1.0 General Information

* Please enter the full title of your study (Spell out acronyms):

Transforming Opioid Prescribing in Primary Care Pilot and RCT (TOPCARE)

* Please enter the Study Nickname you would like to use to reference the study:

TOPCARE Pilot and RCT

* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List departments associated with this study (Note: The primary department should accurately reflect the primary Department or Section of the PI - click on (?) icon for instructions):

<table>
<thead>
<tr>
<th>Primary Dept?</th>
<th>Department Name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMC/BUMC - BMC - General Medicine</td>
</tr>
<tr>
<td></td>
<td>BMC/BUMC - BMC - Medicine</td>
</tr>
</tbody>
</table>

3.0 Assign key study personnel (KSP) access to the study

3.1 * Please add a Principal Investigator for the study:

Lasser, Karen, MD, MPH

Select if applicable
☐ Student
☐ Resident

If the Principal Investigator is a Student, Resident, or Fellow, the name of the Faculty Sponsor must be supplied in Sections 3.3 and 3.4 below.

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Alford, Daniel Peter, MD
Co-Investigator
Liebschutz, Jane M, MD MPH
Co-Investigator
Parker, Victoria Anne, Ed.M., D.B.A.
Co-Investigator
Samet, Jeffrey, MD, MA, MPH
Co-Investigator
Shanahan, Christopher William, MD MPH
Co-Investigator
Xuan, Ziming, Sc.D.
Co-Investigator

B) Research Support Staff

Beers, Donna Resnik, RN, BSN, CARN
Nurse
Cushman, Phoebe Anne, MD
Technician
Gamble, Olivia Tracy, B.A.
Research Assistant
Guara, George, LPN
Nurse
Husain, Jawad Muhammad, B.S.
Research Assistant
Keosaian, Julia, MPH
Project Manager
Larochelle, Marc, MD, MPH
Participating Clinician
O’Connor, Kristen, BSN
Nurse
Park, Christine, BS
Research Assistant
Penti, Brian, MD
Research Assistant
Roy, Payel Jhoom, MD
Research Assistant
Van Ells, Shannon Elizabeth, BA
Research Assistant

3.3 * Please add a Study Contact:

Keosaian, Julia, MPH
Lasser, Karen, MD, MPH

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The study contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Sponsor:

3.5 Please ONLY list the PI’s Department Chair/Section Chief below. The system will automatically route for signoff to any additional “Special Routing” approvals, so please do not list those here.

Samet, Jeffrey, MD, MA, MPH
Department Chair/Section Chief

**Add the name of the individual authorized to approve and sign off on this study from your Department (e.g. the Department Chair or Dean). This should be someone other than the Principal Investigator himself.
3.6 If applicable, please select the Administrative Assistant(s):

List here anyone performing administrative tasks only (not engaged in research and having no contact with subjects or identifiable data; where certification/recertification and COI disclosure form are not required). - Click on (?) icon for more info.

4.0 Review Path Determination

4.1 Review Path Determination

- This project meets the definition of Not Human Subject Research (NHSR). Examples are non-research Quality Improvement/Quality Assurance projects; case reports or case series that include three patients or fewer; studies that involve obtaining anonymous data/tissues or coded data; or BMC/BU Medical Campus is not "engaged" in human subjects research.
- BMC/BU Medical Campus (the Relaying Institution) codes IRB review to another institution (the Reviewing Institution) under an Authorization Agreement.
- The only research activities in this study involve chart reviews.
- This study fits into one or more of the federal Exempt categories or the study does not have external funding and fits into one or more of the Equivalent Protections Exempt categories.
- None of the above. This study requires Expedited review or the review of the Full Board.

4.2 Emergency Use Report

Is this a report of an Emergency Use of an Investigational Drug or Device that has already occurred? Emergency use prior to IRB approval is permitted for use of an unapproved drug or device in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. The patient or legally authorized representative should sign a consent form. The IRB Director should be notified prior to the emergency use if possible, but this notification is not to be construed as IRB approval. Within 5 working days of the emergency use, this application must be submitted to the IRB.

- Yes
- No

4.3 Individual Patient IND

Is this application for an FDA approved Individual patient (single use) IND?

- Yes
- No

4.4 Humanitarian Use Device

Is this application for an FDA approved Humanitarian Use Device?

- Yes
- No

5.0 Human Subject Training and Conflict of Interest

5.1 BMC/BU Medical Campus Institutional Requirements for human subjects training

- The PI confirms the following:
  - All individuals at Boston Medical Center or Boston University Medical Campus who will have contact with subjects or their identifiable data have been listed on this application in Section 3.0
(including those who will obtain informed consent, analyze identifiable data, perform study interventions, recruit subjects, etc.)

- All individuals listed in Section 3.0 have completed their INSPIR profile or have been asked to do so.
- All individuals listed in Sections 3.1, 3.2, and 3.4 are up to date with human subjects training CITI certification and recertification requirements.

5.2 Conflict of Interest Disclosure

I confirm that all those responsible for the design, conduct, or reporting of the proposed program, including at minimum, all Senior/key personnel in the grant application, have completed the financial interest disclosure forms and submitted them to the appropriate office for Boston Medical Center or Boston University

☑ I confirm

Of the financial interest disclosure forms submitted, have any financial interests been disclosed?

☐ Yes ☐ No

6.0 Funding Source

6.1 Funding Source

What is the source of your research funding. If you have multiple sources of funding (including sub-awards), check all that apply.

☐ Student Research with no External Funding
☐ Dept/Internally Funded
☑ Government
☐ Industry
☐ Foundation/Other
☐ Training Grant (e.g. T32, K-award)

6.2 Study Type

This study is:

☐ BU/BMC PI initiated
☐ Other

Does this study meet the definition of a clinical trial as defined by the International Committee of Medical Journal Editors? (See help for definition)

☐ Yes ☐ No

NOTE: Studies that meet the ICMJE definition will not receive final IRB approval until the IRB is provided with the NCT number from clinicaltrials.gov. The responsibility for registering falls to the PI or Sponsor of the trial.
If this trial has been registered, please enter the 8 digit NCT number in the box, below:

01909076

6.3 Funding Details

For instructions on how to complete this section, click on the Help icon.

<table>
<thead>
<tr>
<th>View Details</th>
<th>Sponsor Name</th>
<th>Sponsor Type</th>
<th>Contract Type</th>
<th>BU SAP Grant Number or BMC AU Number</th>
<th>Award Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NIH/National Institute on Drug Abuse (NIDA)</td>
<td>Federal - NIH</td>
<td>Grant</td>
<td>6003269</td>
<td>R01 DA034352-01</td>
</tr>
</tbody>
</table>

Sponsor Name: NIH/National Institute on Drug Abuse (NIDA)
Sponsor Type: Federal - NIH
Sponsor Role: 
Contract Type: Grant
BU SAP Grant Number or BMC AU Number: 6003269
Award Number: R01 DA034352-01
Grant Title: Implementing Opioid Risk Reduction Strategies into Primary Care Practice
PI Name: (If PI is not the same as identified on the study) Karen Lasser

6.4 Grants Office

In the check boxes below, please indicate which grants office is handling your award/sub-award.

☐ BU Office of Sponsored Programs (OSP-med)
☐ BMC Research Finance (RF)
☐ BMC Clinical Trial Office (CTO)
☐ Charles River Campus Office of Sponsored Programs (OSP-CRC)
☐ Other (must list below)

Funding Notifications:
☐ I have received a Notification of Award (NoA)
6.5 Grant Application or Scope of Work

Click on the Help (?) icon for information on what you're required to attach in this section.

No Document(s) have been attached to this form.

7.0 Study Summary

7.1 Provide a brief summary of the project in terms understandable to a non-scientist (in 500 words or less). Do NOT copy from a grant application.

We propose a cluster randomized controlled trial (RCT) of 56 primary care providers (PCPs) at one large Boston Medical Center Adult Primary Care practice and the following community health centers (CHCs; Dorchester House, South Boston CHC, and Boston Health Care for the Homeless), and their estimated 560 patients on chronic opioid therapy. Note that we are considering PCPs and patients to be the study subjects. De-identified patient data will be used to ascertain outcomes. Intervention PCPs will have access to a nurse-managed patient registry, and will receive academic detailing visits (visits from physicians with expertise in chronic pain management that incorporate feedback on PCPs performance managing patients on chronic opioid therapy). Intervention and control PCPs will receive electronic decision support tools to improve adherence to guidelines. Primary outcomes are PCP adherence to chronic opioid therapy guidelines and patient opioid misuse. All main study outcomes and exploratory variables will be obtained from aggregate, anonymous patient-level data from the clinical data warehouse. These data are collected in the routine course of clinical care. Prior to the start of the RCT, all intervention components (nurse managed registry, electronic tools, academic detailing) will be pilot tested with all PCPs in one BMC Adult Primary Care practice as well as with one PCP from each of the CHCs (Dorchester House, South Boston Health Center, and Boston Health Care for the Homeless). The pilot study is part of the current protocol. It should be noted that we have a prior approved protocol (IRB # H-31780) to conduct the baseline analysis of opioid prescribing practices at BMC and the CHCs.

8.0 Navigation Menu

Please note: Questions in the Navigation Menu section determine which subsequent sections will be displayed and which ones will be hidden. If later you make any change to the Navigation Menu section, you will need to click on the "Save and Continue to Next Section" button throughout the whole application to display any new required section or hide any sections that are no longer required.

8.1 Separate Protocol

Is this a new submission with a separate protocol? This protocol must be from the sponsor or cooperative group or be based on the protocol template found on the IRB website, and must include the purpose, inclusion/exclusion criteria, design/procedure, and data safety and monitoring plan. A separate protocol is REQUIRED for all initial submissions of medical or surgical clinical trials. A GRANT APPLICATION IS NOT A PROTOCOL.

- Yes
- No
- Not applicable, this submission is an amendment
### 8.2 International Research

Are any BU/BMC investigators involved in any way in research activities at non-US sites, including oversight of international research activities?

- [ ] Yes
- [ ] No

### 8.3 Subjects Recruitment

Is the PI/study staff recruiting subjects for this study?

- [ ] Yes
- [ ] No

### 8.4 Subjects Consent

Will informed consent be obtained from any of the subjects?

- [ ] Yes
- [ ] No

### 8.5 Genetics

Does this research involve genetic testing, gene therapy, or collection of genetic information?

- [ ] Yes
- [ ] No

### 8.6 Biological Samples Collection

Does this study involve collecting biological samples for research purposes?

- [ ] Yes
- [ ] No

### 8.7 Drugs/Biological Agents

Does this study involve administering drugs or biological agents?

- [ ] Yes
- [ ] No

### 8.8 Devices

Does this study involve the use of one or more device other than for routine measurements or monitoring (e.g., an EKG machine)?

- [ ] Yes
- [ ] No

### 8.9 Radiation

As part of this study, will subjects be exposed to any procedures involving ionizing radiation for research purposes only?

- [ ] Yes
- [ ] No

### 8.10 Samples or Data Retention
Will you be collecting samples that will be retained past the end of this study, or data that will be retained beyond the required data retention period?

- Yes
- No

8.11 StudyFinder Listing

Do you agree to have the study title, summary, and PI name and e-mail address listed on StudyFinder, a publicly viewable medical campus website for general publicity and collaboration purposes? (If you also want to use StudyFinder to recruit subjects, there is another question to answer in the Recruitment section.)

- Yes
- No

9.0 Study Site Information

9.1 Select one:

- Single site research - conducted by BMC/BU Medical Campus investigator(s)
- Multi-site research project - BMC/BU Medical Campus is a research site but is NOT the main study site
- Multi-site research - BMC/BU Medical Campus is the main research site and/or the BMC/BU Medical Campus Principal Investigator is the overall PI of the entire study or the FDA sponsor

9.2 IRB Authorization Agreement – BMC/BU Medical Campus is the Reviewing Institution

Does this study have or require an Authorization Agreement for External (non-BMC/BU Medical Campus) investigators who will rely on BMC/BU Medical Campus IRB review? ***

- Yes
- No

***If this study has or will require an IRB Authorization Agreement where BMC/BU Medical Campus investigators will rely on IRB review by another institution, do not check YES here, but instead, go to Section 4.1 and check the 2nd option, "BMC/BU Medical Campus (the Relying Institution) cedes IRB review to another institution (the Reviewing Institution) under an Authorization Agreement.".

9.3 Provide details of all other research sites involved in this study. PREAMBLE – ALL INDIVIDUALS ENGAGED IN THE RESEARCH MUST HAVE IRB APPROVAL, EITHER FROM THEIR OWN INSTITUTION (UNDER THE BMC/BU Medical Campus IRB) OR AN APPROPRIATE AUTHORIZATION AGREEMENT.

<table>
<thead>
<tr>
<th>Institution &amp; PI Information</th>
<th>IRB approval for site</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PI Name:</strong></td>
<td>IRB approval will be obtained at this site</td>
</tr>
<tr>
<td>n/a</td>
<td>Requesting an appropriate Authorization Agreement for this Relying Institution</td>
</tr>
</tbody>
</table>
PI Name: n/a

Institution Name:
Boston Health Care for the Homeless

9.4 Study Attachments

Here you can attach any study sites related documents. Attach IRB approval letters from other institutions (if any).

<table>
<thead>
<tr>
<th>Version</th>
<th>Title</th>
<th>Category</th>
<th>Last Modified By</th>
<th>Date Last Modified</th>
<th>Checked Out</th>
<th>View Document</th>
</tr>
</thead>
</table>

No Document(s) have been attached to this form.

10.0 Purpose

10.1 Background/Rationale/Purpose

Provide background information, study rationale, and purpose / study objective(s) and/or hypotheses for this study.


The guidelines suggest that patients at “high risk” for misuse be identified through individual patient risk factors, such as a diagnosis of substance use disorder and mental health problems. Once prescribed opioid analgesics for extended periods, ongoing treatment should include an opioid treatment agreement, urine drug testing, frequent prescriber visits, pill counts (to ensure that a patient is not diverting medications), use of state prescription monitoring program (data on individual pharmacy fills of controlled substances), and addressing aberrant opioid taking behaviors. These guidelines have not been systematically implemented at BMC and affiliated CHCs. Since evidence supports these individual components, it is now time to implement and test them collectively, thus addressing the pressing need for an effective clinical approach to the mounting problems of opioid misuse and addiction. Further, with the transition to the patient-centered medical home (PCMH) model, this is an ideal time to develop primary care systems for safe and effective opioid prescribing that can be incorporated into this new delivery system.

Our intervention approach is based on the documented efficacy of the individual intervention elements (electronic tools, disease registry, and academic detailing) in changing provider practices, and in improving patient outcomes. Quality improvement interventions in CHCs which have included disease registries in the setting of the Chronic Care Model, most notably the Health Disparities Collaboratives of the Health Resources and Services Administration (HRSA), have shown improvement in processes of care for asthma and diabetes. Electronic tools such as on-screen, point of care computer reminders have been shown to achieve improvements in provider behavior, in medication prescribing and test ordering. Academic detailing (which includes feedback on PCP performance), has been shown to improve how health care professionals prescribe medications, which may affect hundreds of patients. Both intervention and control PCPs will receive electronic decision support tools within the EMR to facilitate guideline adherence. These tools include validated instruments to assess patient status and also to facilitate physician adherence to suggested monitoring. The intervention PCPs will receive the services of a nurse-managed registry for planning individual patient care and conducting population-based care for patients.
receiving opioids for chronic pain. Nurses will play a central role in patient management to deliver guideline-concordant care. The registry seamlessly interfaces with the electronic medical record (EMR) to optimize both individual and population-based care. In addition, the nurse will be able to look individual patients up in the MA prescription monitoring program (PMP), to determine whether they are “doctor shopping,” receiving opioid prescriptions from different providers at different sites. Finally, in academic detailing visits, trained co-investigators will visit intervention PCPs to provide them with individualized education (including audit and feedback) to change prescribing practice. It will be important to understand barriers and facilitators to implementing these interventions in the “real world.” We will evaluate this implementation strategy on integrating the best available evidence for managing patients receiving chronic opioid therapy for pain into primary care settings. We will evaluate the implementation using qualitative data, collecting observational and interview data about the implementation process and details of the intervention.

All main study outcomes and exploratory variables will be obtained from aggregate, anonymous patient-level data from the clinical data warehouse. These data are collected in the routine course of clinical care.

This project has the following specific aims:

1) Evaluate the relative effectiveness of the intervention compared to the control condition on PCP adherence to chronic opioid therapy guidelines
   Hypothesis: PCP adherence to chronic opioid therapy guidelines will increase more among intervention PCPs relative to control PCPs

2) Evaluate the relative effectiveness of the intervention compared to the control condition on reducing opioid misuse
   Hypothesis: The proportion of patients with opioid misuse will decrease more among intervention PCPs relative to control PCPs

3) Develop a roadmap for widespread dissemination of the implementation strategy, through qualitative assessments.

11.0 Subjects

11.1 Inclusion Criteria

Include age ranges and sex. If study involves different criteria for different cohorts, please list separately.

<table>
<thead>
<tr>
<th>Order Number</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCP subjects</strong></td>
<td>All PCPs (physicians, doctors of osteopathy, nurse practitioners, and physicians’ assistants) at participating sites who have at least 10 patients meeting criteria below: 1) patient age 18 with 3 or more completed visits to the primary care practice; 2) long-term opioid treatment as defined by 3 or more opioid prescriptions written at least 21 days apart within 6 months and 3) an inpatient or outpatient ICD-9-CM diagnosis for musculoskeletal or neuropathic pain.</td>
</tr>
</tbody>
</table>

We will determine the PCPs with ≥ 10 patients meeting above criteria as follows: from the de-identified baseline data set (see Protocol # H-31780) (this data set is at the patient level and has already been assembled in year 1 of the grant), we will identify the PCPs with <10 patients meeting criteria. These PCPs will then be linked by identification number to name and then excluded from the pilot and RCT.

1 Participating PCPs must be willing to sign up for the MA prescription monitoring program (PMP), since one of the intervention components includes a nurse checking the PMP website. In order to detect the efficacy of this component, it is important that both control and intervention PCPs be enrolled in the PMP. Further, MA physicians are now mandated to enroll in the PMP.

**Patient subjects**

All patients of participating PCPs > = age 18 who have 1) 3 or more completed visits to the primary care practice; 2) long term opioid treatment defined by 3 or more opioid prescriptions written at least 21 days apart within 6 months; and 3) an inpatient or outpatient ICD9CM diagnosis for musculoskeletal or neuropathic pain.
11.2 Exclusion Criteria

Include age ranges and sex. If study involves different criteria for different cohorts, please list separately. Do NOT duplicate inclusion criteria; if no additional criteria, indicate "None."

<table>
<thead>
<tr>
<th>Order Number</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Patient subjects currently receiving care for cancer, except non-melanoma skin cancer.</td>
</tr>
</tbody>
</table>

11.3 Race / Ethnicity

Will the expected demographic breakdown of the study population reflect either the Boston population or BMC population?
☑ Yes
☐ No

11.4 Limited- and non-readers

NOTE: This question is new. If this submission is an amendment and your study is still consenting subjects, as a separate step, you must check the signature page of your active consent form(s). If any do not comply with the below requirements, you MUST submit edited consent form(s) meeting these requirements with this submission. See Editing-Signature-Page for more detailed instructions.

1. Limited- and non-readers excluded:
   - No witness signature line AND
   - Subject statement does not say "(or has been read to me)"

2. Limited and non-readers not excluded:
   - Subject statement says "(or has been read to me)"
   - If the study is greater than minimal risk, either a witness signature line appears or another method to assure and document subject comprehension is described in the Consent section

Are limited- and non-readers EXCLUDED from the study?
☑ Yes
☐ No
☐ Not Applicable - No subjects are to be consented for this study (consent will be waived or enrollment is complete)

11.5 Special Populations

Please indicate if ANY (even one) of the following populations will be recruited (Note: Enrollment from any of these categories requires prior IRB approval):

☐ Minors who are wards of the State**
☐ Cognitively impaired subjects (will require use of an LAR, and assessment of ability to consent)**
☐ Employees, students, or trainees under the direct supervision of the PI**
☐ Minors**
☐ Minors independently making their own healthcare decisions**
☐ Non-English speaking subjects**
☐ Pregnant Women**
☐ Prisoners**
☐ Women of child-bearing potential
Please indicate if any of the following populations will be targeted by your research:

- BMC Residents or Fellows
- BU Dental Students
- BU Medical Students and/or Graduate Medical Sciences Students
- BU School of Public Health Students
- Homeless**
- Individuals with psychiatric disorders**
- Terminally ill patients**

**designated as vulnerable

11.6 You have selected one or more vulnerable population (indicated by ** above) that requires special protections. How will you protect their rights and welfare, obtain informed consent, and prevent undue influence and/or coercion? For Minors, Non-English speaking subjects and cognitively-impaired subjects, note that you will be asked additional questions in the Consent Procedures sect which you may cross-reference here rather than repeating.

We will be recruiting PCPs as study subjects, some of whom will be BMC employees. We will obtain written informed consent from PCPs; the consent form will contain explicit language stating that unwillingness to enroll in the study will not affect employment status. In all analyses PCPs will have a unique identification number; they will not be identified by name. In addition, all presentation of study data will be in aggregate; e.g., PCPs will be identified as "intervention PCPs" and "control PCPs." We will do everything possible to protect subjects from deductive disclosure risk. This will include analyzing anonymous data sets that have been stripped of identifiers that could lead to identification of an individual PCP.

12.0 Design/Procedure

12.1 Design and Procedure

Describe in detail the experimental design, including all materials and all procedures to be performed. Do NOT copy from a grant application – your application will be returned to you for revision if you do so.

Please include a clear timeline of the procedures to be performed. Clarify which procedures/test articles are investigational and which are part of standard clinical care. This description may include:

1. methods
2. specific information concerning experimental interventions, such as dose and frequency of drug (and placebo) administration, or deception/debriefing process for social behavioral studies
3. number, frequency and duration of subject contacts (visits, telephone calls, mail outs, emails)
4. entire duration of participation for a single subject
5. any additional requirements of the subject (post treatment follow-up, diary cards, questionnaires, etc.)

(Note: For multiple sites, indicate which of the procedures will be done at any other sites other than BMC/BU Medical Campus (see Study Site Information). Attach, in the Study Attachments section, copies of any surveys, questionnaires, and other data collection instruments.)

Overview. We propose a 4 year project to implement a primary care based intervention to reduce misuse of and addiction to chronic opioid therapy. We currently have IRB approval to finalize implementation tools to promote adherence to the best available evidence to reduce the risks associated with chronic opioid therapy. These include 3 innovations: electronic decision support...
tools, nurse managed registry and academic detailing. Starting in July 2013, we propose to pilot test the system at one site, a BMC Adult Primary Care practice as well as with one PCP at each of the CHCs. Beginning in January 2014, we will conduct a cluster randomized controlled trial (RCT), randomizing 56 PCPs to receive all 3 practice innovations, "Intervention Group" (nurse care managed registry, electronic decision support tools, academic detailing) or to electronic decision support tools alone, "Control Group." We will perform follow-up at 12 months following the start of the intervention, with primary outcomes of PCP adherence to chronic opioid therapy guidelines and evidence of patient opioid misuse. As the intervention development and rollout proceed, we will study the implementation process in order to develop a roadmap for wide dissemination.

Pilot Study: We have identified one hospital-based Adult Primary Care practice at Boston Medical Center to serve as the pilot site; the pilot study will last for six months. The tools and processes will be adjusted and refined, but we do not anticipate major changes that would change the level of risk to subjects. The tools and processes will be made available to the pilot sites at the end of the pilot period. We will pilot the intervention on one or two teams with up to 17 PCPs and 170 patients receiving opioid therapy. We will engage PCPs at the pilot site in the implementation of the electronic tools and registry, in a way that is minimally burdensome. At regularly scheduled provider meetings, we will demonstrate the registry and electronic tools. The implementation of IT tools will be iterative, with feedback from PCPs incorporated into design adjustments. For example, we will ensure that the number and length of assessments available is reasonable to incorporate into a brief office visit. Drs. Liebschutz and Alford will also pilot test academic detailing materials with PCPs at the pilot site. Each PCP will receive one 30-minute individual visit from Dr. Liebschutz or Alford.

Prior to the visit, the care manager will give specific data on the target PCP, and aggregate data for all PCPs at the pilot site to the expert. Visit content will combine elements of audit and feedback (e.g. review registry of individual PCP compared with that of peers and goals) and as well as traditional educational outreach. Specifically, experts will review each aspect of guideline concordant care (assessment of risk and appropriateness for opioid medication, medication dosing, monitoring for harm/adherence, and pain outcomes) to solicit barriers to implementation or lack of knowledge on the underlying evidence for each aspect of care. The experts will work with the individual PCPs to address barriers identified using motivational interviewing as needed to facilitate behavioral change in applying guideline concordant care.

We will implement all intervention elements at the pilot practice, and will compare primary outcomes prior to and following implementation in the pilot practice(s) versus practices that are not involved in the pilot study. In summary, we will pilot test intervention materials in a way that in minimally burdensome to PCPs. Staff input on intervention components will be sought during regular meeting times that are already devoted to quality improvement projects. PCPs will be compensated for any study activities that take place outside of regularly scheduled meetings; they will be given a $50 Amazon gift card for each ½ hour of their time that is devoted to study activities. We estimate that a maximum of one hour of their time will be needed.

In addition to one Adult Primary Care center at BMC, we would like to simultaneously pilot the intervention with one PCP at each community health center starting in July 2013. Pilotng with one provider from each CHC (Dorchester House, South Boston Health Center, and Boston Health Care for the Homeless) would allow us to identify any challenges to conducting the RCT at each of the study sites as early as possible. To verify the accuracy of all outcome variables, both primary and secondary, a random list of 100 electronic medical charts will be generated from Health Care for the Homeless, which study staff will then audit to confirm the accuracy of the clinical warehouse data pull. We received approval on the same protocol amendment in Year 1 for a chart review at Boston Medical Center.

Cluster Randomized Controlled Trial
Study Sites and Participants
Study Sites: We have identified hospital-based Adult Primary Care practices at Boston Medical Center (teams not involved in pilot study) and several CHCs (Dorchester House, South Boston Health Center, and Boston Health Care for the Homeless) to participate in the cluster randomized controlled trial.

Recruitment and Retention
Recruitment and Screening. PCPs at the CHCs and those in the Adult Primary Care practices will be eligible for enrollment in the RCT. We will facilitate recruitment by identifying a PCP clinical
champion at each site. The champion, who is not part of the research staff, will serve as a liaison between the practice and the study staff. S/he will help to troubleshoot problems and facilitate intervention implementation in a way that is minimally burdensome to the practice. We will attend regular PCP staff meetings to present the study. We anticipate that PCPs will be interested in participating, as both control and intervention PCPs will receive assistance in managing patients with chronic pain on opioid therapy, a challenging patient population. We will also provide PCPs with $50 incentives for each hour spent completing a survey or participating in an in-depth interview.

Participant Retention. We expect a small number PCPs will leave the study sites during the study period. Based on Dr. Lasser’s experience directing a primary care practice-based research network of CHCs, we estimate that 11.1% of PCPs will leave the CHCs. Thus we will have at least 50 PCPs and will have adequate power to study both outcomes (PCP adherence to chronic opioid therapy guidelines and opioid misuse) for an intraclass correlation (ICC) < 0.1.

Study Conditions
Control Condition: PCPs randomized to the control condition will receive electronic decision support tools. This content is common to both intervention and control treatment conditions. To maximize uptake of the tools, Drs. Liebschutz or Alford will lead 2 didactic sessions lasting approximately 45 minutes, during scheduled staff meetings. These will present principles of guideline adherent practice with specific emphasis on patient communication. These talks will be based on curricula developed and distributed through Boston University Continuing Medical Education office funded by SAMHSA, available at www.opioidprescribing.com. The control condition standardizes the provision of information regarding evidence-based management of chronic opioid therapy for chronic pain, allowing for a more rigorous evaluation of the nurse care management/registry and academic detailing intervention. We considered having the control group receive usual care, to demonstrate the maximal effect of our interventions. However, when we approached the CHC medical directors, several said that their center would not participate in the study if the control group received only usual care. Electronic decision support tools available to control and intervention PCPs include patient pain assessments, (Brief Pain Inventory, Pain/Enjoyment/General Function “PEG”), substance abuse (DAST, AUDIT), depression (PHQ9), PTSD (PTSD Checklist Civilian), and risk of prescription drug misuse (SOAPP and COMM). The tools calculate scores with recommendation for specific action for each tool, when appropriate. In addition, last urine toxicology screening with results will be available. Clinicians will enter information on date and time of last opioid dose taken to inform same-day urine toxicology screening. There will be a tool to enter pill count results, along with a calculation of how many pills should be available based on date of last prescription refill and number of pills to be taken per day (also called medication possession ratio, MPR. a widely used measure of medication adherence). Additionally, there will be a direct link embedded in the EMR to the MA State PMP website. This program collects prescribing and dispensing information on opioid prescriptions, providing patient prescription history information to prescribers. Prescribers will review this website when starting a new controlled substance prescription (as mandated by Massachusetts law as of August 2012) to identify that the patient is not “doctor shopping” (e.g. obtaining for non-indicated purposes or for the intention to sell) and on a regular basis to make sure the patient is not obtaining multiple prescriptions from other prescribers, an indication of potential abuse or safety concerns. Prescribers will be educated to discuss suspicious behavior with patients, and either cease prescribing, increase monitoring, or document clarification to explain behaviors.

Intervention Condition (nurse care management, registry, academic detailing for intervention PCPs)
Conceptual Framework of the Intervention Approach. We base our intervention on the Chronic Care Model. This model is designed to help practices improve patient outcomes by changing routine delivery of ambulatory care through 6 interrelated system changes (organizational support, clinical information systems, delivery system design, decision support, self-management support, and community resources) meant to make patient-centered, evidence-based care easier to accomplish. The aim of the model is to transform daily care for patients with chronic illnesses from acute and reactive to proactive, planned, and population-based. It is designed to accomplish these goals through effective team care and planned interactions; self-management support bolstered by more effective use of community resources; integrated decision support; and patient registries and other supportive IT. These elements are designed to work together to strengthen the provider-patient relationship and improve health outcomes. Our intervention will employ a
patient registry, a tool to enhance the flow of clinical information for use by patients and clinicians. Access to data (e.g. from the MA PMP, or urine toxicology results) provides clinicians with data to help them to deliver the best care. For example, the PMP can tell them if a patient has been receiving prescriptions from other providers in other health care systems. This information may prompt a clinician not to prescribe an opioid, thereby reducing a patient’s risk for harm. Detailed, current care plans (e.g. for management of suspected opioid misuse) prevent errors through handoffs. Internet accessibility (e.g. to MA PMP) links patient flow with information flow. Finally, summary data (e.g. proportion of patients on opioids with a treatment agreement) provide evidence for clinicians/managers to guide system performance improvement.

Intervention Components and Content.
The nurse/care management intervention will be modeled on BMC’s successful collaborative care office-based opioid treatment (OBOT) program. One fulltime nurse care manager will work with PCPs assigned to the intervention condition. The care manager will be based centrally, in the Section of General Internal Medicine, and will divide his/her time between the 4 study sites. A highly experienced nurse program manager (Ms. Labelle) will train and supervise the nurse care manager, with a physician with opioid risk management expertise (Dr. Liebschutz) providing additional supervision. The main focus of the nurse care manager is to assure that patients are receiving guideline-adherent care, which involves appropriate clinical assessments, opioid treatment agreements, refill management, administering monitoring tools according to risk level (urine toxicology screen, pill counts, PMP data extraction) and timely physician visits to assess pain (minimum every 6 months). To aid in carrying out these tasks, she/he will utilize the electronic tools as well as the registry. When starting the intervention, the care manager will assess the status of each intervention patient with regard to fulfillment of each aspect of guideline adherent care. Each week, the care manager will assess the status of patients scheduled for upcoming clinical visits with the PCP or for medication refills to see what care elements are lacking. The care manager will then contact patients who require agreements, clinical assessments, urine testing, etc. according to the automated recommendations in the registry. This will be largely conducted by phone and recorded in the EMR or registry which will then populate the EMR with any clinically relevant results. The nurse care manager will also prepare prescription refills and visit each site weekly to see patients who require actions such as pill counts, or opioid treatment agreement signing. The nurse care manager will counsel all intervention patients on safe medication storage, and symptoms of addiction. Since the initial assessments will require the largest time investment, the intervention will be rolled out to the 4 sites in sequence, allowing for 12 weeks before an additional site is added. Once all patients have been assessed, the care manager will continue to monitor for ongoing fulfillment of guideline-concordant care according to risk group. Every month, the care manager will prepare individual reports for intervention PCPs on their patients with respect to fulfillment of guideline adherent care. If the care manager is alerted to any (predetermined) high risk results (e.g. urine toxicology screen with unexpected illicit substance), she will contact the PCP and ensure that an action plan be put in place before the patient’s next refill is due. The nurse care manager will facilitate any referrals to addiction treatment, as indicated. The nurse care manager will obtain PCP signatures on prescriptions, prepare the prescriptions for patient pick up, as well as facilitate collection of urine toxicology screens. The nurse care manager will also call patients to notify them of any actions they need to take (e.g. come in to give urine toxicology screen). Finally, the nurse care manager will also facilitate patients to be seen in specialty clinics as directed by the PCP for pain treatment: e.g. orthopedics, physical therapy, behavioral health, neurology, etc. The nurse care manager will work closely with primary care staff to provide seamless care for the patient. The nurse care manager will be given an identification badge at each site and be presented as part of site staff to patients.

A qualitative observer will observe all aspects of the Nurse Care Manager’s interactions with academic detailers, PCPs, nursing staff, and patients. Observational data will be recorded by hand into a structured observation guide, and later typed into an electronic form.

Nurse Care Manager Training and Evaluation. Dr. Liebschutz and Ms. Labelle will deliver a standard training program to the nurse care manager. Training will include information about: 1) Guidelines to manage patients with chronic pain on opioid therapy; 2) Risks of opioid therapy, and risk reduction strategies; 3) Working with patient populations at risk for addiction; 4) Use of the registry; 5) Addiction treatment resources.
IT and Management Plan: We will implement the registry, a freestanding centralized disease management application and registry built using standard database technology. The registry will be populated with patient information via data obtained from the Clinical Data Warehouse (CDW). The CDW will pull into the registry the name, MRN, date of birth, SSN (if available), site (BMC or specific CHC) and name of PCP for the patients of pilot and intervention PCPs at each of the study sites (Adult Primary Care practices at Boston Medical Center, Dorchester House, South Boston Community Health Center, and Boston Health Care for the Homeless), who meet the established eligibility criteria. This system will communicate with the electronic medical record (EMR) at each site. Data that will feed into the registry include clinical data recorded from the EMR (documentation from other clinicians and labs) and data from clinical users entered into the registry via pain and opioid management forms. All clinical user interfaces will provide clinical decision support tools. The care manager will use a custom registry interface to monitor key practice activities across the entire practice at each site. The care manager will use population management tools to provide aggregate measures for quality monitoring and workforce management. All quality metrics can be downloaded in aggregate form for further analysis.

Functional Requirements: The user interfaces work within the existing IT infrastructure and require minimal training. Each interface will be customized to reflect the needs of the users and employ secure EMR or web-based technology to avoid storage of any patient data on a local computer.

Workflow Use Case Requirements: The care manager will enter data into specifically created forms in the registry. While performing care management, the nurse will print reports or enter relevant workflow data.

Key Infrastructure Components: The registry will have been completed using existing IT infrastructure donated in kind from the Section of General Internal Medicine from a previous project performed by this group during the MASBIRT. The system will employ three servers: a central data registry, a test/development server, and a web services server. Both IT staff and clinical users at the sites are highly experienced. As noted above the registry forms will capture key assessment data consistent with guideline adherent care. The IT project lead (Dr. Christopher Shanahan) has an established relationship with BMC IT and extensive experience developing and operating a high volume production data exchange and Internet facing web services (SAMHSA Services Accountability Improvement System webservices). The registry architecture will contain tables that store and manage these key data including: 1. clinical data and 2. care process data (appointment data, PCP and ED visits).

Academic detailing: All PCPs in the intervention group will receive one 30-minute individual visit after project implementation in the PCP’s practice site. Prior studies of academic detailing have shown that as little as one 10 minute visit is sufficient to change PCP practice. The visits will be conducted with at least one of the study experts in pain medication management: Drs. Liebschutz or Alford. Prior to the visit, the care manager will give specific data on the target PCP, aggregate data by site and aggregate data for all to the expert. Visit content will combine elements of audit and feedback (e.g. review registry of individual PCP compared with that of peers and goals) and as well as traditional educational outreach. Specifically, experts will review each aspect of guideline concordant care (assessment of risk and appropriateness for opioid medication, medication dosing, monitoring for harm/adherence, and pain outcomes) to solicit barriers to implementation or lack of knowledge on the underlying evidence for each aspect of care. The experts will work with the individual PCPs to address barriers identified using motivational interviewing as needed to facilitate behavioral change in applying guideline concordant care.

A qualitative observer will attend academic detailing sessions with PCPs and take notes. These observations will be recorded into a structured observation guide.

Qualitative interviews will be conducted with enrolled PCPs from both the intervention and control conditions. Qualitative interviews will also be conducted with academic detailers, nurse care managers, and pilot PCPs. These interviews will collect information about PCPs’ experiences with the intervention, assess possible contamination, and PCP perceptions of the feasibility of intervention components.

Randomization and Blinding. Randomization to the study conditions will be by individual PCP. We will randomize PCPs to condition using random number generators in SAS. To ensure equivalence across treatment conditions, we will stratify random assignment on the basis of four variables: 1) provider type (physician vs. midlevel practitioner; e.g. NP, PA); 2) primary care specialty (family
medicine vs. general internal medicine); 3) whether a provider prescribes buprenorphine (such providers may be more familiar with the risks of opioid treatment) and 4) clinic site, since each of these factors would likely impact study outcomes. We will check the balance of treatment assignment on these factors to assess the result of the random assignment. If imbalance is found and such imbalance may confound our result, we will adjust for these factors in the data analysis stage. The PCPs will not be blinded to intervention condition.

Note that patients receive the care that the PCP is randomized to - if patients leave a intervention PCP for a control PCP they will not be managed by a nurse care manager. We will use intent to treat analysis.

Efforts to Minimize Contamination: We realize that there is a risk of contamination between intervention and control PCPs; we believe we can minimize this risk by having the nurse care manager based centrally in the Section of General Internal Medicine, apart from the clinical sites. S/he will be trained to work only with the intervention PCPs. In addition, control PCPs will not be granted access to the patient registry until after the study is completed. We will develop further strategies to minimize contamination between intervention and control PCPs when we pilot test the project at 1-2 teams of the BMC Adult Primary Care practice as well as with one PCP at each of the CHCs. We anticipate that intervention PCPs may cover control PCP patients and thus may be responsible for writing opioid prescriptions or ordering urine drug tests. For example, at South Boston health center, a “doctor of the day” desktop has been set up in Logician (Centricity), where a different PCP covers messages/requests from the nurses that often include signing opioid prescriptions. We will instruct intervention PCPs that they may not utilize the nurse care manager for these patients; in addition, these patients will not be included in the registry. We realize that for some patients, there is not a clear PCP identified. In these cases, we will develop an algorithm; e.g. we will define the PCP as the provider with whom the patient has had the most visits in the past year. Each health center may have different ways of defining how a patient appears on a PCP’s panel (and in fact, many of the health centers are working on refining the empanelment process as part of the medical home initiative). We will develop our definitions in consultation with the health centers.

12.2 Outcomes

Describe anticipated primary outcome and any secondary outcomes and how they will be measured:

All main study outcomes and exploratory variables will be obtained from aggregate, anonymous patient-level data from the clinical data warehouse.

Primary Outcomes: Our primary outcomes are 1) PCP adherence to chronic opioid therapy guidelines and 2) Opioid misuse by patients, each dichotomous variable assessed at 12 months. Below we define each primary outcome; our definitions are based on outcomes from our prior studies or from the published literature.

1) PCP adherence to chronic opioid therapy guidelines, defined as whether the patient has a) a signed opioid treatment agreement (ever) and b) urine drug testing (at least 1 completed urine drug test for controlled substances at any point during opioid treatment).

2) Opioid misuse, defined as multiple early refills. We define an early refill as being written at least 7 days before the previous prescription for the same medication should have been finished. Our definition of restricted early refills will permit up to one early refill as in previous studies. We will obtain the following data fields from the clinical data warehouse related to our study outcomes:

a) Date of all emergency department visits over the past year

b) Date of all primary care visits in the past year (NP, MD, PA only--NOT RN/LPN e.g. for B212 shot)

c) Date of each opioid prescription written that year, e) Date of every urine drug test in the past year.

We will obtain the date of most recent signed opioid treatment agreement via chart review. Charts will be identified by medical record number (MRN) and reviewed only at Boston Medical Center. Patient identifying information will not be taken from charts. All subject information will be assigned a randomized study ID without identifying information and stored in a password protected Excel file. It will not be possible to connect patient data to the subjects themselves. No link will exist between the master list of MRN numbers used to access charts and the data collection sheet. Each MRN will be removed from the master list after information is removed for

https://inspir.bu.edu/Study_App.jsp?FORM_MODE=PRINT_HTML&tab=full

1/30/2017
each individual. No identifiable data (e.g. name, MRN, social security number, date of birth, etc) will be included on the data collection sheet.

**Secondary outcomes:**
Substance abuse: urine drug tests where there is an illicit substance or something other than the prescribed medication present; Possible opioid diversion: urine drug tests where the prescribed opioid is absent; Questionable activity: patients with missed urine drug screens (urine test ordered but not done); Opioid risk: patients on high dose (> 100 mg/day) of morphine equivalent; Mean total dose of opioid prescribed, per patient, at end of study period; Mean change in opioid dose over study period; Proportion of patients who are terminated from opioids; Use of electronic tools: applicable visits in which the electronic tools were used; Health Care Utilization: Number of emergency department visits over study period; Number of PCP visits over study period; Number of missed orthopedics, physical therapy, and behavioral health visits (number of scheduled appointments where patient did not keep appointment).

**Exploratory variables.** To assess whether the intervention may be particularly effective among certain patient subgroups, we will examine demographic variables, at baseline: age, gender, insurance, and race/ethnic group; mental illness and substance use (at baseline), defined as the presence of diagnosed mental illness/substance use on the problem list, or a visit with an ICD9 code for mental illness/substance use over the study period. Again, these variables will be analyzed from an anonymous data set extracted from the clinical data warehouse. These data are collected in the routine course of clinical care.

### 12.3 Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study? If you are doing qualitative research please state how comparisons will be made.

We will first examine demographic characteristics of the intervention and control PCPs to verify that randomization has resulted in groups with similar baseline characteristics. We will then examine descriptive statistics of the primary outcomes, PCP adherence to chronic opioid therapy guidelines and Opioid misuse, and secondary outcomes. For categorical outcomes, we report percentages and 95% confidence intervals, for continuous outcomes we examine means, standard deviations, and ranges. In order to determine the bivariate relationship of whether the intervention condition achieves greater adherence to guidelines and reduced opioid misuse at 12 month follow-up compared to control participants, we will employ log binomial regression model to determine the main effect of intervention adjusting for baseline measures and use robust standard error estimates adjusting for clustering at the PCP level (Generalized Estimating Equation method) and detect differences that are statistically significant at the p<0.05 level. Analyses will be based on intent to treat. To control for potential confounders identified in bivariate analyses as well as variables of a priori clinical significance (gender, age, race, ethnicity, and insurance), we will further regress the 12month follow-up outcomes on the intervention status with the adjustment of baseline measures and potential confounders. Based on the log binomial regression models, we will examine relative risk with 95% confidence intervals to determine the relative magnitude of the adjusted associations. Independent variables with strong correlations may result in collinearity. To address collinearity, we will assess variance inflation factors and the standard errors estimates for the covariates in the model.

We will conduct an interim data analysis of Shapiro site data for the purposes of grant proposal writing. We will compare the three primary outcomes (agreement, urine drug test, and early refill) between the intervention group and control group using regression approach involving generalized estimating equations to adjust the clustering of patients within PCPs. Only the PI, PM, and data analyst will have access to results of this analysis. Results will not alter study procedures.

Data analysis of qualitative data will be conducted via a content-based analysis. At least two team members will code the data and will meet with their supervisor, Victoria Parker, in bi-weekly analysis meetings to discuss any discrepancies. The software program NVivo v. 10 (QSR International, Cambridge, MA) will be used in data analysis.

### 12.4 Sample Size/Specimens (Click on the Help icon for instructions)

How many subjects (or records, or specimens, or charts) will be enrolled in this study?

Subjects under BMC/BU Medical Center PI (click on the Help icon for instructions)
Sample Size Justification

Indicate why you chose the sample size proposed. Provide your sample size calculations. If this is a pilot study, this justification does not necessarily require a formal sample size calculation, but should provide a rationale for choosing the sample size proposed (e.g. to estimate a mean to a certain accuracy, to determine if the response rate is above a certain percentage, etc.) Note: Once the IRB approves a certain study sample size then you may not enroll beyond that sample size without first obtaining approval from the IRB. Explain how many evaluable subjects you will need to end up with to answer your study question and how many subjects you will need to enroll and consent to achieve this number. The IRB counts study subjects starting when they are consented.

Statistical Power/Sample Size calculations

Our power analysis/sample size calculation is based on the primary study outcomes, PCP adherence to chronic opioid therapy guidelines (use of treatment agreements and urine testing) and opioid misuse (early refills). We have based our power calculations on the following estimates of the outcomes:

1) the proportion of patients with a signed opioid treatment agreement (ever): for usual care, estimates in the literature range from 4% to 11%. In one BMC practice the proportion with an opioid treatment agreement was as high as 75% (unpublished data).
2) the proportion of patients with urine drug testing (at least 1 completed urine drug test for controlled substances at any point during opioid treatment): for usual care, 8%
3) Multiple early refills: Usual care: 23.4% with early refills

Intervention effect estimates from the literature

1) Effects of on-screen, point of care computer reminders on processes and outcomes of care (intervention and control groups)
Median 4% improvement in physicians’ practices and median 3% improvement in patients’ health.
2) Effect of academic detailing (intervention group)
Median 4.8% increase in compliance with desired practice for prescribing (range 3.0%-6.5%) Median 6.0% increase in compliance with other types of professional performance (range 3.6%-16%)
3) Audit and feedback- will be included with academic detailing (intervention group)
Estimates of the effectiveness of audit and feedback vary widely in the literature, with some studies showing a worsening in performance and others showing small to moderate improvements. The relative effectiveness is greater when baseline adherence to recommended practice is low and when feedback is delivered more intensively. We estimate that audit and feedback will not improve provider performance above the effects of academic detailing.
4) Effects of registry/Chronic Care Model: (intervention group only)
16% increase in diabetes patients having assessment of glycated hemoglobin We were unable to find studies that examined effects of registry/Chronic Care Model on our study outcomes. We suspect that improving adherence to opioid prescribing guidelines is more challenging than improving adherence to diabetes guidelines, given the challenges of working with a patient population at high risk for substance use. Therefore, we have conservatively estimated that the registry/chronic care model will improve provider performance by 10%. Based on these intervention effect estimates, we estimate that PCP practice will improve by 4% in control group (4% from point of care reminders) and 19% in intervention group (5% from academic detailing, 0% from audit and feedback, 4% from point of care reminders, and 10% from registry/Chronic Care Model) If we estimate that in usual care, 8% will have both treatment agreement and urine drug testing, our control group will have 12% with guideline adherent care and our intervention group will have 27% with guideline adherent care. If we estimate that in usual care, 76.5% will have no early refills, our control group will have 80.5% with no early refills and our intervention group will have 95.5% with no early refills. Due to the clustering nature of the study design, we provide a set of sample size estimates corresponding to a range of intra-class correlation (ICC) commonly observed in this type of research. Using these effect estimates, we present the power calculations in the Table below. Over a range of ICC, with 56 PCPs, we will have adequate power to demonstrate clinically meaningful changes in PCP practice.

Table - Power Calculations
Outcome 1: proportion of having both treatment agreement and urine drug testing
ICC alphapowerControlIntervention
<table>
<thead>
<tr>
<th>patients per provider</th>
<th>sample size per group</th>
<th># of providers needed per group</th>
<th>total sample size</th>
<th>total # of providers needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05 0.05 0.8 0.12 0.27</td>
<td>10</td>
<td>177</td>
<td>18</td>
<td>354</td>
</tr>
<tr>
<td>0.07 0.05 0.8 0.12 0.27</td>
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<td>199</td>
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<td>398</td>
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<tr>
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<td>464</td>
</tr>
<tr>
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<td>287</td>
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</table>

**Outcome 2: proportion of no early refill**

<table>
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<th>patients per provider</th>
<th>sample size per group</th>
<th># of providers needed per group</th>
<th>total sample size</th>
<th>total # of providers needed</th>
</tr>
</thead>
<tbody>
<tr>
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<td>125</td>
<td>13</td>
<td>250</td>
</tr>
<tr>
<td>0.07 0.05 0.8 0.805 0.955</td>
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<td>141</td>
<td>15</td>
<td>282</td>
</tr>
<tr>
<td>0.1 0.05 0.8 0.805 0.955</td>
<td>10</td>
<td>164</td>
<td>17</td>
<td>328</td>
</tr>
<tr>
<td>0.15 0.05 0.8 0.805 0.955</td>
<td>10</td>
<td>203</td>
<td>21</td>
<td>406</td>
</tr>
</tbody>
</table>

*ICC: intradustercorrelation coefficient*

In the event that some of the estimates we have used to calculate sample size are incorrect, we are allowing for a potential sample size of 125 PCPs in the study.

*We obtained our effect estimates from the published literature. We will refine these estimates after analyzing baseline data at each site on our outcomes of interest (use of opioid treatment agreement, frequency of urine drug testing, and frequency of early refills). If, for example, the baseline use of opioid treatment agreements is very high, we will require a larger sample size to demonstrate an intervention effect.*

For the qualitative data, we expect to collect 50 observations of the NCM, 50 PCP interviews, and 30 observations of academic detailing sessions.

### 12.5 Study Attachments

*You must attach to this application all surveys, interviews, questionnaires, focus group outlines, etc. that will be used in this study. The IRB must review these materials. If these items are included as part of the attached protocol they do not have to be submitted again. Failure to provide this information could result in a delay in IRB review. If some of the materials are not finalized- submit the DRAFT versions. The final versions will need to be approved by the IRB via an amendment PRIOR to use.*

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<th>Last Modified By</th>
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No Document(s) have been attached to this form.

### 13.0 Risks & Benefits & Justification for Approval

#### 13.1 Potential Risk/Discomforts

*List the reasonably foreseeable risks or discomforts to subjects as a result of their participation in the research.*

We believe that this study poses no more than minimal risks to subjects, who are both patients and PCPs. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Risks to PCPs:
The main risk would be breach of confidentiality. PCP data will be measured by predetermined guideline concordant behaviors. Related to breach of confidentiality, it will be important that this information not be shared with supervisors, colleagues or non-research staff. This risk will be minimized through de-identification of data and strictly limiting access to aggregate PCP data that will not identify clinical practice patterns by an individual PCP. Some PCP subjects may think that the surveys, interviews, and/or
observations are personal in nature. However, subjects will have the option not to answer the questions, or withdraw from the study if they so choose. In addition, any survey or interviews will be conducted in a confidential manner in a private room, with appropriate security of the data, and limited access to identifiable data. See below for a more detailed description of the data storage and security procedures. Given these procedures, it would be highly unlikely for any breach to occur and therefore we believe the risk to PCP subjects is minimal. Also, we will put safeguards in place to ensure that PCP subjects are not coerced to participate in the study, by using nonclinical staff to administer informed consent and by emphasizing that they will not be penalized in any way for a decision not to participate. There is also a potential for the PCPs to feel that the surveys and interviews are time consuming. We will minimize this risk by providing multiple options to schedule these within the PCPs’ schedules.

Audio recordings of qualitative interviews may increase the risk of a breach of confidentiality. However, the recordings will be stored securely (detailed below) and any identifiable information would be omitted from the transcript.

Risks to patients: We believe that the project will propose minimal risks to patients and that the sole risk will be loss of confidentiality. Although the study will analyze patient data of a highly sensitive nature, the extensive security procedures in place to maintain confidentiality, including monitoring, will minimize this risk. These procedures are described below.

A secondary risk of loss of confidentiality arises from the list of 100 BMC medical record numbers of patients, who are on chronic opioid therapy, which we propose to generate. This list will be used by study personnel to ensure that the data from the clinical warehouse are accurate and that outcome variables were not incorrectly documented or overlooked in the electronic medical record data pull. This risk is minimized by the following:

1) Only two designated study staff will have access to this list: the PI (Dr. Lasser) and co-investigator (Dr. Khalid), and
2) the list will be stored on a password protected computer on Boston Medical Center’s secure server.

For the chart review we will minimize risk in the same way by taking the following steps:
1) Only trained research assistants will have access to this list and will be under the supervision of the PIs (Dr. Lasser and Dr. Liebschutz).
2) This list will also be stored on a password protected computer on Boston Medical Center’s secure server.

Provide a description of how risks will be minimized.

Protections Against Risks

PCP data: Data confidentiality will be emphasized on the surveys and in-depth interviews, and verbally by the Research Assistant, by the use of sealed envelopes for all completed surveys, and by the use of a unique identification number for each subject. Our team has implemented extensive data protection policies and all data is kept on secure networks which can only be accessed by study staff using password protected computers; hard copies are kept in locked file cabinets in locked offices to which only study staff have access. The surveys and interview data will be coded with ID numbers, not names, in order to further protect confidentiality.

Qualitative interviews will be labeled only with PCP ID numbers and any identifying information on recordings will be omitted from the transcripts of the recordings. Audio recordings will be kept in locked, password protected electronic files.

Secure Firewall for Clinical and Study Data
The entire data system will be maintained in a closed secure clinical database ("Clinical Data Warehouse") operated by Boston Medical Center, on which all hospital clinical systems are located. This is a completely closed system inside a single firewall. The servers sit in Needham, MA, and have three leased, dedicated data lines that have no other electronic traffic (e.g. phone, etc.) on them, and are resistant to hackers, etc.

Access to Registry Information Limited to Authenticated Users
Only 6 authenticated users will be able to access the patient registry, including all individual and aggregate data information: the database analyst (the person who builds the database), the co-investigator in charge of health technology development (Dr. Shanahan), the nurse care manager (TBN), the co-investigator nurse supervisor (Ms. Colleen Labelle), and the principal investigator responsible for supervision of the care manager (Dr. Liebschutz). The co-investigators in charge of academic detailing will be authenticated users who will be able to access single PCP aggregate data in order to present data to the individual PCP ("audit and feedback"). All authenticated users will undergo specific training yearly on data security from
Dr. Shanahan. Of note, no users will be able to access any clinical information about patients in the control condition. When aggregate level data becomes available to guide policies and compare norms, the individual health center directors will not have access to individual PCP level performance data, thus preserving individual autonomy of PCP, and decreasing the possibility of coercion or fear of job security based on research data being made available to higher level supervisors at the site of care.

**Limited Patient Data Set for Research Analysis:**
All data will be stored in a HIPAA compliant manner and data storage techniques will be reviewed biannually by BMC IT staff, overseen by Dr. Shanahan. Specific procedures, which have been approved by our IRB and used successfully in prior research, include protecting participant confidentiality as follows:
- Developing a limited data set for research purposes. This will remove all specific identifiers named in HIPAA regulations (name, social security number, street address, email address, telephone number, fax number, license number, vehicle identification number, personal web page URL, IP address, fullpage photos or other comparable identifying images, medical record number, health plan beneficiary number, other account number, medical device identifier or serial number, biometric identifiers). The data set can include: hospital admission details, age of participant, full five digit zip code or other geographic division such as county, city, precinct, and equivalent geocode—except street address.
- Once this limited data set has been created, any linkage between PCP names/identifiers and clinical outcome data is accessible ONLY to limited study personnel (data analyst, statistician, and PIs).
- Each PCP will receive a unique identification number. All research data collection and data entry forms will be labeled only with this number and will contain no other individual identifiers.
- A file that links the PCP subject names with their study ID numbers will be kept on a password-protected computer that is regularly backed up every 24 hours on a secure server.
- All reports and publications will preserve the subjects' anonymity.
- Any observation notes of NCM interactions with patients will not record any identifiable patient data. Patients will not be identified by name, birthdate, age, or any other protected health information. Patients' PCP will not be identified in any observational notes. Additionally, in PCP interviews, patients will not be described in any identifiable way.

### 13.2 Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the research. (Payments to subjects should not be included in this section.) If there are no direct benefits to individual subjects, you must include a societal benefit that may result from this study.

PCP subjects in the intervention group and their patients may benefit from this study by receiving assistance from a nurse care manager, who can help them minimize the risks associated with opioid therapy in their patients. Control PCPs and their patients may benefit from the PCPs' use of electronic tools to improve their opioid prescribing/monitoring.

An accurate understanding of the effects of this intervention on adherence to guidelines for opioid prescribing is crucial in reducing opioid associated harms. This knowledge could benefit patients and PCPs in the future.

### 13.3 Risk to Benefit Ratio

Describe how risks to subjects are reasonable in relation to anticipated benefits:

In this study, we aim to assess the effects of implementation strategies (a nurse managed patient registry, electronic tools in the EMR, and academic detailing to PCPs) on adherence to guidelines for opioid prescribing. The risks to participants are minimal and mainly include the risk of loss of confidentiality. We will minimize this risk by using study ID numbers on the survey instruments and storing the study instruments in a secure location. There will be a slight time burden, of approximately one hour, to complete study instruments. We will schedule these at a time that is convenient for study participants. The potential benefit of a better understanding of the impact of this intervention on adherence to guidelines for opioid prescribing outweighs the low risk of breach of confidentiality and the minimal time burden.

### 14.0 Data & Safety Monitoring

**A data and safety monitoring plan (DSMP) is meant to assure that each clinical investigation has a system for oversight and monitoring**
of the conduct of the clinical investigation. This oversight is intended to ensure the safety of the participants and the validity and integrity of the data. A DSMP should be commensurate with the risks.

A DSMP can be as simple as the investigator reporting Unanticipated Problems, Adverse Events, and Protocol Deviations to the IRB. A DSMP can be as complex as having a Data and Safety Monitoring Board.

A DSMP can include clinical trial monitoring. Clinical trial monitoring refers to the methods used to oversee the conduct of, and reporting of data from, clinical investigations including appropriate clinical investigator supervision of study site staff. Monitoring activities include communication with the investigator and the study site staff; review of the study site's processes, procedures, and records; and verification of the accuracy of the data.

14.1 For more than minimal risk research, your application needs to include a separate Data and Safety Monitoring Plan. Please check-off one of the options below:

- This study is not greater than minimal risk. Unanticipated Problems, Adverse Events, and protocol deviations will be reported to the IRB as required by IRB policies.
- A DSMP is attached in a detailed protocol (provide page number in textbox below).
- A DSMP is attached in the Study Attachments section below.

14.2 Who will monitor the research for safety of the participants? (check all that apply)

- The Principal Investigator at Boston Medical Center or BU Medical Campus who will report all adverse events and Unanticipated Problems to the IRB in compliance with IRB policy, Federal/State regulations, and sponsor requirements (as applicable ).
- An independent Data Safety Monitoring Board/Data Monitoring Committee
- The Sponsor or Funding Agency
- Other:

14.3 DSMP Attachments

Here you can attach any Data and Safety Monitoring Plan documents including your DSMP, Data Safety Monitoring Board charter, and any other related documents.

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15.0 Recruitment Procedures/Materials

15.1 Recruitment Procedures

Describe in detail how the research population will be identified and your methods for contacting potential subjects.

https://inspir.bu.edu/Study_App.jsp?FORM_MODE=PRINT_HTML&tab=full

1/30/2017
PCPs at all of the sites will be eligible for enrollment in the RCT. We will facilitate recruitment by identifying a PCP clinical champion at each site. We will attend regular PCP staff meetings to present the study. We anticipate that PCPs will be interested in participating, as both control and intervention PCPs will receive assistance in managing patients with chronic pain on opioid therapy, a challenging patient population. We will also provide PCPs with $50 incentives for each hour spent completing a survey.

The Principal Investigator confirms the following:

- No direct or indirect remuneration that constitutes an inducement for recruiting or enrolling subjects will be accepted by any member of the research team; and
- No bonus payments based on the rate or timing of subject recruitment or enrollment will be accepted by any member of the research team; and
- Research involving medical services will comply with federal and state anti-kickback laws and applicable anti-kickback policies of Boston Medical Center and Boston University; and
- No payment or financial incentives (finder’s fees) will be offered to any healthcare providers for referring patients to research studies.

I Confirm

15.2 Recruitment Material

Attach all study related recruitment documents including, but not limited to, materials such as: posters, flyers, newspaper ads, script for in-person or telephone recruitment (if any). You may use this link to download a recruitment script template. Final versions of all materials should be attached. If a video, submit the tape. If a website, provide the URL and attach screenshots for every page.

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15.3 Recruitment using the StudyFinder website

The BMC/BU Medical Campus Study Finder is a medical campus website that lists research studies for public view. If you are using Study Finder to recruit subjects, you should complete the Study Finder Form in the Submission Forms section of INSPIR.

Will you be listing your study in Study Finder to recruit subjects? If "yes," select "yes" below and complete the Study Finder Form (located in the Submissions Forms section of the Study Management view of INSPIR II – click on the (?) icon for instructions).

☐ Yes
☐ No

15.4 Will you be recruiting using one or more Community Health Center (CHC)?

☐ Yes
☐ No

15.5 Screening

Will any sensitive information or protected health information (PHI) collected during the screening without obtaining consent be retained that can be linked to the potential subjects OR does the study require any clinical screening procedures (blood draw, fasting, etc) performed solely for the purpose of determining eligibility in this research?

☐ Yes  ☐ No
Will any potential subjects be directly contacted to obtain screening information?

☐ Yes
☐ No
☐ Not Applicable - all screening activities have been completed for this already-approved study

16.0 Consent Procedures

16.1 Consent Procedures

You indicated in the "Navigation Menu" section that informed consent will be obtained from subjects. Describe in detail the informed consent process, including who will obtain consent and where and how long will subjects have to decide if they want to participate. If the study includes limited- and non-readers and is greater than minimal risk, describe your plan for using an impartial witness or for another method to assure and document subject comprehension (such as a quiz or "teach back") that will be used for limited- and non-readers only or for all subjects.

A trained research assistant will obtain written informed consent in a private room for eligible and interested PCP subjects. The research assistant will advise all potential subjects of their rights as research subjects, study procedures, and risks and benefits of participation. Subjects will be given a week (or longer if necessary) to decide to take part in the study. It will be reinforced to all subjects that they can discontinue participation in the study at any time, for any reason. Study personnel will not inform clinical or supervisory staff whether or not a PCP is participating in the study. However, some clinical staff may become aware if they were to view the medical record of intervention patients who have data entered by the nurse care manager. PCPs may themselves inform anyone they choose about their participation.

The consent form has been edited to include observations and interviews with enrolled PCPs (small paragraphs added on p. 2 and 3). We plan to re-consent currently enrolled PCPs in order to obtain permission to perform these additional data collection procedures.

We are requesting a waiver of informed consent for patients.

16.2 Verbal Consent/Assent - Waiver of Documentation of Informed Consent

Will this research include an informed consent process, but require a Waiver of Documentation of Consent?

☐ No
☐ Yes, because the research presents no more than minimal risk of harm to the participants and involves no procedures for which written consent would normally be required outside of the research.
☐ Yes, because the only record linking the participant to the research would be the consent document and the main risk in the research would be the potential harm because of a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

16.3 Waiver or Alteration of Informed Consent Process

Does the study meet the criteria for a Waiver or Alteration of Consent Process?

☐ No
☐ Yes

In the text box below, please provide study-specific reasons that justify how the study meets each of the following four criteria for Waiver or alteration of Consent:

1. the study is not greater than minimal risk; AND
2. that waiving the requirements for informed consent will not adversely affect the rights and welfare of study subjects; AND
3. that the research cannot be practically carried out without the waiver of informed consent or alteration of the consent process; AND
4. that (if applicable) there is a plan to disseminate pertinent information to study subjects after the study is completed.

We believe that this study meets all four requirements of the Code of Federal Regulations (45 CFR 46.116 (d)) regarding waiver of consent: "Requirements for informed consent may be waived if four conditions are met: the research poses no more than minimal risk; the rights and welfare of subjects are not adversely affected; the research could not be carried out practically otherwise; and, when appropriate, subjects will be debriefed." 1) We believe that this study poses no more than minimal risk to patient subjects. There is no intervention at the patient subject level and for patient subjects the study is solely collecting data. Patient subjects in the control group will have care as usual, whereas patient subjects in the intervention group are likely to have higher level of attentiveness to their medical condition than without the study. Also, we have a very strong data security plan to prevent any data breach, further minimizing potential risks. In addition, all of the patient subject data will have been collected for non-research, clinical purposes. 2) Furthermore, the rights of the patients are not adversely affected. PCPs will not be restricted from prescribing any medication type or dose, and patients will not be required to leave urine toxicology specimen. PCPs will have full autonomy with regard to prescribing. 3) The research could not be carried out practically otherwise. If patients had to sign informed consent, it is likely that patients who had addiction or diversion behaviors would not be willing to participate, and thus the whole set of knowledge would not be testable with this (or any) study design. Because this is an implementation study, we are studying whether changing systems of care affects patient outcomes. The care that will be delivered to both groups (intervention and controls) is standard of care; it is not experimental. Because this is a systems intervention, it is not possible for individual patients to “opt out” if their PCP has agreed to participate (however, it is possible that a patient could decline to speak with a nurse care manager, or might choose to receive their care elsewhere). 4) The trial results will be presented to the community health center staff at trial completion. Again, all of the patient subject data will have been collected for non-research, clinical purposes.

16.5 Consent by Substituted Judgment

Do you intend to obtain consent from a Legally Authorized Representative (LAR) for cognitively impaired/decisionally impaired adult subjects?

☐ Yes
☐ No

16.6 Non-English Language Consent Forms:

Will you obtain consent from subjects who are not fluent in English?

☐ Yes  ☐ No

17.0 Privacy and Confidentiality

17.1 Privacy (Privacy refers to an individual’s control over who has access to him/herself)

Please check one:

☐ The following measures will be used to protect the privacy of subjects and potential subjects:

• The information that will be obtained from and/or about subjects and potential subjects is the minimum necessary to conduct the study; and
• If any interventions and interactions occur with subjects and potential subjects, they will take place in private settings.
17.2 Confidentiality of the Data

Please check all that apply:

☑ All data will be RECORDED as anonymous. There will be no way to link data to individual subjects, even temporarily AND subjects' identities cannot be reasonably ascertained via deductive disclosure.

☑ Study data will be coded. All study documents will be identified by a unique study ID. The unique study ID will be linked to subject identifiers via a master-code or key. Access to the master-code/key will be limited to the researchers.

☑ Study data will contain subject identifiers (data variables that either by themselves or when combined with others, could result in identifying a participant).

☐ There is an alternate plan for how subjects will be identified in study documents. Please specify in text box below.

- If data are not anonymous, please describe in the text box below how you will secure the data (e.g. how the master-code will be stored relative to the study data).
- If the dataset contains protected health information (PHI) and is being stored electronically, please provide explicit confirmation that it will be stored in a HIPAA-compliant BMC-controlled computer that meets BMC's standard for storage of PHI.

All study subjects will be identified by a unique study ID. The unique study ID will be linked to subject identifiers via a mastercode or key. Only research staff will have access to the mastercode/key. The mastercode/key that links study data to identifiers will be stored separately from the study data and protected (locked, separate flash drive, etc) in a secure location in the Clinical Addiction Research and Education Unit at BMC and on secure servers.

To ensure confidentiality for the list of 100 medical record numbers audited for accuracy of the clinical warehouse data pull, 1) Only two designated study staff will have access to this list: the PI (Dr. Lasser) and co-investigator (Dr. Khalid), and 2) the list will be stored on a password protected computer on Boston Medical Center's secure server.

17.3 Release of identifiable data.

Is identifiable data being released outside of BMC/BU Medical Campus? (e.g. to sponsors, because of mandated reporting, etc).

☐ Yes

☐ No

Pertinent findings (related to the aims of the study) and incidental findings (unrelated to the aims of the study): Does the research (including screening) involve any test or procedure done for research purposes only that may yield findings that are of potential health or reproductive importance to the individual subjects (e.g., disease risk, abnormal lab values, imaging abnormalities, genetic results)?

☐ Yes

☐ No

☐ Not Applicable - no additional research results will be collected for this study.

17.4 Destruction of Identifiers
If the data are identifiable and/or if a master-code exists, when and how will the data be de-identified or the master-code be destroyed?

Research data will be kept in a secure location in the Clinical Addiction Research and Education Unit at BMC and on secure servers. PCP data will be stored by study ID numbers; only research staff will have access to the mastercode that links study ID number to name.

Research study data will be maintained by the investigator for a minimum of three years following the completion of the study.

17.5 Certificate of Confidentiality from the NIH

Will you obtain a Certificate of Confidentiality for this study?

Note: If a CoC will be obtained then CoC language is required in the consent form (see the IRB website for the consent form template that contains CoC language.

☐ Yes ☐ No

18.0 HIPAA Compliance

18.1 Do you need access to protected health information (PHI) without signed authorization from the individual whose information you need?

☐ Yes ☐ No

18.2 Do you need PHI (without authorization) only to identify subjects for recruitment?

☐ Yes ☐ No

18.3 Note: All questions below only pertain to data that you are requesting to access without signed HIPAA Authorization from research participants. Do not include information below on data that you will collect AFTER obtaining signed HIPAA Authorization from the participants.

Please indicate your selection criteria for the records: (e.g. all Type 2 diabetics prescribed metformin, all men aged 50-75 with diagnosis of BPH)

We will review charts of all patients of participating PCPs > = age 18 who have 1) Three or more completed visits to the primary care practice; 2) long term opioid treatment defined by 3 or more opioid prescriptions written at least 21 days apart within 6 months; and 3) an inpatient or outpatient ICD9CM diagnosis for musculoskeletal or neuropathic pain.

18.4 Indicate what date range is needed for the records: (e.g. 11/14/98-12/1/13)

1/1/1999 to 5/1/2016

18.5 Please list all data fields that are needed from the medical record or attach the file containing the data elements below:
Charts will be identified by medical record number (MRN) and reviewed only at Boston Medical Center. Patient identifying information will not be taken from charts. Only date of most recent signed opioid treatment agreement, dates of urine toxicology screenings, and dates of prescriptions will be extracted from the medical record. All subject information will be assigned a randomized study ID without identifying information and stored in a password protected Excel file. It will not be possible to connect patient data to the subjects themselves. No link will exist between the master list of MRN numbers used to access charts and the data collection sheet. Each MRN will be removed from the master list after information is removed for each individual. No identifiable data (e.g. name, MRN, social security number, date of birth, etc) will be included on the data collection sheet. Additionally we will obtain the following information from the EMR:

- Reason for discontinuation of opioids from progress notes
- Reason for all ED visits for 1 year following discontinuation of opioids from ED notes
- Reason for all inpatient admissions for 1 year following discontinuation of opioids from admission and progress notes
- Evidence of opioid use disorder (OUD) as stated in problem list or progress notes for 1 year following discontinuation of opioids
- Evidence of treatment for OUD for 1 year following discontinuation of opioids from medication list or progress notes

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18.6 Will you be using the Clinical Data Warehouse (CDW) or will study staff be accessing the records?

- CDW
- Study staff will access records
- Both

18.7 Does your research require access to any of the HIPAA identifiers?

- Yes
- No

18.8 Please describe why the research cannot be conducted without access to protected health information:

Our study outcomes rely on EMR data. Primary care physicians are consented in this study, patients are not explicitly informed that their PCP is involved in our study. Study interventions ended in March of 2016 and we are currently conducting data extraction and analysis only.

18.9 Why is it not practicable to obtain authorization from the participants?

Study interventions (with PCPs) ended in March of 2016 and we are currently conducting data extraction and analysis only.

18.10 What is your plan to protect any identifiable information from use and disclosure by unauthorized parties?

https://inspir.bu.edu/Study_App.jsp?FORM_MODE=PRINT_HTML&tab=full 1/30/2017
No link will exist between the master list of MRN numbers used to access charts and the data collection sheet. Each MRN will be removed from the master list after information is removed for each individual. No identifiable data (e.g. name, MRN, social security number, date of birth, etc) will be included on the data collection sheet.

18.11 When and how will you destroy any identifiers linked to the data?

(Please note: identifiers should be destroyed at the earliest opportunity as consistent with the design of the research study)

Identifiers will be destroyed at the end of the study.

18.12 Please affirm the items below:

☐ I agree that the protected health information will not be re-used or disclosed to any other person or entity, except as required by law, for the authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Regulation (45 CFR 164.512)

☐ I declare that the requested information constitutes the minimum necessary data to accomplish the goals of the research.

19.0 Cost/Payment

19.1 Cost

Please describe how the cost of research visits and procedures will be covered and whether the subject (or the subject's insurance) will be responsible for any research related costs.

N/A

19.2 Payment

Will the subject be reimbursed for participating in this study? (e.g. money, gift certificates, coupons, etc.)

☐ Yes

☐ No

If yes: "Describe the frequency, method, and amount of payment. Please include the total amount paid to subjects and the plan to prorate payment for subjects who withdraw early from the study."

We will provide a §50 Amazon.com gift card to PCPs for each survey they complete. If a participant only completes one interview, he or she will be compensated for that interview.

20.0 Study Attachments

20.1 Attach here any remaining study documents that you have not attached in previous sections.

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