagement is defined as having two or more healthcare services (inclusive of AUD medication) with a diagnosis of alcohol use disorder within 34 days of initiating care[42,43]; initiation is defined as having a healthcare service (inclusive of medication) with a diagnosis of AUD within 14 days of a new AUD diagnosis[43]. A new AUD diagnosis is defined as a healthcare service in which a patient receives a new AUD diagnosis when there has not been an AUD diagnosis for a healthcare service during the prior 194 days, excluding diagnoses assigned in the emergency department/detox[43]. BMC Healthnet Plan (BMCHMP), a longstanding managed care organization under MassHealth, serves under the Boston Accountable Care Organization (ACO) and collects this information based on Medicaid claims. The study will gather data for the primary outcome from BMC ACO Medicaid claims data at multiple time points throughout the study due to the 3–9-month lag time for claims completion. Initial collection of data will be completed as the intervention ends, and conclude with a final request for data approximately 6-months post intervention. Overall, using engagement as the primary outcome balances what is achievable by the intervention, and has the potential to demonstrate improvement on a measure with significant clinical meaning.

4.2.2 Secondary Outcome Measures

There will be several secondary outcome measures. Initiation of AUD treatment (as defined in section 4.2.1 (having a healthcare service (inclusive of medication) with a diagnosis of AUD within 14 days of a new diagnosis)) is a secondary outcome. Initiation alone is a secondary outcome instead of the primary outcome because there are few studies that find improved outcomes associated with initiation compared to engagement. Initiation will be measured using BMC ACO Medicaid data. Additional secondary outcomes for this study will be assessed using primarily BMC Epic data from the BMC CDW (although some measures will use Medicaid claims data) and include the following outcomes among BMC primary care patients with a new AUD diagnosis:

- Patients who have been prescribed AUD medication such as Naltrexone, Intramuscular (IM) Naltrexone, Acamprosate, or Disulfiram[44] within 90 days of a new AUD diagnosis, among patients with a new AUD diagnosis on a clinician's panel. Where possible, we will also look at fills of these prescriptions in Medicaid ACO data.
- Any and number of Boston Medical Center (BMC) outpatient encounters with an AUD billing diagnosis within 90 days of a new AUD diagnosis, among patients with a new AUD diagnosis on a clinician's panel.
- Any and number of visits with a BMC mental health clinician with an AUD diagnosis (encounter with AUD as a billing diagnosis) within 90 days of a new AUD diagnosis, among patients with a new AUD diagnosis on a clinician's panel.
- Any and number of referrals for counseling or specialty AUD care such as the BMC Office Based Addiction Treatment (OBAT), Center for Addiction Treatment for AdoLescent/Young adults who use SubsTances (CATALYST), etc., within 90 days of a new AUD diagnosis, among patients with a new AUD diagnosis on a clinician's panel.

Additionally, we will examine any and number of completed encounters for AUD specialty care as recorded in the EHR within 90 days of a new AUD diagnosis, among patients with a new AUD diagnosis on a clinician's panel. Lastly, we will assess any and number of acute care utilization (emergency department visits and hospitalizations), as well as any and number of acute care utilization (emergency department visits and hospitalizations) with an alcohol-related diagnosis within 90 days of a new AUD

diagnosis, among patients with a new AUD diagnosis on a clinician's panel from Medicaid ACO data to capture care utilization outside of BMC. Initial collection of Medicaid ACO and clinical data warehouse data will be collected as the intervention ends and conclude with a final request approximately within 9-months post intervention. These additional outcomes will help support the primary outcome, and assess additional effects of the intervention.

4.2.3 Exploratory Outcome Measures

We will examine the number of heavy drinking days in the past year reported on the single item screen in the patient's Epic record. Currently, when a patient is seen int the BMC primary care clinic, they receive a single item screening question that asks how many times in the past year have they had greater than 5(males)/4(females) drinks in one day, which is entered into the patient's chart as a numerical result of the number of heavy drinking day episodes the patient has had in the past year. This result is used operationally in the clinic to help identify if a patient is likely to have unhealthy alcohol use and requires additional screening with the AUDIT. Since screening for alcohol use is not consistently completed in the primary care clinic, we will examine number of heavy drinking days as an exploratory outcome.

5 Study Design

The R33 implementation phase of the study will assess feasibility and obtain preliminary effectiveness estimates in a 4-arm factorial randomized trial comparing 1) clinician prompting and decision support (BPA alone), 2) BPA + PHM support, 3) BPA + CCM support, and 4) BPA + PHM + CCM support, to increase engagement in AUD care. Participants in the study are medical clinicians (physicians, nurse practitioners, and residents, and fellows) that provide clinical care to patients who receive care in the BMC GIM primary care clinic. A majority of the enrolled and consented clinicians will be randomized at one time point using a permuted block strategy. Any remaining clinicians enrolled and consented on a rolling basis (until at least 128 participants have been randomized), will subsequently be randomized using a permuted block strategy. Randomization will be stratified by clinician type and patient panel volume to ensure patients are evenly distributed across randomized groups. Clinicians are the enrolled and randomized research participants in the study and will complete informed consent procedures. Patient participants will not complete research study activities, rather, patients may receive improvements in quality of care as a result of the targeted support provided to their clinician (PCP) participants. Patients will not receive investigational or experimental treatments or services as the intervention is designed to increase patient access to standard of care. The RACE study intervention(s) are designed to improve GIM clinician delivery of gold standard evidence-based care for AUD. Identifiable data from patient participants will be collected from the medical record and Medicaid claims.

The conceptual framework/logic of using the EHR to improve AUD care involves collection of data that is otherwise not collected systematically, presentation of those data at the time of a clinician visit when it is relevant in the form of a prompt, provision of clinical decision support to facilitate assessment, brief advice and counseling, medication prescribing, and referral for counseling and AUD specialty care, and a mechanism for measurement-(monitoring-) based care in follow-up (repeat prompts). Although EHR enhancements can improve care, impact is modest. This may be even more likely for AUD, a condition that is associated with stigma, and about which primary care clinicians may have less knowledge and skill than other chronic conditions. Thus, the study aims to expand the potential impact of the EHR with

enhancements that provide additional clinical prompting and support (the PHM and CCM). The EHR for all clinicians will include prompting and decision support through the BPA. For clinicians who receive support from the PHM, the PHM will NOT directly help clinicians manage and implement patient care plans, rather the PHM will provide clinician panel-level feedback from the registry and decision support tools through quarterly reports and weekly summaries of high-risk patients. For clinicians who receive support from the CCM, the CCM is expected to not only suggest potential care opportunities to clinicians for patients with AUD, but also to help facilitate AUD treatment, referral, monitoring, and follow-up through direct interactions with patients. The CCM will be an existing BMC nurse who will facilitate AUD care through existing nursing practices and protocols. The study will not evaluate new systems of care delivered by nursing, but rather it will evaluate having a nurse with dedicated time to support AUD as a chronic disease model of care.

Primary outcome and some secondary outcome data will come from BMC ACO Medicaid claims, and data for secondary outcomes will be obtained from the EHR (BMC Epic) via the BMC CDW as well as BMC ACO Medicaid claims data. The CCM and PHM will also regularly (approximately weekly) complete a Fidelity to the Intervention Checklist, that will supplement EHR assessment of fidelity to the intervention. Additionally, after a clinician consents to participate in the trial, they will be asked to complete a brief socio-demographic survey via a REDCap form. At the close of their time in the study, participating clinicians will be asked to complete a brief follow-up survey, similar to the baseline socio-demographics survey. These surveys will be used to understand baseline characteristics of enrolled clinicians, clinician confidence as it relates to providing alcohol related care, and include an open-ended question on their experience as a participant in the trial. Other relevant clinician characteristics (title, highest degree completed, etc.) will be collected via public data.

6 Potential Risks and Benefits

6.1 Risks

Potential risks for clinician participants include inconvenience related to the time required to participate in the intervention and loss of confidentiality. Potential risks for patient participants include loss of confidentiality. These are minimal risks, consequences are not likely, and will be further minimized by researchers as described below.

Inconveniences: For clinician participants, inconvenience is a potential risk that may occur due to time spent engaging in the intervention activities with the CCM and PHM. It may be inconvenient for enrolled clinicians to take time to review reports and messages from the population health manager and/or clinical care manager and to facilitate and provide additional AUD patient care that they may not otherwise have provided. However, the extent to which enrolled clinicians actively engage with the PHM or CCM, and the reports are up to the clinicians and are entirely voluntary. Additionally, it is routine practice for clinicians to receive information about their performance on healthcare quality metrics, and while the HEDIS initiation and engagement measure (the target of this study) is not currently a routine performance metric shared with BMC GIM clinicians, performance on other similar quality measures such as depression care management, are routinely shared. Thus, we would not consider this risk of inconvenience to be more than minimal, as it would be similar to inconveniences they already encounter outside of the research setting.

To minimize the risk of inconvenience, we will describe the potential burden of time associated with the study and study contacts in the informed consent. It will be stressed that participation is completely voluntary and that they can withdraw from the study at any time. Additionally, when the PHM shares reports clinicians enrolled in the PHM arm(s), they will only get information in 1-on-1 meetings with the PHM, or through emails directly between the PHM and the clinician. Identifiable individual performance, information will never be shared with anyone other than the enrolled clinician. We may share blinded (for practice variability) and/or as aggregate data by suite for providers within a suite who have been randomized to the PHM arm(s). Blinded data would allow people to see where they stand in comparison to their peers, but not actually see who those other individuals are.

Loss of confidentiality: Loss of confidentiality is potentially the most serious risk to clinician participants in the proposed study. Loss of confidentiality for clinician participants could occur is someone sees responses to interview assessments or others quality metric reports, or when research staff make attempts to contact them throughout the study period, though it is very unlikely because specific procedures will be implemented to prevent such disclosure. Additionally, loss of confidentiality is the principal risk for patient participants, however we will not have direct contact with patient participants for data collection. Data will be solely collected through Medicaid data claims and Epic data via the clinical data warehouse (CDW). The risk is minimal because all of this information is already collected in the electronic health record (EHR). Though the information collected is already available in the source databases, and we will take measures to secure data appropriately, it is sensitive information relating to health status and alcohol use.

To assure confidentiality, data will be kept in a secure electronic environment (e.g., REDCap, Box) only accessible to research staff such as the principal investigator, the project manager, and research assistants. Any clinician participant direct identifiers (e.g., names, addresses, contact information, etc.,) and patient direct identifiers will be will be password protected, and accessible only to staff needing the information for appropriate study procedures. Study data collected on paper forms will be stored in locked filing cabinets.

To minimize risk for all clinician participants, they will be informed of the potential for breach of confidentiality during the informed consent process. The CCM and PHM will follow routine GIM clinic and BMC practices, and policies and procedures for ensuring privacy and confidentiality when working with patients and/or accessing PHI. Therefore, any risk of loss of confidentiality for patient-participants will be no greater than minimal risk. To minimize risk of loss of confidentiality to clinician and patient participants, we have a Certificate of Confidentiality from the National Institutes of Health to further protect against loss of confidentiality.

6.2 Potential Benefits

There may be no benefits to any participants from participation in the study. Clinician participants may benefit from increased support and information around the patients on their panel with AUD. Patient participants may benefit from the increased assessment and access to evidence-based, standard of care treatment for AUD. Society, medical science, and the health care system may benefit from the information obtained about advancements to EHR and care innovations provided by the BMC primary care clinic. Particularly, the study has the potential to improve quality of care for patients with AUD.

6.3 Analysis of Risks in Relation to Benefits

The principal risk of participating in the RACE study is loss of confidentiality to clinician and patient participants. The occurrence of this risk is not likely. The anticipated benefits for patient participants include potential for improved quality of care and receipt of evidence-based care through improved identification of unhealthy alcohol use, intervention tools, and targeted support. The anticipated benefits for clinician participants include improved decision support through the EHR, as well as increased targeted support by the CCM and PHM to improve well-being of patients on their panel. The knowledge resulting from this study has potential to help patients and health service organizations as information about the changes in care outcomes will inform future care and future innovations. This information could be useful in understanding the successes and challenges of new interventions, and widely disseminated and implemented in care settings. The opinion of the research team is that the potential benefits outweigh the risks of this study.

7 Study Subject Selection

7.1 Subject Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Primary Care Clinician Subjects:

- Adult (18 years or older)
- Physician or Nurse Practitioner
- Practices primary care at Boston Medical Center in the General Internal Medicine Primary Care Clinic
- Current position in the practice expected to be unchanged for a minimum of 18 months (not a graduating trainee)

Patient Subjects:

Records (EHR, Medicaid ACO claims) from all patients empaneled (patient is assigned to PCP's primary care panel) by study enrolled clinicians who are:

- Adult (18 years or older)
- Have had at least 1 completed visit in general internal medicine at BMC during the last 18 months.
- Eligible for alcohol related care based on high-risk screening results or an alcohol related diagnosis

7.2 Subject Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

- Clinicians who, at the time of study recruitment, are expected to remain in their BMC GIM position for less than 18 months (e.g. resident or fellow trainees expected to graduate within the study time period).
- Limited and non-readers

8 Study Intervention

The RACE study has four intervention groups (BPA only, BPA+CCM, BPA+PHM, or BPA+CCM+PHM) that provide various targeted support to assist clinicians in identifying patients with unhealthy alcohol use and engaging patients in treatment for AUD.

Four-arm randomized control trial:
All groups in the RACE randomized control trial (and all clinicians in the BMC primary care clinic, regardless of RACE trial enrollment) will receive Epic-based prompting, a "best practice advisory" (BPA), that will appear when a clinician opens an Epic record for a visit with a patient who has screened positive on the single item screening question, AUDIT screening survey, or by having past-year utilization with an alcohol-attributable ICD-10 diagnosis code. Most often, alcohol use screening is be done by a medical assistant in the GIM clinical setting as is current standard of care. Medical assistants administer the single item screening tool; if this result is positive the patient will be given the 10 item Alcohol Use Disorders Identification Test (AUDIT). If the single item screening is positive (> 0 <4) and/or the AUDIT is 8-13 (female) or 15(male), the BPA will fire with "Risky Alcohol" decision support. If the single item screening is >= 4 and or the AUDIT > 13/15 or has a sum >=4 on the AUDIT dependence questions (questions 4-6), the BPA will fire with AUD decision support[45]. The EHR prompt that the primary care clinician receives includes the numerical result from patients' responses to self-report alcohol screening questions. From the BPA, the clinician has the option to open a Smart Set which contains clinical decision support for diagnosis and management of risky alcohol use and AUD. Decision support will depend on the screening results but may include the following: 1) suggestion that the clinician assess the patient using the AUDIT or interview the patient about AUD DSM criteria (both of which will be presented on the screen along with EHR data fields for recording findings) and 2) approaches to managing risky alcohol use and/or alcohol use disorder. For those with risky use (positive screen but no current AUD) guidance will be provided regarding brief intervention (feedback, advice to cut down or abstain [e.g. pregnancy or trying to conceive, contraindicated medications or medical conditions, past disorder], goal setting, and follow-up [to measure/monitor by reassessing heavy drinking episode frequency, and AUD symptom appearance]). For those with AUD, clinicians will be presented with a range of options to discuss with patients focusing on 1) medications and how to prescribe them (naltrexone, acamprosate, disulfiram, and topiramate), 2) click-button referrals in the EHR to Office Based Addiction Treatment (OBAT) and Integrated Behavioral Health (IBH), and 3) information and printed patient referral materials for seeking AUD specialty care outside BMC (including links to the NIAAA Treatment Navigator https://alcoholtreatment.niaaa.nih.gov/ posted fall of 2017). Although not treatment, information will be provided on how to connect patients with mutual help groups (Example: alcoholics anonymous).

PHM Description of Activities:
The PHM will use weekly and monthly generated registry and work bench reports to examine the clinician panel-level data on patients with an active AUD (i.e. not in remission) on their problem list, those with suspected AUD on each clinician panel, and to identify high-risk AUD patients who should be targeted for outreach. The lists of identified high-risk patients will be sent to clinicians securely via Epic and/or secure email. The quarterly reports on summary metric data will be sent via email, however, the clinicians will choose how little or much they would like to engage with the PHM and reports. A fidelity checklist will be used to document other information such as the types of work reports pulled, if graphs and charts were sent to the clinician, the frequency of reports pulled, etc.

Additionally, the PHM may use a fidelity checklist to track frequency, types of work reports pulled in Epic, etc., to understand fidelity to the intervention. Particularly, the fidelity checklist may be important

for providing context for reproducibility, and determining aspects of the intervention that were successful to understand reach and acceptability of the intervention.

For clinicians assigned to the BPA and PHM group, they will have access to the following resources:

- Continued access to the existing Epic BPA and Clinical Decision Support (Smart Set) for Risky Alcohol Use and AUD.
    - The BPA will continue to operate routinely, wherein the clinician participant will receive prompting when they open an Epic record for an encounter with a patient who has risky alcohol use, or a possible or confirmed alcohol use disorder.
    - From the BPA, the clinician participant will have the option to open a Smart Set which contains clinical decision support for diagnosis and management of risky alcohol use and AUD.
- The clinician participant will be supported by a **population health manager** who will access an existing registry of patients with possible or confirmed alcohol use disorder and utilize work bench reports to examine outcomes and quality metrics for patients with alcohol use on their patient panel.
    - The PHM will send the clinician participant quarterly reports with summaries of (de-identified) data, charts, and graphs that show the numbers and percentages of patients on their panel who need additional prompting and screening for alcohol use care, as well as the number and percentage of patients on their panel with AUD who have initiated and engaged in treatment for their AUD. These will be circulated via secure email to clinicians.
        - The PHM may offer clinicians the opportunity to review the reports in one-on-one meetings to further assess barriers and facilitators to AUD care, and to help explain and interpret results.
    - When applicable, the PHM will send the clinician participant a weekly Epic message about higher risk patient(s) (patients who were recently (past 7 days) seen in the acute care setting or by BMC Faster Paths for an alcohol-related health problem for whom outreach may be beneficial.
        - In addition to sending this information to the clinician participant via secure Epic staff message, the PHM will send the General Internal Medicine (GIM) front desk staff an Epic message regarding a high-risk patient to facilitate scheduling a GIM visit for the patient within two weeks of their new AUD encounter, and copy the clinician participant on the staff message.
        - The Epic message to the GIM staff will include instructions on what can be communicated to the patient, and the GIM staff will be instructed to inform the clinician and the PHM (and CCM if in the combined PHM and CCM arm), the outcome of the outreach call.
    - The PHM may share aggregated and deidentified data that may be reviewed in group meetings to identify systems barriers or other issues related to clinical care for AUD.
    - Data reviewed may include number and percentage of patients screened with results suggestive of unhealthy alcohol use or AUD, patients with a new AUD diagnosis meeting criteria for initiation and engagement (as defined by the HEDIS measure), and patients with AUD referred to AUD specialty care or behavioral health support.

The effect of PHM is anticipated to be on motivation to respond to the screening prompt and fully engage with the BPA. The PHM helps clinicians know how they are doing managing AUD. However, PHM

does not directly help clinicians with implementation of care with individual patients. PHM has no patient contact.

CCM Description of Activities:
The CCM will use weekly study generated Epic work bench reports to assess and identify patients on the clinician panel who may need additional alcohol related care follow-up. The work bench reports will streamline identification of relevant patients based on certain characteristics as they relate to the study outcomes. For example, Epic work bench reports will include patients who had a new AUD diagnosis and are eligible for initiation and engagement for AUD care. The CCM and the clinician participant will collaborate to assist patients in receiving care for AUD; however, the clinician participant can choose how little or how much to engage with the CCM in providing alcohol use related care to patients.

Additionally, the CCM may use a fidelity checklist to track frequency, types of work reports pulled in Epic, etc., to understand fidelity to the intervention. Particularly, the fidelity checklist may be important for providing context for reproducibility, and determining aspects of the intervention that may have been successful to assist in understanding the reach and acceptability of the intervention.

For clinicians assigned to receive BPA and CCM, they will receive the following resources:

- Continued access to the existing Epic BPA and Clinical Decision Support (Smart Set) for Risky Alcohol Use and AUD.
    - The BPA will continue to operate routinely, wherein the clinician participant will receive prompting when they open an Epic record for an encounter with a patient who has risky alcohol use, or a possible or confirmed alcohol use disorder.
    - From the BPA, the clinician participant will have the option to open a Smart Set which contains clinical decision support for diagnosis and management of risky alcohol use and AUD.
- The clinician participant will be supported by a **clinical care manager** who can assist in identifying patients who need further assessment, those who may be appropriate for AUD medication, counseling, referral, and will assist in conducting outreach to those patients regarding alcohol use care.
    - The CCM will review weekly reports to identify patients who may have had a recent or new alcohol related diagnosis, but have not received follow-up care related to their alcohol use, OR patients with a positive AUDIT score (greater than 13 for women, and greater for 15 for men, or >= 4 on the dependence questions) in the last 7 days but no alcohol attributable visit/encounter diagnosis associated with that encounter. Individuals on these reports may be eligible and appropriate for treatment initiation and engagement
        - Adapting from the HEDIS definition for outreach, we will define a new AUD diagnosis as a new AUD diagnosis in the BMC outpatient setting or acute care settings within the last 7 days when there has been no AUD encounter diagnoses (inpatient or outpatient) in the prior 194 days, excluding diagnoses assigned in the ED/detox.
    - To further identify patients on the work bench reports appropriate for outreach, the CCM may do brief chart reviews of patient charts to determine who to approach and who not to approach (e.g., exclude people in remission, already engaged, in OBAT etc.).

        - The CCM may reach out to the clinician if they have identified a patient to approach in person or over the phone to give the clinician an opportunity to provide further insight and information on the patient.
    - The CCM themselves may conduct outreach to patients to schedule visits, and follow-up about a medication, upcoming appointments, schedule visit, specialty referrals, etc. The CCM will not complete a telephone screening, rather they can facilitate scheduling for further evaluation by clinicians. The CCM may engage in motivational interviewing to help support patients in the initial connection to existing clinical pathways. Using their clinical expertise, the CCM may suggest appropriate care to the patients and will interact with patients to help manage their care.
    - If the CCM has any clinical interaction (in-person or remotely) with the patient, all information related to the interaction will be documented in the EHR using standard general internal medicine documentation procedures using non-billable encounters (no charge clinical documentation encounters).
        - The CCM may create and update care coordination notes for patients who are engaged in AUD care for 1 or more encounter, and may list themselves as a contact for the AUD care.
        - Specifically, telephone calls, whether the patient was reached or not, and in-person encounters will be documented in Epic. This will be used to assist the primary outcome measure in the claims data.
        - The CCM will communicate any relevant information to the clinician, and share clinical encounter notes with the clinician and other team members (e.g., complex care management team, OBAT team, suite nurses, behavioral health team etc.).
    - The CCM will communicate with clinician participants electronically (e.g., Epic messaging, secure email) and in-person to discuss potential care plans, and then assist the clinician in implementing those plans. As needed by the clinician or for efficiency, communication may also occur over secure email or by telephone.
    - Further assistance by the CCM may include facilitating prescription sign-off, assuring refills, finding, selecting, and coordinating specialty AUD care, and contacting patients to facilitate appointments related to care.

The effect of CCM is expected to be to facilitate individual patient care—to suggest it to the clinician and to help make it happen. The CCM may help clinicians get individual care done, and improve reception of quality evidence-based care.

Clinicians assigned to receive the BPA, PHM and CCM combined support will receive prompting from the BPA as described above, the aforementioned data and reports issued by the PHM, and direct patient assistance from the CCM. The PHM reports will be delivered to individual clinicians, and the data reviewed will include elements described above. The CCM will support the clinician and will conduct patient outreach as described above.

9 Recruitment and Retention Procedures

9.1 Recruitment Procedures

To identify potentially eligible clinician participants, research staff may use the following methods:

- Research staff, in collaboration with the BMC primary care leadership team in the general internal medicine unit, will compile a list of potentially eligible clinician participants to invite them to participate in the research study.
- Potential clinician participants may be identified through the professional network of the study team and through clinician referral of colleagues to the study team.
- Research staff will attend a variety of GIM meetings (e.g., suite, clinician, business, etc.)to present information on the study to clinicians. This may occur in person and over Zoom.
    - When meetings occur over Zoom, research staff will ask clinicians to private chat them through the Zoom chat box to sign-up and/or request more information.
    - When meetings occur in person, research staff will bring devices (e.g., tablets, computers) to allow clinicians to review and sign the consent in-person.
        - If approached in a public space (e.g., a charting room, precepting room, etc.), clinicians will be provided with the opportunity to speak with research staff in a private location about the study about any questions or concerns.
        - Though recruitment may take place in person, clinicians will not be required to consent in-person. They will have the option to consent on their own time, and not in a group setting where they may feel pressure to consent and enroll in the study.
    - Research staff will send additional follow-up emails (up to 8 emails over the course of the recruitment period) to GIM clinicians as a reminder of what was discussed, how they can participate, and the benefit of participating in the study.
- Research staff may approach clinicians in-person in charting rooms, precepting rooms, or other work spaces where clinicians congregate or complete administrative tasks to discuss the study, answer questions, and facilitate enrollment/consent into the study. Clinicians will be able to use a QR code or link to access the REDCap eConsent on study devices (e.g., tablets, computers) when recruitment is attempted in-person.
    - If approached in a public space (e.g., a charting room, precepting room, etc.), clinicians will be provided with the opportunity to speak with research staff in a private location about the study about any questions or concerns.
    - Though recruitment may take place in person, clinicians will not be required to consent in-person. They will have the option to consent on their own time, and not in a group setting where they may feel pressure to consent and enroll in the study.

If clinicians are interested in participating, study staff will provide them a link and/or QR code to the REDCap Adult eConsent Form in the Zoom chat box (if interest in participation is expressed during a zoom GIM Meeting) or via email. Potential clinician participants will have the opportunity to read through the eConsent form on their own time, and confirm if they would like to participate by signing the electronic form. If clinicians have questions about the study after reading the eConsent form, they will be provided with contact information of research staff to ask questions via email or request to set-up a meeting or phone call with research staff to ask their questions. Clinician participants will be able to download the consent form from the REDCap page after confirming their participation. To support recruitment efforts, clinicians who decide to enroll into the study will be offered $25 to compensate them for their time and effort.

Patient participants will not be recruited for enrollment in the study.

9.2 Retention Procedures

We anticipate a small number of participating primary care clinicians will leave the BMC primary care clinic during the study period; however, we expect this number to be minimal. We will not enroll clinicians who are expected to leave BMC GIM during the study period due to graduation from clinical training or other expected departures. Additionally, for the patient population we expect attrition to be small because primary care patients largely remain patients at BMC since they are seen regardless of ability to pay, and patients infrequently move out of the region due to socioeconomic status. To assure there is a sufficient number of patients and time for engagement, we chose a study duration of 18-months.

10 Screening Procedures

Clinician participants will not be directly screened (no self-report eligibility screening) for inclusion in the study because the research team we will only approach clinicians deemed eligible by the clinical operations leadership team (based on knowledge of graduation(s) or planned departures). Clinic leadership/expert judgement will be used to help determine if a clinician's current role in the clinic anticipates that they will be working in the clinic for at least 18 months.

The study team or clinican leadership cannot determine if clinicians intend to leave the BMC primary care clinic within 18-month of the study because clinicians may not want to disclose a planned leave, job departure, and plans can change in either direction at any point. Instead, language in the eConsent form will indicate the characteristics (e.g. include clinicians who plan to be in the practice for the next 18-months) of our target population so they can be followed through the duration of the intervention. Providing this language will allow clinicians who anticipate a departure to opt out of participation.

11 Consent Procedures

The study will utilize an eConsent REDCap process using an adult informed consent form because it is the most logistically feasible way to obtain consent from the clinician participants. Obtaining verbal consent would be challenging given time constraints, clinical activities, remote work, and clinicians are more likely to review the eConsent form on their own time.

Clinician participants will confirm agreement to participate in the study by signing the electronic consent form in REDCap. This will be sought by trained research staff (e.g., Research Assistant, Research Coordinator, Project Manager) under the supervision of study investigators. Potential clinician participants will be sent the REDCap link to the eConsent form via Zoom chat box (when the opportunity to participate in the study is presented during a GIM meeting) and/or email, and clinicians will have the opportunity to read and review the information on their own time. Clinician participants will be provided with research staff contact information in case they have any questions or there are elements of the consent they would like to review with study staff. They will have until the recruitment goal (at least 128 clinicians randomized) has been achieved to decide if they would like to participate in the research study. Clinician participants who choose to participate in this RACE trial be able to download a copy of the informed consent document to keep, and those who consent to participate in the study will be offered a $25 ClinCard for their time and effort. Agreement to participate in the RACE trial will be obtained directly before participants complete the brief demographics survey in REDCap.

The REDCap eConsent form will include all required elements: description of study procedures, the potential risks, discomforts, and benefits, the alternative to participating in the study including to not participate in the research, the purpose and duration of the study, confidentiality, the availability of compensation, and that participation is voluntary. Clinician participants who choose to participate will be able to download a copy of the informed consent form for their own records.

We are seeking a waiver of Informed Consent for the patient sample in this study. This study meets the criteria for a waiver of consent with regards to patient participants, i.e. 1) it is minimal risk (e.g., the benign intervention is designed to support and facilitate a patient's clinician in providing standard of care treatment for AUD that already exists in GIM such as providing resources, facilitating referrals to existing treatment programs, and cueing FDA approved prescriptions), 2) the rights and welfare of the subjects would not be adversely affected by the waiver (or alteration) of consent- all information collected from patient participants for use in this study is already routinely collected, recorded, and available in the electronic health record, and the intervention (BPA, PHM, CCM) itself is designed to increase patient access to standard of care, evidence based treatment for unhealthy alcohol use 3) it would not be practicable to carry out the research without the waiver of consent- it would be confusing and an undue burden to participants to be contacted regarding accessing records to seek consent. The primary outcome is engagement in care for AUD (measured using Medicaid claims). If the research team were required to obtain consent from patient participants for record review it would bias our sample for over inclusion of patients who are engaged in care, and would not be representative of the subject population of patients with AUD (undiagnosed and diagnosed) in GIM, 4) the research cannot practicably be carried out without using information in an identifiable format because the study team will perform quality assurance checks on data provided by the Boston Medical Center (BMC) clinical data warehouse (CDW) for research to ensure data integrity prior to conducting analyses, which is not practicable to complete without access to identifiers, and 5) when feasible, subjects are told about the research after the fact- we will not be informing participants of participation in the research after the fact.

12 Study Procedures

See the Appendix for the schedule of events.

Eligibility of clinician participants will be determined and assessed by the primary care leadership team who will provide a list of eligible clinicians to the study team. There will be no screening data collected as part of the study. We will include language in the eConsent form that will indicate the characteristics of our intended population (e.g. include clinicians who plan to be in the practice for the next 18-months) so as to not exclude individuals who do not know or do not want to disclose a planned leave and job departure, and to consider plans may change in either direction at any point.

There are no specific study visits or tests performed as part of the study. After a clinician participant consents, they will be asked to answer a brief socio-demographic survey. The clinicians will also provide contact information to the study team via a separate form in REDCap, which will be stored on password protected and secure servers. This contact information will be collected so clinicians can receive follow-up information about the study, as well as their randomization assignment. At the end of the intervention (up to 18 months from randomization), the participants will be sent a single brief follow-up survey to measure confidence around AUD care and provide feedback.

The CCM and PHM will complete fidelity checklists as part of the study. The CCM fidelity checklists will be used to demonstrate how often the CCM has run and reviewed their reports, performed chart review for patients who may be eligible for outreach, and provide basic numerical totals on how many patients were attempted to be outreached to, how many were not eligible, not reached, etc. The PHM will complete a weekly checklist to demonstrate how often they ran the high-risk patient report, document the number of patients each week eligible on this report, how often they distributed quarterly reports to the clinician participants, if any one-one meetings were held between a clinician participant and a provider, etc.

Study data for the patient sample will be collected through Medicaid claims data, and EHR data accessed via the BMC Clinical Data Warehouse. For the primary outcome, and initiation and acute care utilization we will utilize BMC ACO Medicaid claims data. For all other outcomes we will primarily obtain data from the EHR via the Clinical Data Warehouse. We will use existing clinical source data and source documents from patients on the clinician's panel. This information is generated for purposes outside of research, however, will be used for research purposes. Data from the EHR and from Medicaid Claims will be collected at several timepoints at the end of the study period to account for lag times in data.

Early termination in the study will only be necessary if a clinician participant no longer is employed by BMC primary care during the course of the study or takes a leave of absence and is not providing clinical care in the practice. If this happens, the study team will ask the participant to complete the follow-up survey as they leave the clinic rather than waiting until the end of the study period. The study team will consider how this may impact primary outcome data. The study team plans to complete an intention to treat analysis including clinicians who had early departures in determination of the final outcome. We will request contact information for departing clinicians to allow the study team to send follow-up study survey at study completion.

Overview of Study Contacts:

The RACE trial will not have any formal study visits with clinician or patient participants.

Upon reviewing and signing the eConsent form in REDCap, clinician participants will be asked to complete a brief baseline sociodemographic survey in REDCap. They survey will not be administered for study staff, rather the clinicians will independently complete the survey on their own time. Eligible and consented clinician participants enrolled in the study will be randomized to an intervention group. Randomization may take place at more than one time point as clinician participants consent and enroll (until at least 128 clinicians are randomized). The clinicians will be notified of their randomization assignment by secure email within 2 weeks of randomization.

At the end of the intervention, up to 18 months after randomization, clinician participants will be asked to complete a brief follow-up survey. Clinician participants will be sent a secure email with a link to the follow-up survey in REDCap, and be given approximately eight weeks to complete the survey.

There are no clinical or laboratory evaluations for study-related purposes for clinician or patient participants in the RACE study. Patients included in the patient sample for the RACE study may receive clinical or laboratory evaluations performed as part of their routine clinical care, but no labs or clinical evaluations will be ordered for exclusively research purposes Clinician participants will only place clinical

orders consistent with usual evidence-based care for AUD. Any and all patient care will be documented in the EHR per typical clinical documentation procedures. The CCM role will not be producing billable encounters.

Study Duration:
The study will last a total of three years. In the first year, the research will team hire and train the PHM and CCM staff, develop the protocol and obtain IRB approval, complete clinical trial registration, work with the BMC ACO and the CDW to make plans for future data collection, and work with primary care leadership. Towards the end of the first year of the grant, the research team will recruit and consent all clinician participants from the primary care clinic. Clinicians may be consented and enrolled on a rolling basis until at least 128 are randomized. Clinician participants begin the intervention upon randomization into a study group. The anticipated time between enrollment and end of study activities for each individual clinician participant is up to 18-months. At the end of the intervention, the clinician participants will be sent a brief follow-up survey to answer. Medicaid claims and EHR data collection will last for about 6 months afterwards. Analysis and reporting are planned for the last 6 months of the study.

Randomization:
Randomization may occur at more than one time point. Only participants who remain eligible at the time of randomization will be randomized.

A majority of the enrolled and consented clinicians will be randomized at one time point. Any remaining clinicians enrolled and consented on a rolling basis (until at least 128 clinicians are randomized), will subsequently be randomized. Randomization will be stratified by clinician type (e.g., nurse practitioner, physician, resident or fellow trainee) and by clinician patient panel volume (the mean number of patients eligible for the initiation and engagement outcome per clinician, at the time of randomization or as close to it as feasibly possible). Stratifying by patient volume will help ensure that clinicians with many/few patients with AUD are evenly distributed across randomized groups. To ensure balance with respect to the number of clinicians in each arm, the permuted blocks strategy will be used. Once randomization occurs, clinicians will be informed of their randomization by email, and provided with information on next steps.

Participant Withdrawal:
The research team does not anticipate needing to withdraw clinician-subjects without their consent, however, participation may be terminated for inappropriate behavior towards staff, or if the study is stopped early for any reason. Early termination or withdrawal of subjects may occur if a clinician unexpectedly leaves the clinic during the intervention period. If this occurs, the research team will consider and evaluate for any contamination issues related to the patient panel being divided among clinicians who are assigned to a different group of the study. Study clinicians that leave the practice prior to the close of the study will be asked to complete the follow-up survey as soon as possible.

Blinding:
Clinicians will not be blinded in that they will receive notice when they are randomized with details about which randomization group they have been assigned to.

13 Assessment of Safety and Data Safety Monitoring Plan (DSMP)

13.1 Definitions for Safety Assessment

The following definitions will be used in the assessment of safety:

In a medical study, an *adverse event (AE)* is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

In the context of the RACE study, a non-medical study, an adverse event for a clinician participant may include a breach of confidentiality, inconvenience, invasion of privacy, or emotional distress related to or concerns about perception of job performance related to the study. An adverse event as it relates to a patient participant would be a breach of confidentiality.

Unanticipated Problem is defined as an event, experience or outcome that meets **all three** of the following criteria:

- is unexpected; AND
- is related or possibly related to participation in the research; AND
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research

Unexpected means the nature, severity, or frequency of the event is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
- the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

13.2 Safety Review

Both the risks listed in Section 6.1 and unknown risks will be monitored as follows:

The primary risks in the RACE study are inconvenience due to potential time associated with study team contact for clinician participants, and loss of confidentiality for clinician and patient participants. Though the risk of these occurring is low, clinicians will be provided with contact information of the study team to report any inconvenience on a on a case-by-case basis to the study team. Inconveniences will be reviewed and monitored as they occur by the CCM and PHM as they will be primarily in contact with the study participants. The project coordinator, and director of research operations may assist in monitoring of risks as needed. Loss of confidentiality will be monitored for and reported by all research study team

members as they occur. The PI will be responsible for assuring that study procedures are adhered to regarding data security, and will regularly meet with the study staff.

Adverse events in this study will not be medical. Adverse events will be evaluated for severity, seriousness, relatedness, and expectedness on a form that allows the person who has identified the AE to provide a description of the event, and the Principal Investigator (PI) will review the AE to determine if the event is related to the protocol, expected from the population, and severity. All adverse events will be reviewed by the research team on a monthly basis to determine if a pattern of adverse events exists and suggests a change to the protocol may be necessary. Physicians will not be blinded, and patients will be aware that a CCM is involved in their medical care if they are contacted by them, or if a physician discusses the CCM with the patient. There will be no unblinding required as the study team will know which arm clinicians are associated with.

13.2.1 Multi-Site Safety Monitoring

This is not a multi-site study.

13.3 Reporting Plans

The Principal Investigator at BMC/BU Medical Campus will report unanticipated problems, safety monitors' reports, and adverse events to the BMC/BU Medical Center IRB in accordance with IRB policies:

- Unanticipated Problems occurring at BMC/BU Medical Campus will be reported to the BMC/BU Medical Campus IRB within 7 days of the investigator learning of the event.
- Adverse Events (including Serious Adverse Events) will be reported in summary at the time of continuing review, along with a statement that the pattern of adverse events, in total, does not suggest that the research places subjects or others at a greater risk of harm than was previously known.

13.4 Stopping Rules

The study has no pre-defined stopping rules. Since the study is no more than minimal risk study, and we do not anticipate there being harm associated with the study, we have not built-in stopping rules. The major risk due to the study is inconvenience, however, clinicians can voluntarily end their participation in the study at any point. Though we may gather data during the study, due to the time required for data management, cleaning and quality control procedures, we will not be able to meaningfully analyze the data prior to the end of the study. Therefore, no interim analyses will be performed to determine effectiveness of the different arms in the study.

14 Data Handling and Record Keeping

14.1 Confidentiality

All web and database servers will be housed in a secure, professionally managed server room under the control of the Boston University Medical Camps (BUMC) Office of Information Technology (OIT). Staff from the Biostatistics and Epidemiology Data Analytic Center (BEDAC) and BUMC OIT work to continually

enhance their systems, procedures and processes to ensure compliance with industry and government standards for data security. All central systems are secured and physically behind locked doors with access restricted to key personnel in the BUMC OIT. All data are stored on servers that are password-protected. To protect against security breaches, data will be electronically encrypted so that only the intended recipient can decode. Any PHI will be stored in a HIPAA compliant environment that meets BUMC standards for storage of PHI.

Clinician participants in the RACE Study directly enter data into a REDCap survey that will be attached to clinician participant identifiers (e.g., name, phone number, email). This data will be stored using the security features that allows the system to collect, process, and store data classified as restricted use. The BU REDCAP configuration includes a virtual Restricted Use environment (vRU), a firewall, SSL/TLS encryption, two-factor authentication, and user rights management policies to enhance security and compliance for study data. Additionally, data kept in REDCap will only be accessible to relevant research staff. Paper records will be stored in locked filing cabinets and locked offices.

Additionally, research data will not be collected directly from patient participants. Identifiable patient participant data will be collected solely through electronic health record (EHR) review and through review of Boston Accountable Care Organization (BACO) claims data. Though the information collected is already available in the source databases, and we will take measures to secure data appropriately, it is sensitive information relating to health status and alcohol use. These data will be kept in a secure electronic environment (e.g., Box.com), accessible to relevant research staff need the information for appropriate study procedures. Specifically, Box.com is the HIPAA compliant electronic environment that meets BMC standards for storage of PHI, and is the primary platform the clinical data warehouse (CDW) for research utilizes to data they provide to research teams.

As a National Institutes of Health (NIH) funded study we automatically have a Certificate of Confidentiality to protect participants in this research.

Data will be kept for a minimum of seven years. Identifiable data and/or a master-code provided by the CDW for research that links data to identifiers for clinician or patient participants will be kept for the duration of the study. Once all analyses have been completed and the study PI determines that identifiable data and/or links to identifiers are no longer needed, these identifiers and/or links to identifiers will be destroyed by permanently deleting identifiers from all datasets. If an identifier is deemed important for analysis but is no longer needed for identification purposes (e.g. dates), we will scramble the dates such that they remaining meaningful for analysis purposes (i.e. that an interval can still be determined) but do not remain identifiable.

There are no current plans for external data sharing. The project has been registered on ClinicalTrials.gov., and will be updated during each milestone (e.g., recruitment, randomization, data collection, study closeout) of the study.

14.2 Study Documentation, Source Data, and Case Report Forms (CRFs)

The CCM will utilize non-billable Epic encounter documentation notes to record data that may be used as research data. The CCM will document standard of care clinical processes in the EHR following usual general internal medicine standard documentation processes and policies. Any Epic encounter or progress note documentation will not be used to record research data, but rather for clinical care

coordination and communication in the EMR. If paper copies of work bench reports are printed, the paper copies will be shredded after the work is completed. The PHM will not document in the clinical record.

Data sources in the RACE study include the REDCap baseline and follow-up survey completed by clinician participants, fidelity checklists, and source data: EHR data from Epic and BMC ACO Medicaid Claims data. We may also include clinician use metrics tracked and pulled from email marketing campaign software (e.g., ActiveCampaign) to assess number of clinicians who open the email to view the report, the amount of time a clinician participant views the report, how many clinicians click on the hyperlinks, etc. For the primary outcome, and initiation and acute care utilization we utilize BMC ACO Medicaid claims data for the patient sample. For all other outcomes we will obtain them from the EHR via the Clinical Data Warehouse. We will use existing clinical source data and source documents from patients on the clinician's panel. This information is generated for purposes outside of research, however, will be used for research purposes. The source data will include diagnoses and ICD-10 codes, health care utilization, medications and mentions of medications, counseling and referrals to counseling or specialty care, any EHR fields related to the BPA prompts, and patient demographics (e.g., age, gender, race/ethnicity). These data will be securely sent to the study team per typical CDW and Medicaid claims data procedures with the minimal amount of identifiable information included necessary to complete outcome analyses.

Initial and follow-up socio-demographic information will be collected and directly entered by clinician-participants into a REDCap survey. These surveys are used to understand some baseline characteristics of each clinician participant, confidence as it relates to providing alcohol related care, and impact of the intervention that cannot be collected from the EHR. These will be programmed into a secure electronic platform (REDCap), and managed by BEDAC. Other relevant clinician characteristics (e.g., title, other degrees completed) will be collected via public data sources.

User metrics from the email marketing campaign software (e.g., ActiveCampaign) will be stored on the software platform. Data pulled from the software for research purposes will be stored in Box.com, a HIPAA compliant BMC approved storage software.

Additionally, the CCM and PHM will complete regular fidelity checklists to confirm fidelity to the intervention for replication purposes. This checklist may be completed on a hard copy paper document or electronically. If a paper form is used, the data from this source paper form will be manually entered into the programmed electronic REDCap form within 30 business days. Hard copy documents will be stored in a locked filing cabinet, and electronic forms will be saved on a password protected platform.

Corrections on data collection forms (i.e., fidelity checklist): If any entry error has been made to hardcopy data fidelity checklists, to correct such an error, a single straight line will be drawn through the incorrect entry and the correct data will be entered above it. All such changes will be initialed and dated. There will be no erasures or white-out on hardcopy fidelity checklists. For clarification of illegible or uncertain entries, the clarification will be printed above the item, then initialed and dated. If fidelity checklists are directly entered in the REDCap programmed form, any data entry errors will be captured through the audit trail in REDCap.

See Section 18 Appendix for the following CRFs:

- Baseline Socio-Demographic Clinician Survey

- Follow-up Socio-Demographic Clinician Survey
- CCM and PHM Fidelity Checklist

14.3 Study Records Retention

All study records (e.g., informed consent, REDCap survey records, source data, fidelity checklists) from the RACE study will be retained for at least seven years after completion of the study per Boston Medical Center and Boston University requirements. Data will be managed and retained by the Biostatistics and Epidemiology Data Analytics Center (BEDAC). After the seven years of required data retention, the study PI will determine when the information can be destroyed.

15 Statistical Plan

Note: there will not be a separate attached stastical analysis plan

15.1 Study Hypotheses

Our primary hypothesis is that PHM and CCM separately and combined will improve engagement with AUD care (3 primary comparisons with no PHM or CCM). Secondary hypotheses are that PHM and CCM separately and combined will improve initiation of AUD care, prescription of AUD medication, referral to and receipt of AUD behavioral counseling in primary care, and referral to and receipt of specialty AUD care.

15.2 Sample Size Determination

Sample Size/Power: To define the limits of the study, we present power calculations to assess the differences we will be able to detect with reasonably high power for the primary endpoint of interest, engagement. Calculations assume a 2-sided test, with an overall significance level of 0.05. For the purposes of power calculations, we consider a simple, conservative setting based on a Bonferroni adjustment for multiple comparisons, although in our analyses we will use the Hochberg sequential correction method, an approach that will result in higher power than the Bonferroni method. To maintain an overall type I error rate of 5%, we assume each of the 3 primary pairwise comparisons will be conducted at an alpha level of 0.0167 for the following power calculations. It is expected that at least 128 total clinicians will be randomized in the study (approximately 32 per randomized group), with an average of approximately 8 eligible patients per clinician. We conservatively estimate a total of 1000 patients (approximately 250 patients per randomized group). We expect the interclass correlation coefficient (ICC) will be <0.10 for the outcomes of interest, and conservatively assume a value of 0.10 in the following calculations. Calculations for engagement are based on a chi-square test with continuity correction, with estimates adjusted for clustering based on the inflation factor (also referred to as the design effect). Because the primary outcome, engagement, will be assessed using medical records, there will be no loss to follow-up. Based on rates from BMCHNP and the primary care clinic itself (sources and specifics above under “primary outcome”), we expect 15% of patients with AUD in the BPA only group will be engaged in care. Based on the above assumptions, the proposed study has 80% power to detect an absolute difference of 17% (i.e., 15% in the BPA only group vs. 32% in any of the 3 combined intervention arms) in the proportions with engagement. A difference of this magnitude represents a clinically meaningful effect of the intervention.

15.3 Statistical Methods

For the primary outcome, and initiation and acute care utilization we will access BMC ACO Medicaid data. For all other outcomes we will obtain them from the EHR via the Clinical Data Warehouse. Demographic information from participating clinicians will be collected using REDCap at the time of consent. Sociodemographic patient data will primarily be obtained from Epic, however if there is missing sociodemographic data in Epic, we may use Medicaid claims data to fill in the missing data. Descriptive statistics will be calculated for patient-specific and clinician-specific variables at baseline. All baseline variables will be assessed to see whether there appear to be any differences across randomized arms. This study will use an intent-to-treat analysis including all subjects according to their randomized assignment. The primary goal of this aim is to estimate the effectiveness of the 3 combination interventions (BPA+PHM+CCM; BPA+CCM; BPA+PHM) vs. BPA alone on the primary outcome engagement in care. Randomization and the intervention occur at the clinician level while the unit of observation is at the patient level. Thus, analyses of patients must account for clustering by the clinician. The main analysis evaluating the effect of the interventions on the binary study outcomes (primary: engagement; secondary: initiation, receipt of AUD medication, AUD counseling and specialty AUD care by referral) will use generalized estimating equations (GEE) logistic regression models with empirical (robust) standard errors to account for clustering by clinicians. We will include indicator variables to represent the study arms and will also adjust for the randomization stratification factors clinician type (attending/nurse practitioner vs. resident) and clinician volume (above the median, or below the median by clinician type) to improve efficiency, and explore suite effects not already accounted for. In addition, the models will control for important baseline characteristics (individual-specific, clinician-specific, or both) that differ between groups to avoid confounding. An additional analysis will be further adjusted for the duration of time each clinician spent in the study, accounting for late study entry and early withdrawal to see if this has any impact on the treatment estimates. Secondary, confirmatory analyses will be conducted using mixed effects logistic regression models, sometimes referred to as random effects models or hierarchical regression models accounting for clustering by including a random effect for clinician. Spearman correlation coefficients will be obtained to identify pairs of variables that may be collinear ($r>0.4$) and would therefore not be included together in regression analyses. In addition, the variance inflation factor (VIF) will be assessed to detect possible collinearity. The 3 pairwise comparisons of primary interest are between each combination intervention vs. BPA alone and we will adjust for the multiple comparisons using the Hochberg sequential test procedures.

For the trial, our plans to randomize and analyze groups by intention to treat, have outcome assessment done by those unaware of group assignment, the likelihood of minimal loss to follow-up, and an adequate power and sample size will support the validity of the results. It is possible that the interventions tested could be too weak to have an effect. However, PHM and CCM are effective approaches for other conditions and are feasible. More intensive models are more difficult and costly to implement. BPA, PHM and CCM balance intervention strength and feasibility well. We will attribute patients to their assigned primary care clinician when they meet eligibility for initiation of AUD treatment (e.g. have a new AUD encounter diagnosis, as per the HEDIS definition of new AUD diagnosis). There is a small possibility that individual patients will be reassigned to a different clinician (potentially in a different treatment arm) during the follow-up period for the outcomes, which could introduce contamination. We feel that this will be rare occurrence and that it will not interfere with the pragmatic intent-to-treat analysis using the clinician at patient inclusion in the study. But, we will perform additional secondary analyses allowing time-varying clinician assignments to verify that changes in clinician assignment do not compromise the treatment effect estimates. Otherwise, contamination is

unlikely because clinicians, while they may be aware that other clinicians are receiving PHM or CCM, will not be receiving it. The primary outcome of the trial, engagement in AUD treatment, will have to have technical specification modified (as has been done for prior research to define the index visit). It is also different from data fed back by PHMs to clinicians from the EHR in real time (because engagement is collected at the end of the trial). Results are likely to apply widely to similar settings.

16 Ethics/Protection of Human Subjects

This study is to be conducted according to applicable US federal regulations and institutional policies (which are based in federal regulations, guidance, and ICH Good Clinical Practice guidelines).

This protocol and any amendments will be submitted to the Boston Medical Center and Boston University Medical Campus IRB for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator.

All clinician subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB. The consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. Consent will be documented as required by the IRB.

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18 Appendix

18.1 Schedule of Events

Activities	Months															
	0-3	3-6	6-9	9-12	12-15	15-18	18-21	21-24	24-27	27-30	30-33	33-36	36-39	39-42	42-45	45-48
Recruitment				X	X											
Consent				X												
Baseline Survey				X												
CDW Data Pull				X	X											
Randomization					X											
PHM Monthly Data Pull and Review					X	X	X	X	X	X						
PHM Quarterly Reports					X	X	X	X	X	X						
PHM 1-on-1 meetings (as requested)					X	X	X	X	X	X						
PHM Weekly Reports					X	X	X	X	X	X						
CCM Weekly Reports					X	X	X	X	X	X						
CCM Chart Review					X	X	X	X	X	X						
CCM+ Clinician Communication/Collaboration					X	X	X	X	X	X						
CCM + Patient Communication					X	X	X	X	X	X						
CCM Epic Clinical Interaction Documentation					X	X	X	X	X	X						
Fidelity Checklist Documentation (PHM + CCM)					X	X	X	X	X	X						
Adverse Events					X	X	X	X	X	X						
Complete Follow-up Survey											X					
Gather BMC ACO Medicaid Claims Data											X	X				
CDW Request											X	X				
Data Analyses												X	X	X	X	