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TITLE: **“Preventing Risky Drinking in Veterans Treated with Prescription Opioids”**

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14. ABSTRACT Veterans who are taking prescription opioids for chronic pain and are engaging in risky drinking are at heightened risk for drug interactions, including overdose and other negative effects, particularly if they are also using benzodiazepines. In this application, we propose to test an integrated prevention intervention, designed to reduce rates of risky drinking in veterans receiving prescription opioids to treat their chronic pain. This adaptive, patient-centered intervention provides integrated clinical assessment, brief intervention, monitoring, and extended prevention services delivered through a combination of clinical visits, telephone calls, and text messages. We propose to conduct a study in which returning OEF/OIF individuals and other veterans receiving medical care at the Philadelphia VAMC (N=300) who are on daily doses of prescription opioids and screen positive for risky alcohol use will be randomized to receive 12 months of an adaptive integrated prevention intervention (IPI) or to standard care (SC), which consists of a Brief Intervention (BI) with 2 follow-up contacts. Potential participants will be veterans at the Philadelphia VAMC who, based on pharmacy records, are using opioids daily to treat chronic pain. An initial evaluation will identify individuals who also engage in risky alcohol use based on NIAAA-recommended guidelines and meet other inclusion criteria to be enrolled in the study. The evaluation will also identify the use of other medications (e.g., benzodiazepines) that could interact negatively with opioid use. For veterans randomized to the IPI condition, a BI is first provided to reduce alcohol to non-hazardous levels and the effects are monitored for one month. Veterans who reduce alcohol use to non-hazardous levels during this one-month period continue in a monitoring track, consisting of tailored text messages and brief monthly telephone contacts. Veterans who continue to drink at risky levels are instead placed in a track that provides tailored text messages and more frequent telephone calls. In addition to monitoring, these calls provide further prevention/BI services to help the veteran reduce alcohol use to non-hazardous levels. Key components of these services are motivational enhancement and development of more effective ways to cope with stress and other triggers for risky alcohol use. All participants will be followed up at 3, 6, 9, 12 and 18 months after baseline. The primary outcome at each follow-up point will be a dichotomous measure of any risky drinking since the prior follow-up (yes/no). Secondary outcomes will include self-reported frequency of heavy drinking, biological measures of alcohol use, other drug use as determined by urine toxicology tests, opioid overdoses, and ratings of depression and pain. Repeated measures analyses will compare the IPI and SC conditions on primary and secondary outcomes assessed across an 18-month follow-up. Analyses will also test hypothesized moderation and mediation effects.					
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1. Introduction

Veterans who are taking prescription opioids for chronic pain and are engaging in risky drinking are at heightened risk for drug interactions, including overdose and other negative effects, particularly if they are also using benzodiazepines. In this application, we propose to test an adaptive prevention intervention, designed to reduce rates of risky drinking in veterans receiving prescription opioids to treat their chronic pain. This adaptive, patient-centered intervention provides clinical assessment, brief intervention, monitoring, and extended prevention services delivered through a combination of clinical visits, telephone calls, and text messages. We will conduct a study in which returning OEF/OIF individuals and other veterans receiving medical care at the Philadelphia VAMC (N=300) who are on daily doses of prescription opioids and screen positive for risky alcohol use will be randomized to receive 12 months of an adaptive prevention intervention (API) or to standard care (SC), which consists of a Brief Intervention (BI) only. For veterans randomized to the API condition, a BI is first provided and the effects are monitored for one month. Veterans who reduce alcohol use to non-hazardous levels during this one-month period continue in a monitoring track, consisting of tailored text messages and brief monthly telephone contacts. Veterans who continue to drink at risky levels are instead placed in a track that provides tailored text messages and more frequent telephone calls. These calls provide monitoring and further prevention/BI services to help the veteran reduce alcohol use to non-hazardous levels. Key components of these services are motivational enhancement and development of more effective ways to cope with stress and other triggers for risky alcohol use. Veterans in the API condition who are initially placed in the monitoring track but whose drinking increases again during the 12 month intervention are transferred to the more intensive prevention track, until their alcohol use has again decreased. API is hypothesized to produce better alcohol and other drug use outcomes than SC over an 18-month follow-up.

2. Key words

veterans, opioid medication, pain treatment, risky drinking, prevention, brief intervention, monitoring, adaptive interventions, benzodiazepines, overdose, follow-up

3. Accomplishments

Major Goals of the Project

The goal of the proposed study is to test an adaptive prevention approach designed for returning OEF/OIF individuals and other veterans who are engaging in risky drinking while being treated with prescription opioids for chronic pain. We propose to conduct a study in which returning OEF/OIF individuals and other veterans receiving medical care at the Philadelphia VAMC (N=300) who are on daily doses of prescription opioids and screen positive for risky alcohol use will be randomized to standard care (SC) or to 12 months of the adaptive prevention intervention (API) described above. The primary outcome at each follow-up point will be a dichotomous measure of alcohol use status (any risky alcohol use since the prior follow-up: yes/no). Secondary outcomes will include self-reported frequency of heavy drinking, biological measures of heavy drinking, urine toxicology tests to assess other drug use, opioid overdoses, depression, and pain.

Objectives and Hypotheses

a. Primary objective: To compare the effectiveness of a 12-month adaptive prevention intervention (API) with standard care (SC) over an 18-month follow-up period, for veterans treated with prescription opioids and who are engaging in risky/hazardous drinking, as defined by NIAAA guidelines (5).

- *Hypothesis 1:* API will produce better outcomes than SC, as indicated by lower rates of risky/hazardous alcohol use across the follow-up period.

b. Secondary objectives: To examine secondary outcome measures, moderator effects, and mediation effects:

- *Hypothesis 1:* API will produce better outcomes than SC on frequency of heavy drinking, biological measures of heavy drinking (i.e., GGT and CDT), urine toxicology tests to assess other drug use, depression, and pain.
- *Hypothesis 2:* Rates of opioid overdoses will be lower in API than in SC
- *Hypothesis 3:* Intervention effects will be greater in higher-risk veterans, including those with higher prescription opioid dosages, co-occurring benzodiazepine use, poor social support, and low readiness for change.
- *Hypothesis 4:* Results favoring API over SC on risky drinking will be mediated by greater readiness for change, self-efficacy, and coping.

Milestone	Base Line Plan Date
Task 1: Prepare the text messaging system for the study, and finalize all manuals for the adaptive prevention intervention (API)	15-Oct-2014
Task 2: Pilot test methods to identify veterans with chronic pain who are receiving daily opioid medication through VANC pharmacy records, and the screening procedures to detect risky alcohol use in these individuals	15-Oct-2014
Task 3: Complete training for the two prevention counselors in API, and identify and begin training a third prevention counselor	15-Oct-2014
Task 4: Begin enrollment of study participants	15-Jan-2015
Task 5: Complete enrollment of study participants	01-May-2017
Task 6: Complete all 18-month follow-ups	15-Oct-2018
Task 7: Complete and submit all main outcome papers	30-Jun-2019

Progress Toward Year 2 Milestones:

There were no milestones specific to Year 2. The main tasks in Year 2 were to continue to enroll veterans in the study, deliver the intervention, and perform follow-up interviews.

Major Activities in Year 2:

- Recruitment at the Corporal Michael J. Crescenz Medical Center (Formerly the Philadelphia VAMC)
 - Reviewed 3,000+ electronic medical records to identify potentially eligible Veterans.
 - 24% were eligible for recruitment letter
 - 58% reported no alcohol use
 - 18% were ineligible based on other exclusion criteria
 - Mailed 1051 letters
 - The majority of letters went to Veterans who reported some alcohol use on the most recent administration on the AUDIT-C by medical staff within the VA system.
 - As an experiment, we also mailed 255 letters to Veterans who reported no alcohol use, hoping to find Veterans who were under reporting. This resulted in only 1 Veteran who was eligible to enroll.
 - Performed 690 phone screens
 - Positive screens (N=28)
 - Enrolled 21 (see below)
 - 7 requested time to think about the study/talk to doctor first
 - Screening/enrollment failures (N=662)
 - 51% did not meet criteria for risky drinking
 - 32% not interested in participating in the study
 - 6% not taking daily opioids
 - 4% reported travel difficulties
 - 3% scheduled baseline but did not follow through
 - 3% met criteria for moderate or severe SUD, and were referred to treatment
 - 1% did not have a cell phone capable of receiving text messages
 - 1% other
 - Enrolled 21 Veterans
 - Active: 18
 - Current Condition
 - Prevention Intervention: 9
 - Standard Care: 9
 - Dropout: 3
- Submitted three modifications to the Corporal Michael J. Crescenz Medical Center IRB
 - Modification approved 08/04/2015: We removed mention of risky alcohol use from recruitment script and recruitment letter. We changed the protocol to allow recruitment of Veterans who received mental health services from the Mental Health Clinic and Veterans who were referred to us by the Behavioral Health Lab.

- Modification approved 11/09/2015: We made the integrative part of the intervention optional and changed the consent form and protocol to reflect that. Also updated the recruitment script further to include more motivational interviewing principles.
- Modification approved 03/10/2016: Added two sites, Pittsburgh VAMC and the University of Pennsylvania. Changed website and server used for data collection. Added a research specialist to the study staff to aid with recruitment.
- Continuing review at the Corporal Michael J. Crescenz Medical Center approved on 08/05/2015
- Submitted three modifications to the University of Pennsylvania IRB
 - Modification approved on 12/14/2015: Added two sites, Pittsburgh VAMC and the University of Pennsylvania. New versions of the consent, protocol, recruitment brochures, recruitment script, and a list of Philadelphia-area organizations to recruit from were included.
 - Modification approved on 03/01/2016: Edited site name on consent forms when the Philadelphia VAMC became the Corporal Michael J. Crescenz Medical Center.
 - Modification approved on 03/16/2016: Approved study profile to post to iConnect, a University of Pennsylvania website that allows research participants to find studies for which they may be eligible.
- Continuing review at the University Pennsylvania approved on 08/17/2015
- New sites:
 - Submitted an initial proposal to the Pittsburgh VAMC IRB to open a site at their facility
 - Gained approval to send electronic recruitment materials for listserv distribution from Veterans Upward Bound at the University of Pennsylvania, Montgomery County Community College, Camden County Community College, Community College of Philadelphia, Villanova University and Drexel University.
 - Contacted 30+ community organizations, colleges, and universities to begin recruiting from the Veteran community outside of the Philadelphia VA hospital.

Opportunities for Training and Professional Development

Nothing to report

Dissemination of Results

Nothing to report

Plans During the Next Reporting Period to Accomplish Goals and Objectives

The main goal for the third year of funding is to greatly increase recruitment of study participants. As is described in detail in the Changes/Problems section, changes in the VA's policy regarding alcohol and drug use in veterans receiving opioids for pain, which were instituted just as we began recruitment, have produced a situation where veterans on opioid medication are very reluctant to admit any alcohol use, for fear of losing their opioid prescriptions. This has sharply impacted our recruitment efforts at the Philadelphia VA. Therefore, for the third year of funding, we will be implementing several new recruitment initiatives (pending DoD approval). First, we are now in the process of expanding recruitment to include veterans in the Philadelphia area who do not get their treatment at the Philadelphia VAMC or its CBOCs. This modification was approved by the DoD and the UPENN IRB, and we have already begun to contact various veterans groups and organizations that provide services to veterans (e.g., colleges and universities, Vet Centers, etc.) to initiate recruitment of veterans at these sites. Second, we have put in a modification to the DoD to be able to recruit veterans at the Pittsburgh VA, and hope that this will be approved as well. The protocol is currently under review by the Pittsburgh VA IRB, and should be approved soon, allowing for rapid implementation of this second recruitment site if the DoD approves it. Finally, we are in the process of gathering information on numbers of veterans who are being treated for pain at the Philadelphia VA who are on medications other than opioids for which alcohol use is contraindicated, such as benzodiazepines and muscle relaxants, and are drinking at hazardous levels. If those numbers look promising, we will put in a modification to the DoD to expand recruitment to these veterans. Enrolling these veterans would be consistent with the goal of the grant, which is to reduce hazardous alcohol use in veterans with pain diagnoses who are receiving medication that interacts negatively with alcohol.

4. Impact

Development of the principal discipline of the project:

Nothing to report

Other disciplines:

Nothing to report

Technology transfer:

Nothing to report

Society beyond science and technology:

Nothing to report

5. Changes/Problems**Changes in approach and reasons for change:**

As indicated above, we have made several changes to increase recruitment, and hope to make several more in the near future. During the past year, we eliminated language from the informed consent in which the prevention intervention was referred to as “integrated” with primary care. We also removed the term “risky drinking” from our script, and instead refer to “safe use of opioid medication.” These changes were made to address concerns of prospective participants regarding negative labeling and the possibility that information that they provided to our prevention counselors or research staff concerning alcohol use would be conveyed to their primary care physicians via the electronic medical record. We have also just started efforts to recruit veterans in the Philadelphia area who are not receiving medical care at the Philadelphia VA (see above).

Actual or anticipated problems or delays and actions or plans to resolve them:

As is detailed in several sections above, our major problem is the low participant enrollment rate. Due to changes in policy at the VA regarding the prescribing of opioid pain medication to veterans who report alcohol or other drug use, there is a marked reluctance on the part of veterans receiving opioid prescriptions at the VA to admit to any drinking. Therefore, we have expanded our recruitment efforts in a number of ways and are currently seeking to further expand our efforts, as is detailed in above sections of this report. These are: (1) recruiting veterans in the Philadelphia area on opioids for pain who are receiving treatment outside of the Philadelphia VA, (2) recruiting veterans on opioids for pain at the Pittsburgh VA, and (3) recruiting veterans at the Philadelphia VA who have pain diagnoses and are receiving medications other than opioids that also interact negatively with alcohol. We are confident that these modifications, once implemented, will greatly improve our recruitment efforts, while staying within the primary goal of the grant, which is to reduce the incidence of risky drinking in veterans being treated for pain with medications that interact negatively with alcohol.

Changes that had a significant impact on expenditures:

Nothing to report

Significant changes in use or care of human subjects:

Nothing to report

6. Products

Nothing to report