Trial Protocol documentation

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2. Original grant submission: Approach section
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An organizational readiness intervention and randomized controlled trial to test strategies for implementing substance use disorder treatment into primary care: SUMMIT study protocol

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Abstract

Background: Millions of people who need treatment for substance use disorders (SUD) do not receive it. Evidence-based practices for treating SUD exist, and some are appropriate for delivery outside of specialty care settings. Primary care is an opportune setting in which to deliver SUD treatment because many individuals see their primary care providers at least once a year. Further, the Patient Protection and Affordable Care Act (PPACA) increases coverage for SUD treatment and is increasing the number of individuals seeking primary care services. In this article, we present the protocol for a study testing the effects of an organizational readiness and service delivery intervention on increasing the uptake of SUD treatment in primary care and on patient outcomes.

Methods/design: In a randomized controlled trial, we test the combined effects of an organizational readiness intervention consisting of implementation tools and activities and an integrated collaborative care service delivery intervention based on the Chronic Care Model on service system (patient-centered care, utilization of substance use disorder treatment, utilization of health care services and adoption and sustainability of evidence-based practices) and patient (substance use, consequences of use, health and mental health, and satisfaction with care) outcomes. We also use a repeated measures design to test organizational changes throughout the study, such as acceptability, appropriateness and feasibility of the practices to providers, and provider intention to adopt the practices. We use provider focus groups, provider and patient surveys, and administrative data to measure outcomes.

Discussion: The present study responds to critical gaps in health care services for people with substance use disorders, including the need for greater access to SUD treatment and greater uptake of evidence-based practices in primary care. We designed a multi-level study that combines implementation tools to increase organizational readiness to adopt and sustain evidence-based practices (EBPs) and tests the effectiveness of a service delivery intervention on service system and patient outcomes related to SUD services.

Trial registration: Current controlled trials: NCT01810159

Keywords: Implementation, Organizational readiness, Evidence-based substance use disorder treatment, Primary care, Collaborative care, Care coordination, Medication-assisted treatment, Extended-release injectable naltrexone, Vivitrol, ®Buprenorphine/naloxone, Suboxone, ®Motivational interviewing

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Background

Substance use disorders (SUD) continue to be under-identified and under-treated [1]. In 2013, 22.7 million people aged 12 or older needed treatment for an illicit drug or alcohol use problem; of these, 20.2 million did not receive it [1]. The consequences of untreated alcohol and drug abuse are great and include increased risk of disease, injury, disability, and death [2,3] as well as hundreds of billions of dollars in costs to the criminal justice, social welfare, and health care systems [4-6]. Historically, treatment of SUD has taken place in residential and outpatient specialty care settings. Although specialty care settings play an important role for individuals with severe dependence, long waiting lists, stigma, and the lack of public funding for patients without insurance coverage have contributed to the lack of access. Further, many people who need treatment are not aware that they need it, are not ready for treatment, or do not know how or where to seek treatment [7].

Primary care clinics are a feasible and opportune setting in which to identify and provide treatment to people with SUD. Studies suggest that the prevalence of alcohol use disorders and use of illicit drugs is higher among primary care and emergency room patients than it is in the general population [8,9]. Further, most individuals (82%) visit a health professional at least once a year, thus providing ample opportunity for providers to identify patients in need of treatment [10]. Research suggests that integrating SUD treatment and general health care can result in less utilization of inpatient care and fewer emergency room visits [11] and that integrated care is acceptable to patients with an SUD [12].

However, despite the potential benefits of providing SUD screening and treatment in primary care and the existence of evidence-based practices (EBP) suitable for delivery in these settings [13-21], uptake of evidence-based SUD treatments in primary care has been slow. Accordingly, patients are unlikely to receive treatment for their SUD in primary care [20-24]. Some of the organizational barriers to providing SUD treatment in primary care settings include lack of insurance reimbursement, perceived lack of time to fully assess and discuss substance use, and lack of administrative buy-in for integrating SUD care into medical practices [25,26]. At the physician level, perceived barriers to SUD treatment adoption include negative attitudes toward people with SUD, lack of confidence among physicians in their ability to treat SUDs, lack of adequate role models and access to decision support consultants, and deficiencies in training and expertise in addiction treatment [13,25-28].

Research on introducing new practices into health care and other organizations suggests that intervention at both the organizational level (i.e., to increase organizational readiness to adopt new practices) and service delivery system level (i.e., reorganizing how care is provided to support the new practice) may both be necessary to integrate and sustain EBP [29-31]. Organizational readiness refers to "the extent to which organizational members are psychologically and behaviorally prepared to implement organizational change" [32]. Interventions that increase an organization's commitment to change and the ability of the members of the organization to visualize how the new practice could be adopted and incorporated into existing practices are both important to increasing organizational readiness and adoption of EBP [33]. However, even when an organization exhibits high organizational readiness, change may not be successful unless attention is paid to how the new practice is supported and integrated into existing care practices. Further, adapting new practices to fit the nuances of a setting is a key component of whether the practice is ultimately accepted and adopted. As Damschroder et al. note, "without adaptation, interventions usually come to a setting as a poor fit, resisted by individuals who will be affected by the intervention, and requiring an active process to engage individuals in order to accomplish implementation [30]."

To address the need for change at two levels—organizational and service delivery system—to increase the intent and ability of primary care providers to identify and treat opioid and alcohol use disorders (OAUD), we designed a multi-level study to create and evaluate change at both levels. We call this study substance use motivation medication integrated treatment (SUMMIT) and focus on alcohol and opiate use disorders because of their relevance to the clinic population and availability of effective medications. At the organizational level, we test the effects of an organizational readiness intervention on the organization's readiness to identify and treat individuals with opioid and alcohol use disorders. At the service delivery system level, we use Wagner's Chronic Care Model [34] to reorganize and guide how care for OAUD is provided and supported; we call the service delivery intervention integrated collaborative care (ICC). Integrated, collaborative approaches have been successful in improving outcomes for patients experiencing a variety of different chronic illnesses, including diabetes [35], asthma [35], and depression [36]. ICC has improved implementation of evidence-based treatments and quality of care [37], lowered costs [38], improved patient outcomes [39-42], and is thought to be feasible for and sustainable in primary care clinics [43]. We test the effects of the organizational readiness intervention using a repeated measures pre-post design and the impact of the service delivery intervention on patient-level outcomes using a randomized controlled trial (RCT) to compare the service delivery intervention (ICC) with "service as usual" (SAU) on service system and patient outcomes. We hypothesize that provider (providers include administrators, medical

and mental health providers, and other staff) readiness to implement the EBP and patient-centered SUD care will improve from the pre-organizational readiness intervention period (year 1) to the post-readiness intervention periods (years 2–5); that patients in the ICC condition will report more integrated, patient-centered evidence-based care for their opioid and/or alcohol use disorders, will be more likely to receive OAUD care, and will have lower overall health care utilization (e.g., emergency department and medical visits) than patients in the SAU condition; and that provider adoption of EBP will increase from year 2 to years 3 and 4 and that providers will still be delivering OAUD EBP a year after completion of the study in year 5. We also hypothesize that patients in the ICC condition will report less substance use, fewer SUD consequences, higher health and mental health functioning, and greater satisfaction with their SUD care 6 months after enrollment than SAU patients.

The evidence-based practices that we are introducing into the clinic are two medications—buprenorphine/naloxone (BUP/NX) (trade name Suboxone®) for opioid dependence and extended-release injectable naltrexone (XR-NTX) (trade name Vivitrol®) for alcohol dependence—and a motivational interviewing (MI)-based behavioral treatment for those with abuse or dependence of either substance. BUP/NX has been proven effective for patients with opioid (heroin as well as prescription opioid) dependence and is feasible for delivery in office-based settings [12,44-49]; XR-NTX has been found effective for people with alcohol or opioid dependence and also is feasible for delivery in primary care [50-54]. Due to greater complexity for administration for opiate dependence, in this study, XR-NTX is used only to treat alcohol dependence. MI-based interventions have improved SUD treatment outcomes [18,19,55,56].

In this article, we present our methods, including study setting; conceptual framework; study design; participant recruitment; a description of the interventions, which consist of the organizational readiness intervention and the service delivery intervention; as well as our measures, data collection procedures, and analysis plan. We conclude with a discussion of the study's unique design and its relevance to implementation of OAUD treatment in primary care, and we note the study's limitations.

Methods/design

Study setting

We are conducting the study in a large urban, federally qualified health center (FQHC) in Los Angeles that serves approximately 20,000 patients annually. The study is taking place at the FQHC's two largest sites. We elected to hold the study in an FQHC because of the expected influx of patients into publicly funded clinics due to expanded coverage, an increased funding and an increase in the number of clinics due to the Patient Protection and Affordable Care Act (PPACA) [57], and the greater opportunity to reach more individuals who need treatment. The clinic currently has integrated mental health services and provides treatment for anxiety and depressive disorders; however, prior to the study, the clinic did not conduct any screening or treatment for SUD. If substance misuse was identified, patients were sometimes, but not systematically, referred to specialty care.

Conceptual framework

In our conceptual framework, illustrated in Figure 1, the organizational readiness intervention increases provider readiness to use each of the EBP for OAUD (the two medications and the MI-based behavioral therapy) as well as readiness to adopt ICC (the service delivery intervention) to deliver the three EBP. The organizational readiness intervention consists of well-studied "implementation" tools, designed to increase the readiness of an organization to implement and deliver new practices. Our measures of organizational readiness are provider acceptability of the EBP, provider perceptions of EBP appropriateness and feasibility, and provider intention to adopt each EBP. In addition, because an aspect of organizational readiness is the ability of providers to visualize how the new practices can be adopted and integrated into the existing workflow [33], a final measure of readiness is the development of locally tailored EBP protocols and an ICC protocol that shows how the EBP will fit into clinic workflow.

In the second part of the conceptual framework, the service delivery intervention (ICC) facilitates the uptake of the EBP and affects service system outcomes (e.g., patient-centered SUD care, measured at the level of the patient and provider, and service utilization, measured at the level of the patient) and patient functioning outcomes (e.g., substance use, consequences of use, both measured at the level of the patient). While organizational readiness may improve immediately following the organizational readiness intervention, we expect that once the three EBP are implemented through ICC and the staff sees improved patient outcomes, a feedback loop will occur, leading to even greater staff acceptance of the new practices.

Study design

The study is designed to test the combined effect of both an organizational readiness intervention (which includes a 1-year organizational preparation period and an 8-month pilot of the ICC condition study) and a service delivery intervention (see Figure 2). We examine the effects of the interventions on organizational readiness, service system, and patient outcomes, all of which are believed to be important in understanding the uptake of new practices [58]. To test the unique effects of the

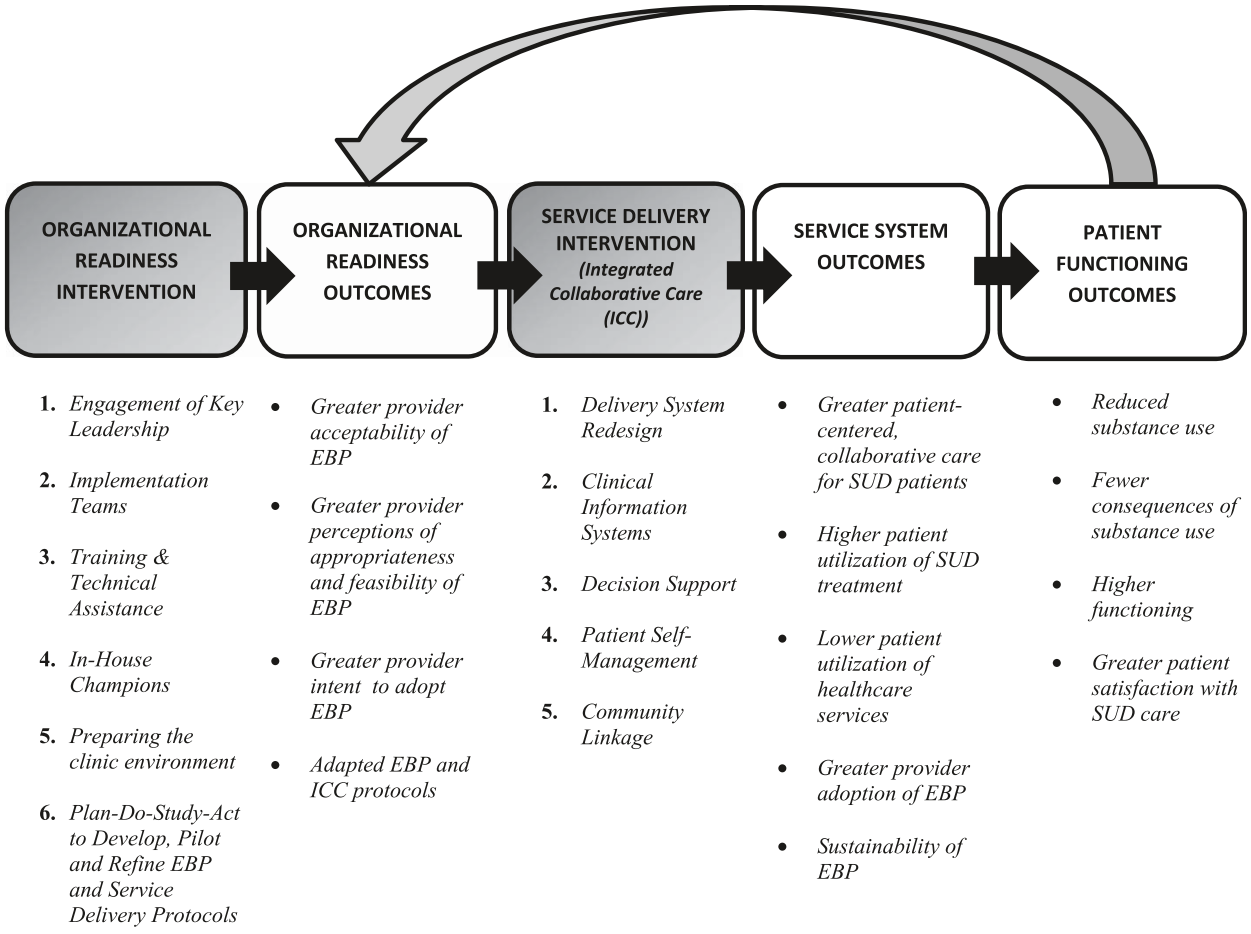

Figure 1 SUMMIT conceptual framework for integrating SUD EBP into primary care.

organizational readiness intervention on provider outcomes, we use a pre-post-intervention design and measure these outcomes at the beginning of the study and then again at the end of year 1. At the end of year 1, we implement an eight-month pilot test of ICC. During the pilot test, providers gain experience with the protocols, and the protocols are iteratively adapted and refined based on provider feedback. Because we hypothesize that readiness outcomes may continue to improve as providers gain experience with ICC and the three treatments, we continue to measure organizational readiness outcomes annually at years 2–5. Thus, changes in outcomes between year 1 and years 2–5 reflect the combined effect of both the organizational readiness intervention and ICC on provider outcomes. To test the effects of the interventions on service system and patient-level outcomes, we are conducting an RCT to compare the effects of ICC with SAU. Service-system outcomes are patient-centered collaborative care, utilization of SUD treatment, patient utilization of health care services, provider adoption of EBP, and sustainability of EBP. Patient-level outcomes include substance use, consequences of use, physical and mental health functioning, and patient satisfaction with SUD care.

For the RCT, all patients are screened for drug and alcohol use by clinic staff as part of usual care; eligible consenting patients (i.e., those with risky use or worse) are referred for further eligibility screening by the research staff, and eligible patients ($N = 400$) are invited to participate in the study. After consenting and completing the baseline interview at one of the study sites, patients are randomized to the ICC or SAU study condition. We use a concealed randomization protocol so neither patient nor research staff is aware of the randomization until after the baseline interview is completed when research staff open sequentially numbered envelopes that contain the randomization assignment. Assignments were made in advance by a statistician using R software. Patients complete a follow-up interview by telephone 6 months after the baseline interview.

The design is a variation of a "hybrid type 2" study, which Curran et al. [59] describe as the "simultaneous testing of a clinical intervention and an implementation intervention/strategy." In this case, the organizational

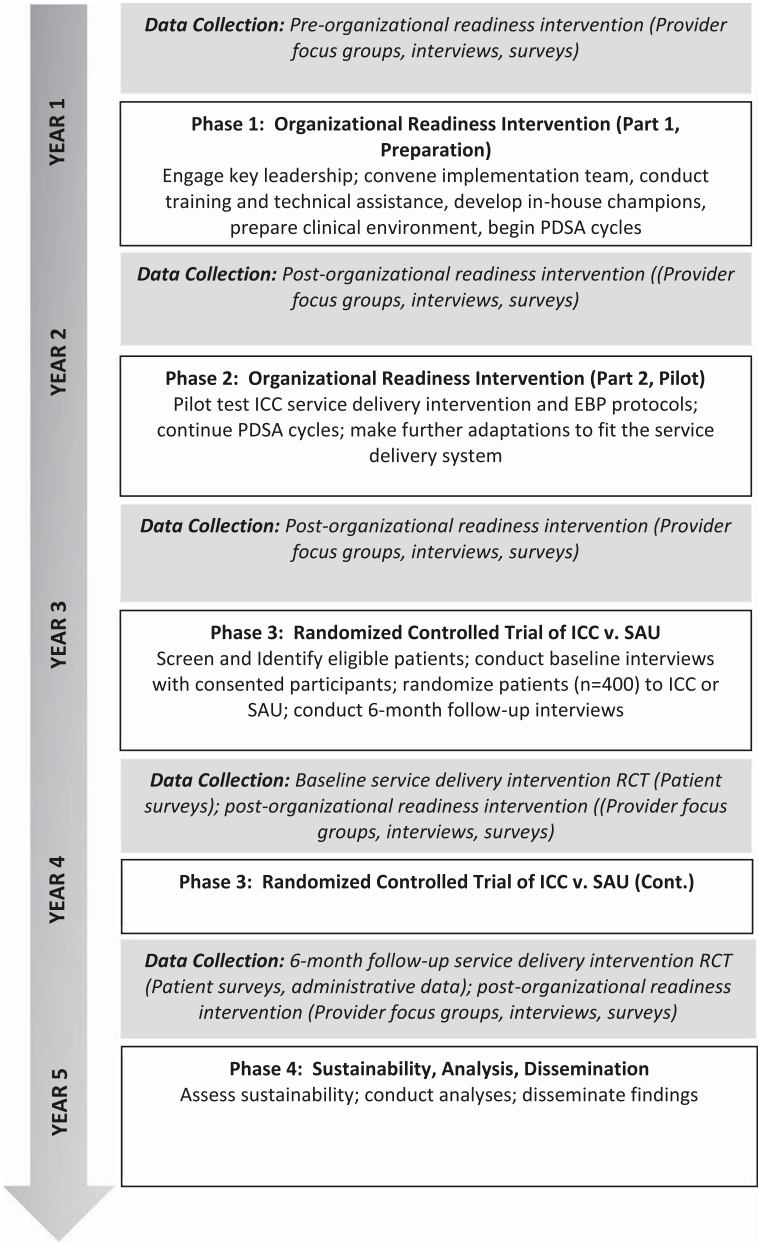

Figure 2 SUMMIT study design and timeline.

readiness intervention is the implementation intervention/strategy and the ICC service delivery intervention is the clinical intervention. The design, which incorporates implementation outcomes such as intention to adopt EBP as well as service system and patient outcomes, follows the recommendations for implementation research outcomes suggested by Proctor et al. [58].

Study participants

Organizational readiness intervention

Organizational readiness intervention participants are full-time clinic administrators, medical and mental health providers, and other clinic staff, including medical assistants, discharge coordinators, and front desk and security staff who agree to participate in interviews, focus groups and/or surveys ($N = 70$).

Service delivery intervention

Service delivery intervention participants are full-time medical and mental health providers (not including residents) as well as patients who come to the clinic for a medical visit; the participants initially screen positive for risky (or worse) alcohol or opioid use using an adapted NIDA Quick Screen [60] and then meet all study

eligibility criteria and consent to participate in the study ($N = 400$). To be eligible for the study, patients must be 18 years or older; meet the "Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM IV)" criteria for abuse of or dependence on alcohol or opioids (heroin or prescription opioids) (assessed using the WHO ASSIST [61]); must not have marked functional impairment from bipolar disorder or schizophrenia; speak English or Spanish; and are not currently in treatment for SUD.

Interventions

Organizational readiness intervention

To create organizational readiness to provide evidence-based treatment for OAUD, we employ multiple tools and activities known to facilitate adoption of EBP as follows: (1) engaging (and obtaining buy-in from) key administrators through regular administrator and board briefings about the proposed study and how to best prepare the organization to implement the ICC intervention and providers to adopt the EBP [29,62]; (2) convening an implementation team that includes key clinical leadership to develop the ICC service delivery intervention and EBP protocols that fit the clinic [29,63]; (3) selecting and training physician and therapist champions to serve as role models for adopting the EBPs [29]; (4) providing trainings for the staff and providers on the ICC intervention and evidence-based treatment for opioid and alcohol use disorders [64,65]; and (5) preparing the clinic environment to identify patients with SUD by instituting universal screening and brief intervention procedures. After preparing the organization, we then conduct the final part of the organizational readiness intervention—piloting the EBP and ICC protocols and making iterative adaptations using plan-do-study-act (PDSA) cycles [66,67]. PDSA cycles offer a structured approach to engaging staff in making iterative, feedback-based changes in service delivery [65,66].

Service delivery intervention

We use Wagner's Chronic Care Model (CCM) [35] as the theoretical basis for the service delivery intervention (ICC). The ICC intervention is comprised of five components that have been shown to result in improved patient outcomes; each component supports the delivery of the planned care for opioid and alcohol use disorders: (1) redesigning the delivery system to support the delivery of the EBP and establishing a care coordinator; (2) modifying clinical information systems to provide alerts to indicate that patients have problematic substance use and developing a patient registry used by the care coordinators to monitor and track patients; (3) providing expert consultation to therapists for complex cases; (4) offering patients self-management tools; and (5) identifying and establishing linkages with community resources. These components are thought to lead to productive patient-provider interactions, which, in turn, lead to improved service system and patient outcomes. The ICC components are described in greater detail in Additional file 1.

Outcomes, procedures, measures, and analysis plan

Next we describe our data collection procedures, measures, and analysis plans for the organizational readiness and service delivery interventions.

Organizational readiness intervention

Procedures We use qualitative and quantitative methods to study our organizational readiness outcomes as follows: 1) *Provider focus groups and semi-structured interviews*. We conduct focus groups with medical and mental health providers and one-on-one interviews with key administrators to inform the development of our intervention and EBP protocols and to understand perceptions of acceptability, appropriateness, feasibility, and intention to adopt the ICC and EBP protocols. For both the focus groups and the interviews, we follow a semi-structured protocol guide that asks "grand tour" questions related to each domain (i.e., general thoughts about ICC and the EBP), and includes specific probes for more detailed responses. 2) *Provider Surveys*. We also conduct surveys in years 1–5 with all the staff and providers to assess changes in organizational readiness outcomes throughout the study. The survey includes validated measures as well as "home-grown" items about specific activities, such as whether providers prescribed a medication and any barriers to doing so. Surveys are web-based, or, for providers with less access to email, through in-person, paper and pencil surveys.

Measures We measure organizational readiness using outcomes for implementation research recommended by Proctor et al. (2011) [58]. We will evaluate the following outcomes specifically related to our organizational readiness intervention: (1) *Acceptability*. Acceptability refers to satisfaction among implementation stakeholders with the complexity of an EBP or new practice (such as the ICC intervention) and relative advantage over current practices [58]. To assess acceptability we adapted items for the staff survey from Moore and Benbasat's [68] validated instrument which maps onto parallel elements of Roger's elements of successful diffusion (i.e., complexity, relative ease of use) [69]. An example of these items is: *Prescribing extended-release injectable naltrexone for patients with alcohol use disorders at this clinic would be relatively easy to do*. We also include locally developed items in the survey to capture barriers to use as well as items from the National Center for Addiction and

Substance Abuse's (CASA) National Survey of Primary Care Physicians and Patients on Substance Abuse [70] that capture providers' opinions about the effectiveness of OAUD EBP, as well whether providers find it difficult to discuss OAUD with their patients. We ask specific questions about acceptability in the focus groups and interviews, such as: *How easy or difficult would it be for providers to prescribe and administer extended-release injectable naltrexone? What are some of the barriers? What changes would have to be made to make it more acceptable?* (2) *Appropriateness*. This refers to the "perceived fit, relevance, or compatibility" [58] of the EBP and ICC intervention in the clinic. We have adapted items from Moore and Benbasat [68] that measure compatibility of EBP and the ICC intervention with the clinic and with current work style (also an element of Roger's diffusion theory) [69]. This includes items such as: *I think the ICC intervention will fit with the way I like to work*. We also include items from the "Substance Abuse Attitudes Survey (SAAS)" to measure changes in provider attitudes about people with substance abuse disorders [71]. The focus groups and interviews also capture reasons why the EBP or ICC intervention may or may not be perceived as compatible with work style and with other approaches to managing patients with OAUD or introducing new practices into the clinic. (3) *Intent to adopt the EBP*. We assess intention to adopt EBP in several ways. First, we incorporate into the survey the *EBP Attitude Scale (EBPAS)*. The EBPAS is a brief (15-item), valid, reliable measure that assesses general attitudes toward adoption of new clinical practices [72]. Next, we use items from Moore and Bensabet's scale that measure elements associated with successful adoption of new EBP [68]. To measure intention or willingness to adopt, we use the "demonstrability" scale, which asks questions such as "*I believe I can communicate to others the consequences of using extended release injectable naltrexone*." Finally, we ask questions in the focus groups and interviews about intent to adopt. (4) *Feasibility*. Feasibility is the actual fit, utility, and suitability of a program within an organization: the practicability [58]. We assess feasibility retrospectively by asking participants in focus groups and interviews whether the EBP and ICC intervention were successfully implemented and whether poor resources, training, or other barriers impeded use. We also ask about feasibility in the provider survey using items from CASA's National Survey of Primary Care Physicians and Patients on Substance Abuse that capture how prepared providers feel they are to treat patients with SUD [70]. (5) *Adapted EBP and intervention protocols*. Our final measure of readiness is finalized, adapted protocols for each of the three EBP and the ICC service delivery intervention, which describe how the EBP fit into the clinic workflow. Adapted, finalized protocols are key to ensuring that staff can visualize how the EBP and ICC intervention will be implemented.

Analysis plan The semi-structured interview and focus group data will be analyzed to identify key facilitators and barriers to implementation using classic content analyses. Our quantitative analysis of survey items will consist of pre-post, one-way repeated measures ANOVA comparisons of survey responses between pre- and all post-intervention periods.

Service delivery intervention

To examine the effect of our service delivery intervention, we examine service system and patient functioning outcomes.

Procedures We use a combination of administrative records, patient interviews and staff surveys to evaluate service system and patient outcomes, as follows: 1) *Administrative records*. We collect three administrative files every 6 months—appointments (all appointments scheduled whether or not they were kept), encounters (including medical and therapy visit reasons and diagnoses), and medication orders. 2) *Patient interviews*. The patient interview contains an assessment of SUD diagnoses, substance use frequency and quantity, consequences related to use, and health and mental health functioning items. We administer patient interviews at baseline and 6 months after enrollment. 3) *Staff surveys*. Staff surveys are described above.

Service system measures We are analyzing five service system outcomes: (1) *Patient-centered, collaborative SUD care*. We measure patient experiences using a locally developed measure based on the validated Patient Assessment of Chronic Illness Care (PACIC) [73]. Provider perceptions of collaborative SUD care are measured using the Assessment of Chronic Illness Care (ACIC) [74]. (2) *Patient utilization of SUD services*. This refers to patient linkage to and usage of appropriate treatment. We measure this by examining clinic administrative records that capture all patient encounter dates, types and providers, and by patient self-report of clinic services on the follow-up survey. (3) *Patient utilization of health care services*. This refers to utilization of emergency department and health care services. We measure this by examining clinic administrative records of clinic health care visits and by patient self-report of emergency department visits. (4) *Provider adoption of EBP*. This is a measure of provider use of the EBP (either of the medications or the brief therapy). Although adoption is sometimes thought of as an implementation (or readiness) outcome, we include it with service system outcomes because we believe that both interventions—organizational readiness and service

delivery—are needed for adoption of EBP. We measure adoption by examining administrative records for prescription of either medication or use of the therapy and by asking providers to self-report use of the EBP in the survey. (5) *Sustainability of EBP*. This is the extent to which the three EBP are still being utilized during year 5 of the study. Following the end of patient enrollment in the RCT, we will continue to monitor clinic practices to examine whether the EBPs are still being utilized following the end of the RCT.

Patient outcomes We are examining four primary patient outcomes. Patient outcomes are: (1) *Changes in quantity and frequency of substance use*. We measure this using the Timeline Follow-Back (TFLB), a validated instrument that uses a calendar to facilitate recall of substance use over the past 30 days [75]. (2) *Consequences of substance use*. To assess consequences, we use the Shortened Inventory of Problems Alcohol and Drugs (SIP-AD), a validated instrument that assesses consequences related to substance use in the past 90 days [76]. (3) *Functioning*. We assess overall health functioning with the SF12 version 2, four-week recall [77]. We use the Patient Health Questionnaire-9 (PHQ-9) [78] to assess depressive symptoms and the generalized anxiety disorder (GAD) [79] to assess symptoms of anxiety. (4) *Satisfaction with SUD care*. We use an adapted standardized patient satisfaction survey [80] to assess patient satisfaction with SUD services at the clinic.

Analysis plan Our quantitative analysis of provider survey items and administrative data related to service system outcomes will consist of pre-post, one-way repeated measures ANOVA comparisons of survey responses between pre- and all post-intervention periods. To analyze patient-level outcomes, we use an intent-to-treat approach. We will first conduct a bivariate analysis to estimate the uncontrolled association between being in the ICC group and outcome. In addition, even though our design randomly assigns patients, we will assess any possible imbalance in covariates between ICC and SAU groups including age, gender, race/ethnicity, and education that affect the impact of the ICC intervention on the outcomes. In cases where observed imbalances are attributable to sample attrition, we will correct for potential bias due to attrition at follow-up using response weights. In addition, characteristics related to an outcome at a conservative significance level of $\alpha = 0.2$ will be considered covariates in a multivariate analysis for reduction of bias if imbalanced or for efficiency gains. For the multivariate analyses, we will infer about the impact of ICC on an outcome by fitting hierarchical models using SAS Proc Mixed, R LME4, and Winbugs. These models take into account the multi-level structure of the data: two repeated measures over time (baseline and 6 months) nested within patient and patients nested within clinics. Sensitivity analyses will be conducted testing model functional forms, the covariates to be used, and the impact of influential outliers in the analyses results. For outcomes assessed only at month 6 (e.g., treatment satisfaction), we will use cross-sectional analyses (such as linear and logistic regression) to estimate the effect of ICC relative to SAU. This study was designed to estimate sufficient effect sizes that can be detected with a power of at least 80% when comparing the outcomes of patients randomly assigned to the two conditions in an end-status analysis at month 6 for a 5% significance level. For continuous outcomes, the study will be able to detect effect sizes of about 0.30–0.32 standard deviations. These are the kind of effects that can be expected for an intervention like ICC [42]. For dichotomous outcomes, we will be able to detect a difference of 13–14 percentage points under the assumption that the SAU group has a 15% rate of receiving the outcome.

Trial status

The RCT is currently in month 11 of 18 planned months of active enrollment and data collection.

Discussion

The present study responds to several critical gaps in health care services for people with SUD—the need for greater access to SUD treatment, the need for more evidence to support the growing emphasis on collaborative, integrated care for SUD in primary care settings, and the call for broader dissemination and adoption of evidence-based treatments for SUD in general and in medical settings in particular. To meet these diverse and complex needs, we designed a multi-level study that (1) combines well-studied implementation tools into an intervention to increase organizational readiness to adopt and sustain SUD EBPs in primary care and (2) tests the effectiveness of a service delivery intervention (ICC) on service system and patient outcomes related to SUD services.

Our hybrid type 2 design [59] allows us to support and study important organizational changes thought to be critical for the adoption and sustainability of new practices and to add what we believe is a necessary component of integrating SUD EBP into primary care—a service delivery intervention tailored to meet clinic specifications and the complex needs of patients with SUD treated in these settings. The study's unique design takes into account the complexity of introducing new EBPs into a clinical setting, the barriers to integrating SUD EBP into primary care, and the chronic nature of SUD and the corresponding complex needs of SUD patients. We believe that our 18-month organizational readiness phase, starting with preparing the organization for SUD

EBP delivery and ending with a pilot phase to ensure that the ICC intervention (i.e., service delivery system intervention) and EBP protocols fit the environment will ensure greater organizational readiness and thus greater likelihood of adoption and sustainability. We believe our multi-level approach—addressing organizational change plus SUD-specific service delivery—is necessary for adoption and sustainability of SUD EBP in primary care. The organizational readiness outcomes will allow us to assess whether our organizational readiness intervention improves provider perceptions of and intention to adopt the EBP while the service delivery intervention will help determine whether the ICC delivery system improves quality of care and patient outcomes compared to service delivery as usual.

Despite the study's strengths, there are some limitations. One limitation is the lack of provider randomization to test the effects of ICC on provider outcomes. This was determined to be infeasible, due to potential contamination across study conditions and lack of provider and patient support for asking patients to switch providers to match their study condition. Additionally, because we are testing the combined impact of the organizational readiness intervention with the ICC intervention, we will not be able to draw conclusions about the unique contribution of either intervention on EBP implementation, sustainability, or patient outcomes. Moreover, both the organizational readiness and the ICC interventions are complex, containing multiple elements. We will be unable to tease apart the impact of particular elements of the interventions (e.g., the effect of the decision support system from the self-management support) on outcomes. Given the emphasis on examining two complex interventions simultaneously, we elected to examine them initially in one FQHC serving a diverse population in a large metropolitan area in California. It is important to note that this occurred during a time of rapid health care reform especially in California, a state that was an early adopter of Medicaid expansion. We will not know whether our study results will be applicable to other FQHCs or in other geographical locations.

Additional file

Additional file 1: Integrated collaborative care intervention (ICC). This file contains a detailed description of the elements of the ICC intervention.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AJO contributed to the design and implementation of the study and drafted the manuscript. KW contributed to the design and implementation of the study and provided substantial input on the manuscript. SH contributed to the design of the study and provided substantial input on the manuscript. KL contributed to the design and implementation of the study and carried out the service delivery intervention. ML contributed to the design and implementation of the study and carried out the service delivery intervention, CMS contributed to the evaluation and analytic plan and provided input in the manuscript. All authors read and approved the final manuscript.

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APPROACH

Overview. We propose a 5-year mixed methods study to test and compare how two strategies, ICC and E&R, affect implementation, service system and patient outcomes, and costs. We also assess the process and extent of ICC and E&R implementation. Our approach includes document review, focus groups, semi- structured interviews, and surveys for obtaining data on the adoption process and implementation outcomes; analysis of patient electronic health records (EHR) for obtaining service system outcome data; a combination of EHR and patient surveys for evaluating patient outcomes; and analysis of provider financial records, EHR, and patient surveys for estimating costs. We also will evaluate fidelity of MET and MAT using the EHR and audio-tapes of MET sessions. Administrators and providers will be asked to participate in data collection activities prior to, during and following implementation. Patients will be asked to complete baseline, 3-month, and 12 month interviews. We have set up a Scientific Advisory Board to review study procedures and progress (see letters of support).

Study Setting. We will collaborate with the VFC, COPE Health Solutions, and LA+USC Healthcare Network and White memorial hospitals. VFC provides primary health care and specialty care to over 24,000 patients, with more than 106,000 visits annually. COPE Health Solutions, an implementation consulting group, will help to plan and coordinate the research in the hospitals and primary care clinics. We will recruit patients from two hospitals: LAC+USC Healthcare Network – the nation's largest academic medical center and one of the largest acute care hospitals in America; and White Memorial Medical Center – a 353-bed teaching hospital providing a full range of patient services to the Los Angeles community. The 5 VFC clinics we are working with are a convenience sample and are likely representative of clinics serving very poor, ethnic minorities.

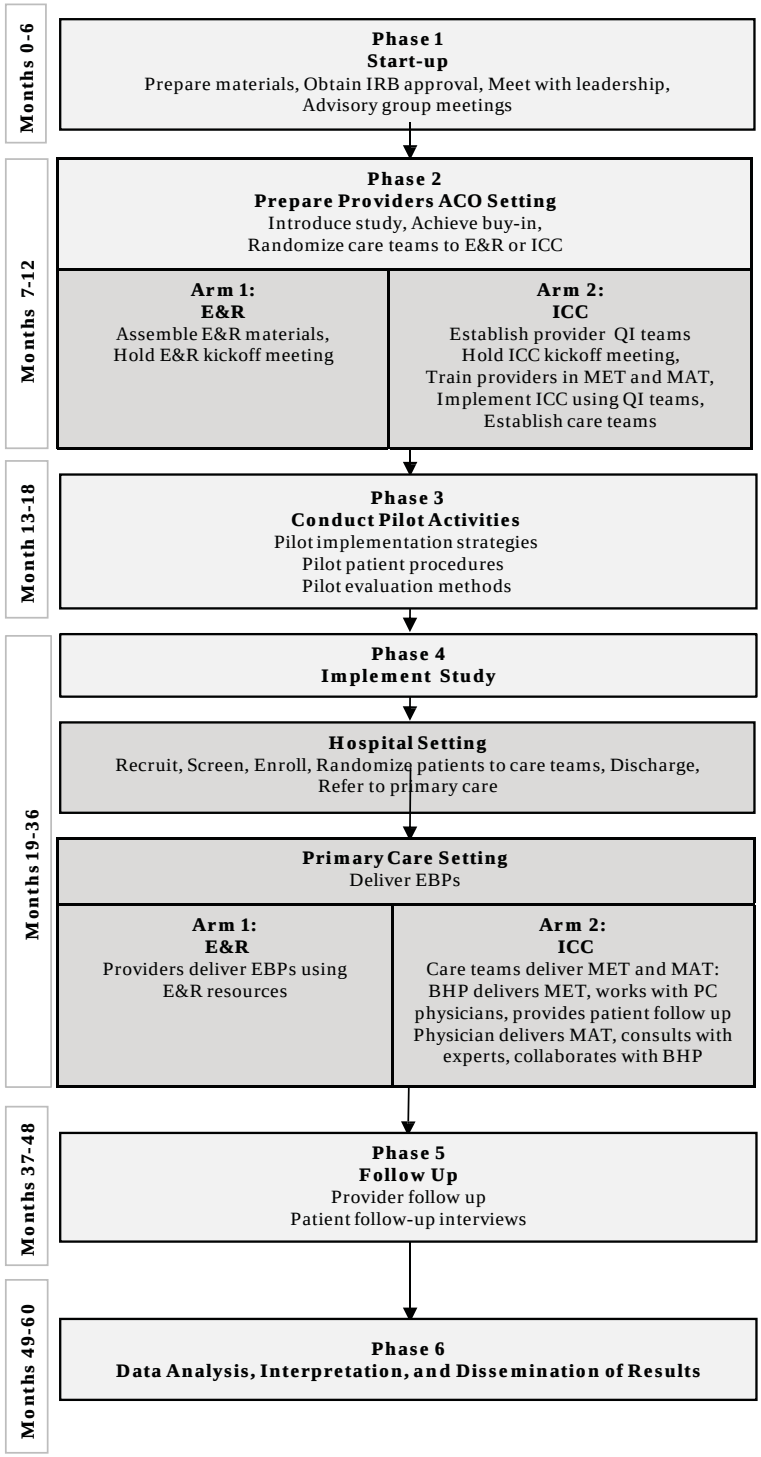
Study Design. Figure 1 provides an overview of our study design and timeline. We will use a two-step randomization design to select care teams (comprising one or more physicians, a nurse practitioner, registered nurse and/or a physician's assistant, and a BHP) and patients for participation. Within each primary care clinic, all care teams will be randomly selected to implement either ICC or E&R. The care teams will not overlap, and there will be one BHP for each condition in each clinic. We will recruit patients from one of the two hospitals who had an admitting diagnosis of an OAUD; consenting patients will select a clinic to attend and will be randomized to a care team within that clinic. Among the 5 clinics, the number of physicians ranges from 4 to 13; we conservatively estimate at least 4 care teams per clinic, or 20 total teams.

The proposed study design offers advantages for estimating the causal impact of ICC compared to E&R. Because there are multiple care teams within a clinic, some delivering ICC and some delivering E&R, any clinic characteristic that is associated with either strategy and that could affect outcomes will be controlled for. Randomly assigning care teams to ICC or E&R and then randomly assigning patients to care teams will reduce bias, increase external validity of the observed impact, and may make results generalizable to clinics beyond

the study clinics--possibly to other urban FQHCs and free clinics. In addition, with multiple patients in each clinic receiving either ICC and E&R, any possible correlation among outcomes of patients attending the same clinic will be controlled for. This will also increase the effective sample size since clinics will be used as blocks in the design.

Our design has potential limitations. Randomizing care teams to either ICC or E&R can lead to contamination across teams. We believe this is highly unlikely: care team staff do not overlap, use different examination and treatment rooms, and have separate team meetings. The clinical information system can be programmed so that only providers in the ICC condition will receive clinical reminders and have access to the registry functions. In general, each element of the ICC model must be provided by an appropriately trained team; thus ICC cannot be accidentally delivered. During focus groups and interviews, we will ask staff about sharing information between study conditions; any contamination found will be noted and controlled for in all analyses.

Figure 1: Project Overview and Study Design



ACN- Accountable care network; E&R - Education and resources; ICC - Integrated collaborative care; QI - Quality improvement; MET - Motivational enhancement therapy; MAT - Medication assistance therapy; BHP- Behavioral health professional

Project Phases. The study has 6 phases. *Phase 1* includes identifying materials and resources, obtaining IRB approval, conducting pre-implementation provider and administrator interviews and focus groups, and holding advisory group meetings. *Phase 2* includes meeting with VFC leadership, establishing care teams, randomizing providers to care teams, and holding kickoff meetings. For the ICC arm it also includes establishing quality improvement (QI) teams, training providers in MET and MAT, and using the QI teams to adapt ICC for the local setting. We will discuss infrastructure and agency processes related to implementation of ICC, help to set up decision support and update clinical information systems, and define guidelines for linkages between the PCPs and community resources. During *Phase 3* we will pilot patient identification and enrollment procedures and the evaluation methods to ensure providers are prepared for implementation. Providers will try the new procedures, and suggest changes to make them more efficient. We will provide coaching and feedback on MET and MAT as providers use these EBPs. We will also pilot the collection of utilization and cost data and the fidelity testing of the EBPs. *Phase 4* includes enrolling patients and observing the effects of ICC and E&R on outcomes. We will measure the extent of ICC and E&R implementation, using provider focus groups and patient and provider surveys. *Phase 5* includes collecting three and twelve-month follow-up interviews with patients. Upon completing the twelve-month patient interviews, we will gather post-study data from providers and administrators. During *Phase 6*, we will collect final administrative data, analyze qualitative and quantitative data, interpret results, and prepare multiple papers to disseminate results. Our papers will focus on description of the process and extent of strategy utilization by providers/clinics (Aim 1), the impact of the strategies on implementation outcomes

(Aim 2a), service system outcomes (Aim 2b), patient outcomes (Aim 2c) and costs (Aim 3).

Strategies. We now describe E&R and ICC, our conceptual framework for how ICC is hypothesized to influence outcomes, and our approach to helping PCPs implement and use the strategies. Both strategies consist of research team activities to introduce (and in the case of ICC to support) the strategies, as well as local implementation and both promote the same evidence-based treatment--MET and MAT.

1)Education and Resources*:* The E&R strategy is commonly used in primary care to promote adoption of EBPs.[15,16] E&R will include a 1/2-day kickoff conference where all E&R providers will receive information about the study; an overview of EBPs for OAUDs; and toolkits, including manuals, screeners, and training resources available online or in the community. Senior VFC management will promote how the study aligns with the clinic's mission, and the use of care teams to integrate SUD care into primary care. E&R providers will receive no follow-up support for organizational change, coordination of care teams, or MET/MAT supervision.

2)Integrated Collaborative Care (ICC): Figure 2 shows our hypotheses about how ICC improves outcomes. Our study is powered to test how the ICC strategy as a whole affects our outcomes of interest; we will not have the power to detect the relative influence of any single model component on outcomes. ICC is typically considered a model or framework for evidence-based care delivery; we consider it a strategy because components of ICC are hypothesized to increase the delivery of EBPs. We are aware that our version of ICC is a hybrid of a strategy and a clinical practice, since the BHP will deliver MET as well as act to change clinical practice. To address this issue, we examine multiple levels of outcomes. Our conceptual framework specifies factors that can influence delivery of evidence-based OAUD treatment; we use a QI approach to implement ICC. ICC is grounded in the collaborative care model of chronic disease management,[58-60] which is based on diverse theories including social influence theory[61-63] and social learning theory.[64] Our approach to QI is informed by the organizational transformation model, developed in the RWJ Pursuing Perfection initiative and adapted by Lukas.[65,66] Key model elements are active commitment of top leadership; alignment with system priorities, infrastructure and resources; and multi-disciplinary evidence-based clinical process redesign. We describe the components of ICC below.

Figure 2. Conceptual Framework: How the Integrated Collaborative Care Model Improves

	Health System Organization	Delivery System Design	Decision Support	Clinical Information Systems
Implementation				
Acceptability	√		√	
Adoption	√	√	√	√
Appropriateness		√	√	√
Feasibility		√		√
Sustainability	√	√	√	√
Service System				
Quality of care	√	√	√	√
Utilization	√	√	√	√
Costs	√	√	√	√

1. Health system organization**.** Organizational change requires senior leadership support: They have the decision-making authority to align system strategies and organizational priorities with staff responsibilities and rewards.[65,67] We will involve VFC leadership in planning, training for, and implementing ICC.

2. Delivery system design**.** Delivery system design refers to changing the organization of care delivery to support reliable and routine delivery of evidence-based care.[11,68] Essential elements include clinic-specific protocols describing what and how care will be delivered, by whom, when, and where. Care teams, anchored by a BHP and associated PCPs, will provide evidence-based OAUD treatment. The BHP will function as a care

manager, developing a treatment plan with the patient, coordinating patient care, tracking and following up on patient treatment progress and adherence, and communicating with ICC team members. With the PCP, the BHPs will integrate OAUD treatment into primary care for all health needs and deliver MET if indicated.

3.Decision support. Promoting decision support will involve expert consultation, training, and supervision for following the EBPs. We will help providers obtain buprenorphine certification, train and supervise the BHP in MET, conduct monthly case conferences, and provide support via an existing e-consultation system

4.Clinical information systems to track progress and provide clinical reminders. We will work with VFC information technology staff to incorporate a clinical registry into its existing NextGen EHR, which is locally modifiable to support clinical trials. This will help care teams monitor progress and adherence, and will incorporate clinical guidelines and reminders to support effective care and team coordination. We will train providers to collect and use patient outcome data to evaluate patients' response to treatment and guide decisions regarding treatment changes. Patient outcome data will be incorporated into MET delivery.

5.Linkages between the healthcare system and the community. Patients with OAUD often require referrals to services usually not available within primary care. Thus linkages to appropriate agencies and services may be a cost-effective way to obtain important resources for patients, as well as strengthen organizational linkages to the community. To facilitate linkages, we will invite community stakeholders to the kickoff conferences.

Implementation of ICC. During phase 2, VFC leadership will designate ICC providers to participate in QI teams; research team members (Ms. Chen; Drs. Heinzerling, Ngo, and Watkins) will conduct site visits to each clinic to introduce the ICC care model and work with the QI teams to develop a detailed implementation plan. We will follow up with monthly site visits and weekly telephone calls. By the end of phase 2 we will have a clinic-specific protocol that describes —who does what to whom, when, where and how‖. We will pilot test the protocol in phase 3. The QI teams (with researcher participation) will assess discrepancies between the implementation plan and execution. We will use patient and provider experiences during the pilot to adapt or refine the original implementation plan and protocol. We will monitor MET/MAT fidelity, providing additional training/supervision as needed. We will keep detailed notes to document the implementation process.

Evidence-based Practices. The goal of both ICC and E&R is to increase delivery of motivational enhancement therapy (MET), and medication assisted treatment (MAT). Substantial research supports their effectiveness.

Motivational Enhancement Therapy (MET). MET is a registered,[69] brief[25] EBP for SUD based on principles and strategies of motivational interviewing.[70] Motivational interviewing is a directive, client-centered counseling style for eliciting behavior change for a range of problematic behaviors, including substance use.[69,71] It has been tested extensively in treatment evaluations of alcohol consumption, drinking intensity, and other drug use/misuse (e.g., marijuana, nicotine, and opiates).[69,72-78] MET can be applied in a single session[69,72-78] or in a series of sessions,[72,73,77,79] and is effective even when delivered by non-mental health providers.

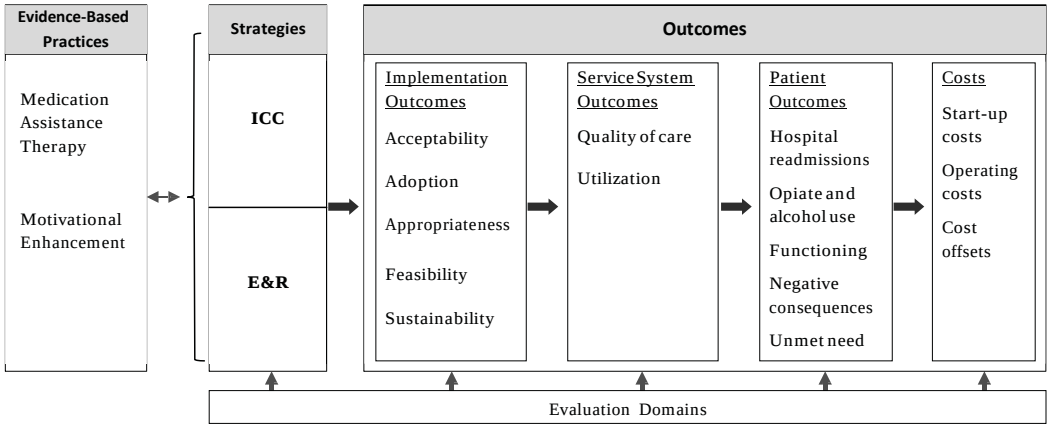
2. Medication-Assisted Treatment (MAT). Evidence suggests that medications can improve treatment outcomes for individuals with alcohol[80-82] and opiate disorders,[83-85] particularly when combined with psychosocial counseling.[86] For alcohol use disorders, the FDA recommends Naltrexone for treatment in primary care.[87-90] For opiate disorders, the FDA recommends Buprenorphine and/or Naloxone.[55,83,85,91-97] Multiple resources support physicians and nurses in office-based delivery of buprenorphine.[96,98,99]

Training in MET and MAT. Both ICC and E&R providers will receive written information about MET and MAT, and an introductory lecture. BHPs in the ICC condition will be provided motivational interviewing (MI) and MET training by Elizabeth D'Amico, PhD.[91,167,168, 22] A 2-day overview workshop will include presentations, demonstrations, practice exercises, and role plays of practice sessions based on the MET Project Match clinical research guide.[71] During the pilot phase, every MET session[22,90,169] will be recorded and 20% scored for fidelity to MI.[100] BHPs will receive weekly supervision with coaching and feedback.[170] BHPs are expected to follow the protocol and, by the end of training, provide competent MET and follow the protocol. Supervision will be available throughout, in response to provider request. *MAT Training* for the ICC condition will be led by Dr. Heinzerling, who is board certified in Internal Medicine and Addiction Medicine and directs the UCLA Primary Care Addiction Medicine clinic. The trainings will consist of 1) an introductory overview of office-based treatment of opioid and alcohol dependence, 2) one or more sessions observing office-based addiction medicine procedures at the UCLA Primary Care Addiction Medicine clinic, and 3) ongoing mentoring and technical support during service implementation. Curriculum will draw on SAMHSA's Treatment Improvement Protocols for buprenorphine[101] and naltrexone.[102] Participants will receive a packet of reference materials (progress note templates, patient questionnaires, patient education handouts) to help implement the services in their clinics. Following the initial sessions, physicians will also complete the American Society of Addiction

Medicine online buprenorphine training (http://www.buppractice.com/) and obtain the DATA 2000 waiver to prescribe buprenorphine. During the pilot and the implementation phase, Dr. Heinzerling will provide ongoing technical support and clinical mentoring to ICC providers via phone/video conferencing or site visits.

Evaluation Design.

Figure 3. Study Overview and Evaluation Domains



SOURCE: Adapted from Procter, et al. 2008

Figure 3 shows our evaluation domains. First, we will measure the implementation process and extent to which the strategies are used (Aim 1). As recommended by Michie et al (2009),[53] we will document the components of the E&R and ICC strategies that the care teams use and investigate barriers and facilitators. Using a modified version of Proctor et al. (2011)[55,56] innovative model for implementation research, we propose four types of study outcomes: implementation, service, patient (specified in Aim 2), and costs (Aim 3).[103]

Implementation outcomes. We define implementation outcomes as —the effects of deliberate and purposive actions to implement new treatments.‖[55] Implementation outcomes serve three important functions: 1) they are indicators of implementation success; 2) they are proximal indicators of implementation processes; and 3) they are key intermediate outcomes in relation to service system or patient outcomes, because a treatment will not be effective if it is not implemented well. We will evaluate the following 5 implementation outcomes for both MET and MAT. 1) *Acceptability:* the perception among implementation stakeholders that a given EBP is acceptable; 2) *Adoption*: intention to use the EBP; 3) *Appropriateness:* the —perceived fit, relevance, or compatibility‖[103] of the EBP in the organization; 4) *Feasibility:* the extent to which the EBP can be successfully used within a given setting; 5) *Sustainability:* the extent to which a newly implemented EBP is maintained within a service setting's ongoing, stable operations.‖[103]

Service system outcomes. We evaluate two service system outcomes; 1) quality of OAUD care, including linkage with primary care, utilization of MET and MAT and the patient's experiences with care (patient-centeredness and timeliness); and 2) utilization of physical and mental health care. Because of extensive co-morbidity between physical, mental and substance use disorders, providing EBP for OAUDs may also affect use of physical and mental health care.[1,12]

Patient outcomes. Primary outcomes include hospital readmissions, and OAUD-specific outcomes such as quantity and frequency of use, patient functioning, negative consequences from use, and unmet treatment need. Secondary outcomes include productivity and satisfaction.

Cost outcomes. Cost outcomes include startup costs for implementing each strategy, operating costs after startup (including labor costs for healthcare and administrative staff, supplies, and IT services), and medical and psychiatric cost offsets. Summing across these categories, we will produce estimates of the total costs of ICC and E&R for providers, costs per patient, and costs per FTE physician.

Data Sources, Measures, and Procedures

Table 1 summarizes the evaluation domains by level of analysis, data source, and study phase.

Evaluation Domain	Level of Analysis	Data Source					Study Phase
		Focus Groups	Semi-Structured Interviews	Admin Data/ EHR	Audio-Tapes/ Checklist	Patient Interview/ Provider Survey	
ICC AND E&R USE							

Implementation process	Administrator, Care team	X	X				Pre-, Mid-Study
Extent	Administrator, Care team	X	X				Pre-, Mid-Study
IMPLEMENTATION							
Acceptability	Administrator, Provider					X	Pre-, Mid-, Post-Study
Adoption	Provider					X	Pre-, Mid-, Post-Study
Appropriateness	Administrator, Provider	X	X				Pre-, Mid-, Post-Study
Feasibility	Provider			X	X		Mid-Study, Post-Study
Sustainability	Provider		X	X			Post-Study
SERVICE SYSTEM							
Linkage w/ primary care	Patient			X			Post-Study
Quality of OAUD treatment	Patient; Provider			X	X	X	Mid-,Post-Study
Mental and physical health treatment utilization	Patient			X		X	Post-study
PATIENT							
Hospital readmissions	Patient			X			
Opiate and alcohol use	Patient					X	Baseline, 3-Month, 12-Month
Functioning	Patient					X	Baseline, 3-Month, 12-Month
Negative consequences from substance use	Patient					X	Baseline, 3-Month, 12-Month
Unmet need	Patient			X		X	Baseline, 3-Month, 12-Month
COST							
Start-up costs	Organization, Provider			X			Pre, During,
Operating costs	Organization						During, Post-Study?
Cost offsets	Organization					X	During, Post-Study

Measures of ICC and E&R Implementation and Use (Aim 1) We will use administrative records that document any trainings, training attendance records, and access to MET/MAT resources and will review all meeting minutes. In the provider interviews and focus groups, we will ask about their awareness of the ICC and E&R models, their participation in any related trainings, and access and utilization of ICC and E&R materials. We will use components of the Assessment of Chronic Illness Care (ACIC)[104] to assess the level that each component of the ICC model is being implemented within each care team. Respondents (practice teams) are asked to rate the degree to which each component is being implemented within their system. We may also assess validated care team process measures covering domains of team communication,[105] psychological safety,[106,107] coordination,[105] role clarity,[108] team identification,[108] team climate,[109] leadership,[105,110] and perceived team effectiveness.[111] Dr. Friedberg and the RAND SRG have experience with assessing these domains, in a currently funded project (R18 HS20120-01). *Facilitators and Barriers*. We will use items adapted from Scheier et al.[112] and will systematically query staff abut experiences with each intervention. We will develop additional items based on standard barriers and facilitators for delivering EBPs.[113]

Measures of Implementation Outcomes (Aim 2a). *Acceptability.* To assess acceptability we will utilize the *EBP Attitude Scale (*EBPAS) and the *Substance Abuse Attitudes Survey (*SAAS). The EBPAS is a brief (15-item), valid, reliable measure that assesses general attitudes toward adoption of EBP.[94] SAAS is a reliable and valid measure of physician attitudes towards alcohol and drug misuse.[114] *Adoption.* We will assess intent to adopt using a survey instrument[115] that asks whether staff attended EBP training, obtained access to the EBP written materials and implementation support tools, and intended to use the EBPs. We will use the EHR to measure the *proportion of providers* who delivered any of the EBPs during the study. *Appropriateness.* We will adapt Moore and Benbasat's[116] validated instrument for the current study. The focus groups will capture reasons why the intervention was or was not perceived as advantageous, complex, and compatible with other approaches. *Feasibility.* We will assess feasibility retroactively by asking participants whether the intervention was successfully implemented and whether poor recruitment, retention, resource or training requirements or other barriers impeded use. *Sustainability.* We will assess whether providers continued to use the ICC care model and EBPs one year after the end of research support for the strategies.

Measures of Service System Outcomes (Aim 2b) *Quality.* We will use previously developed quality indicators.[117,118] The indicators cover the Institute of Medicine domains of effectiveness and timeliness. We will use the Patient Assessment of Chronic Illness Care (PACIC) to assess patient-centeredness.[119] To measure MAT fidelity, we will examine patient EHR to determine whether providers delivered the EBP according to protocol. To measure fidelity to MI for MET, we will use the Motivational Interviewing Treatment Integrity (MITI)

scale.[95,120-122] *Mental and physical health care utilization* will be measured by examining the EHR and by patient self-report given the possibility that patients may use services outside of VFC.

Measures of Patient Outcomes (Aim 2c)

Baseline Characteristics and Possible Covariates. The Composite International Diagnostic Interview (CIDI)[123] will be used to diagnose substance use disorders, and can be administered by non-clinicians. The CIDI will be assessed at baseline and used as a covariate. We will also assess background characteristics (age, gender, race/ethnicity, education, income, history of SUD treatment, HIV status, depressive symptoms using the PHQ-9,[124,125]) and presence of co-morbid physical disorders as potential moderators of the treatment effect.

Primary Outcomes All patient-reported outcomes will be collected at baseline, 3-month and 12-month interviews. *Hospital Readmission.* We will measure readmissions using hospital claims data and patient self-report. *Substance Use.* We will use the TimeLine FollowBack (TLFB) method[126] to assess substance use. The TLFB uses a calendar to ask clients to retrospectively estimate their patterns and frequency of substance use for a period (e.g., 90-days) prior to the interview date. *Negative Consequences from Use.* We will assess negative consequences associated with alcohol and illicit drug use using the Shortened Inventory of Problems (SIP-AD).[127] *Functioning.* We will use the 12-item Short-Form General Health Survey (SF-12)[128] , a reliable measure of changes in mental and physical health and functioning, to assess quality of life and functional status.[170,171] We will also use the EQ-5D,[172] and a single item visual analogue scale as an assessment of global quality of life.[173] *Unmet Need.* We define unmet need as ongoing substance abuse without appropriate care.

Secondary Outcomes*. Productivity.* We will measure productivity by including assessments from the Unutzer et al (2001)[37] collaborative care study, including questions regarding employment and nonmarket employment (e.g., caregiving and volunteer work). *Client Satisfaction.* We will measure patient satisfaction using the Client-Satisfaction Questionnaire (CSQ-8), a self-report measure of satisfaction with health and human services. The measure has demonstrated good reliability[129] and validity[130-132] and is responsive to measuring change over time.[133] Analysis of these data will be part of the analyses of patient level outcomes.

Measures of Costs. We will collect the following costs: startup costs (e.g., recruitment of the BHP and infrastructure investments such as IT); operating costs including labor costs for staff, supplies, and IT services; and medical and psychiatric treatment costs. The primary sources of cost data will be measurement of work hours in each staff category via survey, administrative financial records on physician and other professional fees, electronic health records (EHR) and patient surveys on services provided, and provider estimates of infrastructure investments and capital costs. To extrapolate our cost estimates to the national level, we will use secondary data on average compensation for physicians from the MGMA Physician Compensation and Production Survey or AMGA Medical Group Compensation and Financial Survey.

Data Collection Procedures

Focus Groups and Provider Surveys*.* We will conduct focus groups with the care teams to assess how ICC and E&R were implemented and perceptions of the appropriateness and feasibility of delivering MET and MAT in primary care settings. We will conduct separate focus groups for providers assigned to E&R and ICC. The focus groups will be conducted yearly during the study (Please see timeline). Clinical team members will complete paper and pencil surveys at the time of the focus groups to assess acceptability, adoption, and appropriateness. We will assess fidelity of MET using audiotaped therapy sessions for both conditions.

Administrator Semi-Structured Interviews. We will conduct individual interviews with clinic administrators to assess how and whether ICC was adopted, perceptions of the appropriateness of ICC, E&R, and MET/MAT, and feasibility of delivering MET/MAT in the local setting. We will build on an informant interview protocol used in previous implementation research[115,134] to develop a semi-structured interview guide. The interviews will follow a broadly accepted format—an initial grand tour question, followed by standard probes to generate lists of responses and short qualitative answers. We will use multiple strategies to decrease the possibility of bias, including use of standardized instruments along with semi-structured interview protocols.

Fidelity Data We will have BHPs in both conditions audiotape therapy sessions and will randomly select one session from each patient for fidelity assessment. Drs. D'Amico and Ober will use the MITI scale to evaluate fidelity to MET.[95] A randomly selected 20-minute segment will be coded from 20% of the audiotaped sessions conditions and 20% will be randomly selected to double code for reliability. Raters will receive 40 hours of training and will meet weekly to discuss coding discrepancies.

Organizational Records. We will examine documentation from each clinic on meetings and/or trainings in the EBP and implementation strategies (e.g., ICC components), attendance rates, and access to EBP resources.

We will abstract the EHR for each participant from the VFC system to assess exposure to MET, MAT, other health care utilization for physical and mental health concerns, and hospital readmissions.

Patient Surveys/interviews*.* We will conduct patient interviews at baseline (prior to hospital discharge), and at 3 and 12 months after baseline. SRG will conduct all interviews. *Participant Recruitment, Screening, Randomization, Baseline Patient Interviews*. A COPE staff member will identify patients with an admitting diagnosis of an OAUD disorder and will ask them if they are willing to receive information about the study. Interested patients will be contacted by the SRG; patients with an OAUD diagnosis will be screened for eligibility. Criteria include: 1) 18 or older; 2) understands English; and 3) does not already have a PCP or is willing to switch to another PCP. RAND staff will randomize patients and conduct the baseline interview while patients are still in the hospital. RAND staff will also inform the hospital discharge coordinator of the implementation condition; all patients will be discharged according to usual discharge practices. Patients in the ICC condition will receive a ―warm handoff‖ (i.e., appointment reminders, phone calls, a personal visit in the hospital) from the ICC BHP at the clinic to which they are referred to improve linkage of the patients between the hospital and the clinic. Flow Rates. Based on the rates of OAUD admission and discharge diagnoses in 2009 (approximately 58 per month), we anticipate a total of 30 eligible patients per month enrolling in the study. See SRG budget. Study Assignment Procedures. Patients will be randomized to one of the two strategies. We will use a blocked randomization stratified by clinic. The statistician will keep the block size hidden to prevent gaming. The random assignment of each patient to either condition will happen after the baseline interview is conducted. The statistician will generate and give SRG sealed envelopes containing the random assignment for each enrolled patient. This procedure will ensure an approximately equal number of patients assigned to each condition within each clinic. Even when participants are randomly assigned to conditions, it is possible that characteristics of participants, of the research setting, of the design, and differential rates of refusal and treatment dropout across conditions[135] may not be balanced, potentially compromising the ability to draw strong causal inferences. We will consider using case-mix to adjust for pre- existing participant differences.

Costs. We will obtain cost data from administrative financial records and provider work logs. To facilitate data collection, we will design a questionnaire similar to the DATCAP and SASCAP.[43,136] We will collect data on patient treatment utilization from the EHR and patient surveys. Providers will document work hours related to study patients during a random sample of weeks during the study.

Analyses by Specific Aims

Aim 1: To measure the process and extent of ICC and E&R implementation.

Strategy Use. Two raters will examine the extent to which care teams successfully implemented the components of the two strategies as reported in agency documentation, semi-structured interviews, and the provider survey. We will create a composite measure from the ACIC of ICC strategy utilization. Psychometric properties of such composite score will be studied. Data from the semi-structured interviews with staff will inform us about the facilitators and barriers to implementation. *Facilitators and Barriers.* We will use classic content analysis to analyze the notes from the open-ended interview questions to determine the reported facilitators and barriers to implementation.[112,113] The interviewer and notetaker will collaboratively develop field notes.[137,138] We will sort the narrative text sections of the notes by themes to identify issues common across interviews. The interviewer and notetaker will first read sections from the interviews to identify themes[139]. After review, a coding system will be developed that includes a description of each theme, inclusion and exclusion criteria for sorting sections, and typical and atypical exemplars.[140] We will use Microsoft Excel to organize and analyze the field notes. Inconsistencies will be discussed to determine a final consensus coding decision.

Aim 2A: Implementation outcomes

Acceptability, Adoption, and Appropriateness. There will be a total of at least 20 care teams. Since these outcomes are collected at the care team level, we can conduct only descriptive quantitative analyses (there will be a total of 80 members of the care teams, but implementation outcomes within each care team will be highly correlated, and so effective sample size will be smaller--40 to 50). We will use the Fischer's exact chi-squared test appropriate for small sample size comparison when comparing categorical characteristics and a t-test for continuous variables. The test statistics will test the hypothesis of whether an outcome such as appropriateness is better for ICC compared to E&R. We will also examine whether care team characteristics, (gender, race) are associated with these outcomes. We will also measure ―fidelity‖ of ICC implementation using the ACIC and correlate it with different team characteristics. *Exploratory Hypothesis: We hypothesize that higher ratings of acceptability, adoption, and appropriateness will be correlated with higher levels of*

implementation, as measured by the ACIC. We will test this hypothesis by regressing each client team-level outcome (e.g., for appropriateness we will examine the *relative advantage, compatibility, observability and trialability)* on ACIC score, while controlling for baseline values of these measures. ***Feasibility and Sustainability (qualitative data).*** This analysis will draw on principles of grounded theory,[141,142] which involves examining narrative data, searching for patterns and themes that explain a given phenomenon, and coding the data to further corroborate or modify themes. Using the major domains specified in the focus group and interview protocols, Drs. Hunter and Ober will separately review the recordings to identify patterns. A codebook will be developed that identifies and defines each theme, range, and central tendency described, using verbatim quotes as exemplars.[164] We will assess intercoder reliability. To guard against bias, we will ask respondents to review findings.[165] We will explore the relationship between feasibility, sustainability, and strategy use, and the influence of organizational and team-factors on these outcomes.

Aim 2B and Aim 2C: Service system and patient outcomes

We discuss the analysis of service system and patient outcomes together since both are measured at the patient level and use the same type of analysis. *We hypothesize that patients in the ICC condition will have improved service system and patient outcomes relative to patients in the E&R condition*.

Preparatory Analyses. For each variable to be used in the multivariate analyses described below, we will identify missing values and evaluate the distributions and patterns of gaps. We will impute missing values using a method such as hot-deck imputation or multiple imputation.[143,144] Where appropriate, we will develop scale variables and examine the distributions and psychometric characteristics of those variables. ***Use of Intent-to-Treat Analysis.*** We assume each care team will follow their implementation strategy with all their components. If, however, care teams differentially implemented the strategies, we will use an intent-to-treat analysis. Such intent-to-treat analysis will compare all patients who complete the baseline interview as if they were in the group to which they were assigned, regardless of whether they actually complete treatment or of the intensity of the treatment. Additional efforts will also be made to control for implementation intensity when necessary. We will consider using instrumental variables with randomization as instrument in the case of severely uneven implementation strategy across care teams. ***Loss to Research Follow-Up.*** We expect a response rate of 90% and 80-85% at the 3 and 12 month follow-ups respectively based on previous SRG experience.[145] We will compare attriters versus completers on baseline characteristics. If differences exist, we will account for loss to follow-up by employing multiple imputation or nonresponse weights.[144]

Analytic Approach. ICC and E&R will be implemented in every clinic, controlling for most confounders. This analysis will estimate the causal difference between the two strategies in the population commonly covered by the VFC. For **binary outcomes** such as unmet need and hospital readmission, a bivariate analysis will first be conducted to estimate the uncontrolled association between being in an ICC group and outcome. In addition, even though our design randomly assigned patients, we will examine the association between outcomes and covariates that can affect the outcome while being also related to the ICC implementation, including age, gender, race/ethnicity, education. Characteristics related to the outcome at a conservative significance level of α=0.2 will be considered covariates in the multivariate analysis. For the multivariate analyses, we will infer the relationship between outcome and ICC by fitting growth curve/hierarchical models using SAS Proc Mixed, R LME4 and Winbugs. These models take into account the multilevel structure of the data: three repeated measures over time (baseline, 3 and 12 months) nested within patient and patients nested within care teams and clinics. Since the clinics are a convenience sample, they will be treated as fixed effects. For binary outcomes, a logistic regression will be used. Using hospital readmission as an example, where 1 is the value of readmission and 0 if not, the model will be specified as

$$\Pr ob(\mathrm{Re}\, admission_{it} = 1) = \frac{1}{1+\exp(\pi_{0i} + \pi_{1i} T_t)} \qquad \text{(Equation 1)}$$

$$\pi_{0i} = \beta_{00} + \beta_{02} Z_i + r_{0i} \qquad \text{(Equation 2)}$$

$$\pi_{1i} = \beta_{10} + \beta_{11} ICC_i + \beta_{12} Z_i + r_{1i} \qquad \text{(Equation 3)}$$

where $Readmission_{it}$ is the readmission outcome of patient i at time t (0, 3 or 12 months), T_t is the time value assumed continuous, ICC_i the implementation assignment taking value 1 for ICC and 0 for E&R, and Z_i represents all the covariates included in the model including the clinic fixed effect. Additional approaches of covariate adjustment including propensity score methods,[146] or double-robust estimation methods [143,147,148] will also be considered, depending upon the number of measures Z_i for which there are significant baseline

differences between the two study conditions. In this model, equation 1, estimates the likelihood that a patient is readmitted and it is assumed that the log-odd impact of readmission changes linearly over time by a factor π_{1i} for each patient i. At baseline, the log-odd of readmission is also assumed to be estimated at π_{0i} for each patient. Equations 2 and 3 model the dependence of the baseline and time trend impact in readmission as a function of whether a patient was under ICC or not (only for π_{1i} since no ICC impact should be expected at baseline) and other patient characteristics summarized in Z_i including clinic level fixed effect. The parameter β_{12} estimates the log-odd of the impact of ICC on readmission over time and a chi-squared test will be used for inferring about whether or not such impact is statistically different from 0. Similar analysis will be conducted for other outcomes. Even though clinic fixed effect will be included to account for the clinic to clinic variability, a sensitivity analysis of clinic random effect will also be considered and the proportion of variability explain by clinics will be estimated. For **continuous outcomes** such as days of OAUD use, quality of care or functioning, equation (1) about will be replaced by a linear model counterpart of the form

$$Severity.of.abuse_{it} = \pi_{0i} + \pi_{1i} T_t \qquad \text{(Equation 1')}$$

For such model, inference will be made similarly with the exception that the parameter β_{12} will now estimate the incremental change in the outcome score when comparing ICC to E&R patients. Similar sensitivity analyses will be conducted for the continuous outcomes. For **Outcomes Assessed only at Month 3 and/or 12** we use cross-sectional analyses (such as linear and logistic regression or chi-square tests) to estimate the effect of ICC relative to E&R. We will correct for potential bias due to attrition at follow-up with non-response weights.

Fidelity. We will estimate interrater reliability for MET using the prevalence-adjusted bias-adjusted kappa.[149] The hierarchical model described above will be used to estimate the difference in MET and MAT fidelity between ICC and E&R.

Power analysis for outcomes measured at the patient level We expect to enroll 400 patients and estimate the effect sizes that can be detected with a power of at least 80% when comparing the outcomes of patients randomly assigned to the two conditions in an end-status analysis at month 12 using tests with 5% significance level. This is likely to be conservative because it does not utilize all 3 waves of data and uses only the projected retained sample at month 12 (about160-170 patients per condition). For continuous outcomes, we will be able to detect effect sizes of about 0.30-0.32 standard deviations. These are the kind of effects that can be expected for an ICC type of intervention.[150] This is equivalent to one fewer drink on a drinking day for the ICC strategy versus E&R when the standard deviation of the number of drinks per drinking day is about 3.2.[151] For dichotomous outcomes, we will be able to detect a difference of 13-14 percentage points under the assumption that the E&R group has a 15% rate of receiving the outcome.

Aim 3 To estimate provider costs for each strategy.

We estimate the direct costs of implementing ICC and E&R from the provider perspective. Providers will be financially discouraged if the strategies are not economically viable—or if there is a large degree of uncertainty about intervention's economic impact. From the provider perspective, the economic impact has two components: impact on operating costs and impact on payments received. The primary expenses from ICC and E&R are fixed startup costs including recruitment, training, and infrastructure investments and ongoing operating costs. To measure labor costs we will a. estimate the average salary, overhead, and benefits costs across sites for each member of the care team; b. use the EHR to estimate the number of billable office visits and encounters with study participants c. estimate time spent recruiting the BHP, training the care team, redesigning the care delivery system and in QI team meetings, from provider logs. By combining the estimates described above, we can compute the total labor cost of the intervention over the study period. We will adjust the labor cost estimates from our California providers using MGMA or AMGA data to produce nationally representative estimates. We will also estimate the direct costs of implementation materials such as training and educational guides, in addition to the infrastructure and service costs for the IT components of the intervention. Summing across these categories, we will compare the total costs of ICC and E&R, costs per patient, and costs per FTE physician.

We will generate rough estimates of cost offsets by calculating total non-OAUD medical costs. To capture the costs of service use from out-of-practice providers we include the costs of patient-reported counts of emergency room visits, mental health and physical health visits, and medications. We will assign costs to outpatient services using Consumer Price Index-inflated cost estimates from the Medical Expenditure Panel Survey or MGMA data. Concordance between self-reports and provider records can be reasonable.[152]

Amendment since the last HSPC full committee review on 5/23/13:

- **(AM03) reviewed at the 5/23/13 meeting and approved on 9/05/13**
  Notification of HSPC Approval indicated the following:

On 9/5/2013, the study met the contingencies on the 5/23/2013 HSPC approval of the Phase 3 pilot of the Randomized Controlled Trial. The HSPC approved the revised consent form and the Data Safeguarding Plan (pages 1-8 of the Data and Safety Monitoring Plan).

Remaining Contingencies:

- Further HSPC review and approval of Phase 4 RCT before Phase 4 participant recruitment and data collection begin.
- Further HSPC review and approval of Phase 5 follow-up data collection from RCT participants and post-study data collection from providers and administrators before Phase 5 participant recruitment and data collection begin.
- Further HSPC review and approval of Phase 6 administrative data acquisition before Phase 6 data acquisition begins.

- **(AM05) submitted on 2/12/14 and approved on 2/21/14**
  Notification of HSPC Approval indicated the following:

On 2/21/2014, the HSPC approved the amendment including:

1. Revision of the study design to remove medical (physical health care) provider randomization. Mental health care (therapy) providers will remain randomized. All medical providers will have the opportunity to receive the same level of training and support so patients can continue to see their own providers, regardless of patient study condition. In addition to continuing to see their regular medical provider, intervention patients interested in medication will also see a medical provider who specializes in the particular medication.

2. Revision of form for clinic-administered universal screening for substance use disorders, which will be used to identify patients eligible for study participation (revisions are not substantive).

3. Revision of eligibility criteria to exclude patients with bipolar disorder (diagnosed and received medications or were hospitalized in the past year) and schizophrenia (diagnosed) only if they also indicate "marked" or "exteme" impairment (a self-rating of 7 or more in any of three domains--work/daily activities, social activities, care of self/family/house) of the Sheehan Disability Scale.

4. Revision of eligibility criteria to remove the requirement that patients must be willing to change providers for the length of the study.

5. Revision of consent form to: remove language indicating patients might have to change medical providers: add language that participants who receive medication may have to see a doctor who specializes in the medication in addition to seeing their regular provider; and add language clarifying that patients who are currently receiving mental health services may have to see a different therapist during study participation.

Remaining Contingencies:

- Further HSPC review and approval of Phase 4 RCT before Phase 4 participant recruitment and data collection begin.
- Further HSPC review and approval of Phase 5 follow-up data collection from RCT participants and post-study data collection from providers and administrators before Phase 5 participant recruitment and data collection begin.
- Further HSPC review and approval of Phase 6 administrative data acquisition before Phase 6 data acquisition begins.

Amendment since the last HSPC full committee review on 3/25/14:

- **(AM06) reviewed at the 3/25/14 meeting and approved on 5/08/14**
  Notification of HSPC Approval indicated the following:

On 5/8/2014, one of the contingencies on the 3/25/2014 HSPC approval of the full RCT was met: "HSPC subcommittee review and approval of the consent form, revised to reflect the certificate of confidentiality would provide protection from subpoena 'if granted' and to include standard RAND language pertaining to exceptions for possible disclosure of information regarding intent to harm self or others to those who can protect against such harm."

Also on 5/8/2014, the HSPC approved the following revisions: increasing the baseline survey payment amount from $25 to $50 (to cover time spent on initial screening, consent to contact, eligibility screening, and enrollment in addition to the baseline survey); revisions to other study documents (protocol, consent to be contacted, FAQ, HIPAA form); and revisions to the RHINO Study form (to reflect the increase in payment and that the RAND Survey Research Group will administer the baseline survey).

The remaining contingency is: "Application for a certificate of confidentiality and notification of the HSPC of the outcome." [Certificate issued on 8/21/14]

I am completing the amendment workflow at this time (7/15/2014) at the request of study staff so that another amendment may be submitted.

- **(AM07) submitted on 7/23/14 and approved on 8/04/14**
  Notification of HSPC Approval indicated the following:

On 8/4/2014, the HSPC approved the amendment to:

1. Conduct a single follow-up interview at 6 months after baseline rather than follow-up interviews at 3 and 12 months.
2. Post flyers around the clinic to advertise the study.
3. Post stickers that advertise the study on existing substance use posters at the clinic.

The HSPC also approved: revised consent form; revised FAQ; revised Data and Safety Monitoring Plan; "Welcome to SUMMIT" handout (ER and ICC versions); flyer; and sticker.

- **(AM08) submitted on 3/17/15 and approved on 3/17/15**
  Notification of HSPC Approval indicated the following:

Marilyn Yokota verified that the Data Safeguarding Plan uploaded on 3/17/2015 is the same version (attached to Event Report 2012-0193-RE02) that was approved by the HSPC subcommittee by email on 3/17/2015.