TITLE OF RESEARCH: Reducing Prescription Opioid Misuse: ROPEs Pilot Trial

NCT NUMBER: NCT03691948

DOCUMENT DATE: September 20, 2018

DATE UPLOADED: September 17, 2020

PROTOCOL TITLE:

Reducing Prescription Opioid Misuse: ROPEs Pilot Trial

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1.0 Objectives / Specific Aims

The objective of this study is to conduct a small-scale pilot randomized controlled trial comparing a newly developed web-based continuing dental education (CDE) intervention - Responsible Opioid Prescriber Education (ROPEs) - targeting increased prescription opioid (PO) misuse screening, use of existing prescription drug monitoring programs, and provision of patient-education to attention control condition.

The pilot trial aims to: (1) establish the feasibility of ROPEs delivery; (2) identify and address potential issues with subject recruitment and retention; (3) develop and validate assessment instruments and procedures; (4) collect preliminary data regarding pre-to-post changes in knowledge, motivation, and behavioral skills pertaining to the use of risk mitigation strategies when prescribing opioids in dental practice; and (4) collect preliminary data regarding the sustainability of changes at one-month follow-up assessment.

2.0 Background

Many individuals who go on to develop opioid use disorders, including those individuals who ultimately transition to heroin use, report that early exposure to opioids was through a legitimate prescription or prescription shared from family or friends (Canfield et al., 2010; Butler et al., 2016). Research suggests that lifetime non-medical use of prescription opioids is highly correlated with, and most often preceded by, medical use of prescription opioids (McCabe et al., 2016). This risk is particularly highlighted among adolescents and young adults (McCabe et al., 2016).

Dental prescribing has played a role in the ready availability of immediate release opioids - like hydrocodone - throughout previous decades (Gupta et al., 2018; Janakirim et al., 2018; Levy et al., 2015; McCauley et al., 2016a; McCauley et al., 2016b). Opioids account for a nearly one-third of prescriptions issued by dentists (Levy et al., 2015). Due in large part to the commonality of third molar extraction procedures, dental opioid prescribing is particularly frequent for adolescent patients, a group at increased risk for misuse (Denisco et al., 2011; Gupta et al., 2018; Mutlu et al., 2013). Patients often report having unused medication leftover from their post-procedural prescription (Maughan et al, 2016), and a notable segment of dental patients report at least some nonmedical use of pain medications (Ashrafloun et al., 2014) and approximately one-in-five dental patients report recent substance abuse, including problematic alcohol use or illicit drug use (Ilgen et al., 2012).

Despite dentists' regular experience with opioid prescribing and the risks such prescribing confers, research suggests that dentists do not regularly implement recommended risk mitigation strategies - including screening for prescription drug abuse/misuse, querying a prescription drug monitoring program (PDMP; enacted in all US states except Missouri), and providing thorough patient education regarding safe use, storage, and disposal when prescribing opioid medications for pain management (Herman, 2011; McCauley et al., 2016a; McCauley et al., 2018a). The leading reasons cited by dental prescribers for not accessing their PDMP include lack of awareness of the existence and lack of knowledge regarding how to register for and/or use their state's PDMP (McCauley et al., 2016b). Further, growing evidence and recent guidelines support the use of ibuprofen and/or acetaminophen as first-line analgesic options for managing acute dental pain (ADA, 2018; Moore et al., 2018).

Recently, our group conducted a large-scale survey of dentist members of the National Dental Practice-Based Research Network regarding their prescribing behavior, risk mitigation implementation, and training relevant to opioid analgesics entitled, *Reducing Prescription Opioid Misuse: Dental Provider Intervention Development Survey* (McCauley et al., 2018a; McCauley et al., 2018b). Briefly, results demonstrate that a minority of network dentists reported prescribing opioids only (11%) or opioids in combination with

recommendation for NSAIDs/Acetaminophen (18%) to half or more of their patients needing management of acute pain. Higher opioid prescribing was significantly associated with less-consistent implementation of PDMP use and patient education. A majority of dentists reported infrequent PDMP use and inconsistent counseling of patients regarding risks, storage, and disposal of opioids. Higher frequency of opioid prescribing was associated with less-consistent risk mitigation implementation. Nearly half (n=388) of respondents reported that they had never accessed their state PDMP. The most often reported reasons for not accessing were lack of knowledge of the program's existence (58% of non-users) and lack of knowledge regarding how to register and access the program (25% of non-users). The majority of PDMP users reported use to be very helpful (58%) or somewhat helpful (32%), whereas only 6% reported program use as not very helpful or not helpful at all. Dentists reported that PDMP use most often did not change their intended prescribing behavior (40% of users), led them to not prescribe an opioid (34% of users), or led them to prescribe fewer doses of an opioid for pain management (26% of users). Dentists practicing in states with mandated PDMP use policies (compared to those living in states without such a policy) reported more-frequent use of their PDMP prior to prescribing to new patients, high-risk patients, prior to issuing refills, and prior to any opioid prescribing for pain management.

Training and education in opioid prescribing and prescription drug abuse is recommended by leading practice organizations, including the American Dental Association (ADA, 2018; Dana et al., 2018). Data from the network survey demonstrate that training relevant to prescription drug abuse is associated with safer opioid prescribing practices; however, fewer than half of dentists have training specific to identification and assessment of drug abuse/addiction and only one-quarter of dentists reported training in identification of prescription drug diversion (McCauley et al., 2018a). Importantly, nearly all respondents (96%) identified continuing dental education as being somewhat or very valuable practice resource regarding controlled substance prescribing.

As the culmination of our team's prior mixed methods research regarding dental opioid prescribing practices and training preferences, we developed the Responsible Opioid Prescriber Education (ROPEs) course. ROPEs is designed as a self-directed, web-based continuing dental education intervention targeting: (1) more-conservative reliance on opioid analgesics for post-procedural, acute dental pain management; (2) more-consistent use of PDMP data prior to prescribing opioids; and (3) more-consistent provision of comprehensive patient education regarding the risks associated with opioid use and misuse, as well as the appropriate way to store and dispose of medication. This intervention was iteratively developed with frequent consultation of a dental advisory group, has been alpha and beta tested in dentist-comprised focus groups, and the current protocol is for a pilot evaluation of this online continuing dental education intervention.

3.0 Intervention to be studied

The ROPEs intervention is a self-guided, web-based continuing dental education intervention. Consistent with ADA recommendations, ROPEs consists of seven modules of active content: (1) Overview; (2) Background on the Opioid Epidemic; (3) Dental Pain Management and the Role of Opioids; (4) Universal Precautions Approach; (5) Screening, Monitoring, and PDMP use; (6) Providing Patient Education; and, (7) Case Vignettes. All key intervention content is delivered via a video-based platform and includes a range of downloadable practice aides (e.g., patient education handouts) and resources (e.g., ADA recommendations, brief substance abuse screening instruments, etc.). Active ROPEs content (excluding pre-test and post-test) can be completed in 60-80 minutes. While dentists will be encouraged to complete the ROPEs intervention in one sitting (and required to complete the intervention within 2 weeks), all participants will have their unique log-in credentials that will enable them to complete ROPEs (or attention control) in multiple sessions, as well as return to the content at any time subsequent to completion (e.g., to

print patient resources, review materials). The attention control condition will be a web-based version of the Centers for Disease Control Guideline for Prescribing Opioids for Chronic Pain.

4.0 Study Endpoints

This is a randomized controlled pilot trial to establish methodological feasibility and determine whether a web-based, continuing dental education intervention regarding opioid prescribing risk mitigation strategies - consistent with ADA guidelines - produces pre-to-post changes in knowledge, motivation, and behavioral skills pertaining to the use of risk mitigation strategies when prescribing opioids in dental practice. The current study involves completion of a self-report pre-test (dentists), randomization to complete ROPEs or attention control intervention, completion of a self-report post-test (immediately following intervention/control completion), and completion of 1-month self-report follow-up assessment.

Primary outcomes are intended to establish methodological feasibility and include: (1) recruitment rates; (2) time to complete ROPEs and completion rates; and (3) follow-up assessment completion rates. Web analytic metrics will include average time spent on the site for both intervention and control participants.

Secondary outcomes will include: (1) changes in dentists' knowledge regarding the dentists' role in curbing PO misuse, initiation to abuse, and diversion; (2) changes in knowledge regarding recent released guideline recommendations for standard pain management in dental practices; and (3) changes in knowledge of risk mitigation strategies, such as PO misuse screening and use of their state's PDMP.

5.0 Inclusion and Exclusion Criteria/ Study Population

Participants will be licensed dentists and dental residents (N=60) recruited from MUSC, the state of South Carolina Dental Association, the local (Charleston-area) community, and the National Dental Practice Based Research Network. Vulnerable populations (e.g., minors, underrepresented minorities) will not be targeted for recruitment; minors will not be recruited and racial/ethnic representation will result from random sampling.

*Inclusion Criteria**:***

1. Male or female; any race or ethnicity; age 21–85 years.
2. Able to comprehend English.
3. Be either a licensed dental practitioner currently practicing or a Resident enrolled in the College of Dental Medicine at the Medical University of South Carolina or a practicing dentist in the Charleston-county area or a licensed dental practitioner currently participating in the National Dental Practice Based Research Network (NDPBRN).
4. Report having ever prescribed an opioid analgesic to a patient
5. Must have Internet access
6. Must have a valid, usable email account
7. Must agree to complete all study measurements.

*Exclusion Criteria**:***

1. Unable to provide informed consent due to mental or physical limitations.
2. Participation in ROPEs intervention development focus groups.

6.0 Number of Subjects

A total of 60 participants (30 per condition) will be recruited for the current study.

7.0 Setting

All assessment and intervention/control condition completion will take place via either secure web-based platform (pre-test, intervention/control, post-test) or REDCap (1-month follow-up) platform. Participating dentists will enter data/responses directly into the web-based platform. Data will be housed on a secure MUSC server using Secure Sockets Layer 128-bit encryption. Prior to analysis, data will be downloaded from the secure platform in comma separated values (csv) file format and imported in a statistical software program for analysis.

8.0 Recruitment Methods

The study will be managed from the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina. Data will be collected via online response and housed on secure servers at the Medical University of South Carolina. Participants for the proposed research will be recruited from the South Carolina Dental Association, dental practices participating in the NDPBRN, dental practices located in the Charleston-area community and broader state of South Carolina, and from the MUSC College of Dental Medicine through use of the following recruitment approaches: (1) Listserv announcements, advertisements, and emails through the NDPBRN, South Carolina Dental Association, the MUSC College of Dental Medicine, and the MUSC College of Dental Medicine Alumni Association; (2) mailed invitations to existing dental practices; (3) flyers posted in College of Dental Medicine; and (4) personal contact and/or professional networking/direct emails through mentorship team (e.g., Dr. Leite). Individuals interested in participating in the study will be asked to email the study PI (at ropesadmin@musc.edu) expressing interest. At that time, eligibility criteria will be confirmed and interested individuals will be engaged in the consent process *described below*.

9.0 Consent Process

Participants will be a total of 60 licensed dentists and dental residents recruited from the state of South Carolina and the National Dental Practice Based Research Network. Interested individuals (those emailing the study PI) will receive an email response that reiterates eligibility criteria, provides information commensurate with informed consent for participation in the study, and asks individuals to confirm their eligibility and interest in participation via email response. Following confirmation of eligibility and interest in participation, participants will be emailed a hard copy of the study information sheet (attachment) and log-in credentials for participation.

A waiver of written consent is requested for the current study. The main risk associated with participation in this study is loss of confidentiality and waiver of written consent is one step to diminish this risk. Whereas login credential will be contained in email (a non-secure form of communication), this log-in information will not be linkable to participant USERID credentials (used for data storage) without access to the linkage key document. Only IRB-approved study personnel will have access to this linkage document.

10.0 Study Design / Methods

Consenting participants will be emailed log-in credentials and instructions for accessing the ROPEs/control intervention site. Participants will be randomized at the time of log-in to receive either the ROPEs intervention or a web-based attention control condition. The attention control condition will consist of a website containing printed content of most recent best practice guidelines provided by the Centers for Disease Control and Prevention Guideline for Prescribing Opioids for Chronic Pain. It is anticipated that the web-based intervention will take approximately 60-80 minutes to complete, excluding pre-test and post-test completion. Outcomes will be assessed at three time-points: (1) pre-intervention; (2) post-intervention; and, (3) one-month post-intervention. Assessment inventories will take approximately 15 minutes each to complete. Pre- and post-intervention assessments will be embedded into the intervention/control website. Participants will be re-contacted (via email) at one-month post intervention, and asked to complete the one-month follow-up assessment on the secure REDCap platform. Participants will receive $50 for their time

completing pre-intervention assessments, $50 for their time in completing post-intervention assessments, and $100 for their time in completing one-month post-intervention follow-up assessments. Remuneration will be provided via email in the form of an Amazon gift code link.

11.0 Specimen Collection and Banking

Not Applicable to the current study.

12.0 Data Management

Data for the pilot trial phase of this study will be obtained from online self-report measures and web-analytic metrics. Data will include: (1) recruitment rates; (2) time to complete ROPEs intervention and completion rates; and (3) follow-up assessment rates; as well as changes in dentists' knowledge regarding: (1) role in curbing PO misuse, initiation to abuse, and diversion; (2) recent released guideline recommendations for standard pain management in dental practices; and (3) risk mitigation strategies, such as PO misuse screening and use of their state's PDMP. Web analytic metrics will include time spent on the site, number of log-ins, and activity completion. The participant will directly enter data into the web-based platform during completion of ROPEs (or attention control). Data will be housed on a secure MUSC server using Secure Sockets Layer 128-bit encryption. Further, assessment (pre-intervention, post-intervention, one-month follow-up) data for this study will be stored electronically in de-identified manner using participant identification numbers (USERID). Only members of the study team will have access to the linkage document associating USERID with identifying and contact information. Identifying information will be used only for the purposes of participant reimbursement and contact for follow-up. Participants' identifying information and linkage to data USERID will be stored on a secure MUSC server in a password protected file and will be destroyed at the conclusion of the study.

Outcomes will be assessed at three time-points: (1) pre-intervention; (2) post-intervention; and, (3) one-month post-intervention. Key outcomes include enhanced knowledge regarding: (1) dentists' role in curbing PO misuse, initiation to abuse, and diversion; (2) recent released guideline recommendations for standard pain management in dental practices; and (3) risk mitigation strategies, such as PO misuse screening and use of their state's PDMP. *It is important to reiterate that the primary aim of the pilot RCT is to demonstrate the feasibility of methodology. We do not anticipate the pilot to be adequately powered to produce meaningful between-group effect sizes*. Nonetheless, we do anticipate that ROPEs will result in significant within group increases in knowledge. We will also make a direct comparison of the efficacy of the ROPEs intervention versus the attention control in increasing knowledge of risk mitigation strategies. The main predictor will be intervention assignment. We hypothesize that ROPEs will result in significantly improved knowledge regarding recommended risk mitigation strategies measured via provider self-report at immediately post-intervention and one-month follow-up time-points.

Handling of Missing Data. Given that the majority of analyses will be descriptive in nature (rather than hypothesis testing), the extent of missing data will be reported for each query of interest. With respect to hypothesis driven analyses, there are multiple techniques available for managing missing data in a sample of this nature. In brief, if the pattern of missing data is independent of values of other observed variables, then it is considered missing completely at random (MCAR). Participants with missing data patterns that are MCAR are thought of as a random subsample of the original sample. If the missing mechanism is MCAR, we can exclude participants with missing responses without being concerned about bias. If the missing mechanism is differential (common with longitudinal designs), we will consider data imputation techniques including introducing dummy variables for the missing variables, as well as the mean, mode, or median substitutions as appropriate.

13.0 Provisions to Monitor the Data to Ensure the Safety of Subjects (if applicable)

This pilot trial is intended to establish the methodological feasibility of a randomized controlled trial of an educational intervention targeting changes in dental opioid prescribing practices. Since the current pilot is a non-medication trial, all unexpected Adverse Events (AEs) will be reported to the MUSC Committee on Human Research and NIDA only, and not to the FDA.

Definition of AE and SAE.
Adverse events are defined as any untoward medical occurrence that may present itself during treatment or administration of an intervention, and which may or may not have a causal relationship with the treatment. Serious adverse events are defined as any medical occurrence that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect.
  OR
- Requires intervention to prevent one of the above outcomes.

All AEs will be reported as soon as possible and within ten working days of the investigator first learning of the event. Serious AEs (SAEs) will be reported within 24-business hours. The MUSC IRB AE reporting requirements are as follows: All deaths that occur during the study or 30 days post termination from the study are required to be reported as adverse events even if they are expected or unrelated. Other adverse events are reportable to the MUSC IRB if the AE is unexpected AND related or possibly related AND serious or more prevalent than expected. All three criteria must be met for an AE to be reported to the MUSC IRB. The IRB definition of unexpected is that the AE is not identified in nature, severity or frequency in the current protocol, informed consent, investigator brochure or with other current risk information. The definition of related is that there is a reasonable possibility that the adverse event may have been caused by the drug, device or intervention. Reportable AEs are reviewed by the IRB Chair and reported to the IRB Board at the next meeting. The proposed pilot trial will investigate changes in knowledge, motivation, and self-efficacy of dental providers' implementation of risk mitigation strategies when prescribing opioid analgesics. Study outcomes do not assess clinical outcomes among participants (dentists). It is extraordinarily unlikely that a participant in the proposed trial will experience a medical occurrence meeting the aforementioned criteria for AE/SAE as a result of their participation in this trial.

Reporting Mechanisms of IRB Actions to NIDA. Any significant actions taken by the local IRB, as well as protocol changes, will be relayed to NIDA. AEs and SAEs occurring during the course of the trial will be collected, documented, and reported in accordance with reporting requirements (see above). All research staff involved with adverse event reporting will receive general and protocol specific AE/SAE training including identification, assessment and evaluation, and documentation and reporting.

Report of Changes or Amendments to the Protocol. Any significant actions taken by the local IRB - including but not limited to requested protocol changes, amendments, and progress reports - will be relayed to NIDA in a timely manner.

Trial Stopping Rules. Given that this is a pilot feasibility trial, *we do not anticipate that results will show statistically overwhelming significant differences between groups, particularly at interim analysis points*; however, if they do, the blind will the candidate will consult with her mentorship team regarding the decision to break the blind and terminate the pilot trial at that time.

Collection and Reporting of AEs and SAEs. AEs/SAEs will be documented and reported as per protocol and IRB requirements. The candidate and research/mentorship team will identify adverse events and obtain all available information to assess severity, seriousness, study relatedness, expectedness, outcome and the need for change or discontinuation in the study intervention. Adverse events will be documented on AE Logs and AE Case Report Forms (CRFs). Additional relevant AE information, if available, will be documented in a progress note in the research record as appropriate to allow monitoring and evaluating of the AE. If the AE meets the definition for serious, appropriate SAE protocol specific reporting forms will be completed and disseminated to the appropriate persons and within the designated timeframes as indicated above. For each AE/SAE recorded, the research staff will follow the AE/SAE until resolution, stabilization or until the participant is no longer in the study as stated in the protocol.

In the unlikely event that a reportable SAE is identified, the PI will initiate an SAE form, and the following individuals will be notified by facsimile transmission within 24 hours of the PI's initial knowledge of the SAE:

i. The Principal Investigator (Dr. McCauley, a clinical psychologist) and Primary Mentor (Dr. Brady, a psychiatrist) will provide oversight, consultation, assessment and documentation as appropriate of the SAE.
ii. The research staff will notify the MUSC institutional review board (IRB) and complete the AE report form in conjunction with the PI. Communication with the IRB is through email, memos, official IRB forms, and online reporting.
iii. The NIH program officer.
iv. The data safety monitoring board members.

If complete information is not available when the initial 24-hour SAE report is disseminated, follow-up information will be gathered to enable a complete assessment and outcome of the event. This information may include hospital discharge records, autopsy reports, clinic records, etc. The research staff will attach copies of source documents to the SAE report for review by the PI and for forwarding to the NIH program officer as appropriate within 2 weeks of the initial SAE report. In addition, the PI will provide a signed, dated SAE summary report, which will be sent to the NIDA Medical Safety Officer within two weeks of the initial SAE report.

We will report adverse events to the MUSC IRB online as soon as possible, but no later than 10 working days after the investigator first learns of the event. The MUSC IRB AE reporting requirements have been presented above. In brief, MUSC's policy for reporting serious adverse events is as follows: It is the investigator's responsibility to report all serious adverse events to the HIC (Human Investigators Committee) and the sponsor within 24 hours after learning of the event. An "Adverse Event Report Form" must be completed and submitted to the HIC office. A description of the serious adverse event and treatment, if any, must accompany the form. The HIC chairperson, designated representatives, or the full HIC, as determined by the chairperson, reviews the report. If the reaction is severe, the investigator may be requested to discontinue the research pending further review by the HIC. Investigators must ensure that the NIH is informed of actions, if any, taken by the IRB as a result of its continuing review. Any adverse event will be reported to NIDA in an individual adverse event report.

Management of SAEs or Other Study Risks. Adverse events will be monitored throughout the study and any event will be followed to resolution or stabilization. All serious adverse events will be reported immediately to the IRB and NIDA. The PI (Dr. McCauley) will provide continuous, close monitoring with prompt reporting of adverse events to the IRB and NIDA, and will follow MUSC's adverse event reporting policy. In addition, Dr. McCauley and the mentorship/consultation team will evaluate the progress of the study at bi-weekly study team meetings, including periodic assessments of data quality and timeliness, participant

recruitment and retention, participant risk versus benefit, and other factors that can affect study outcome. We will also consider factors external to the study, such as scientific or therapeutic developments that may have an impact of the safety of participants or the ethics of the study.

Protection of Confidentiality. All data will be stored in a confidential manner (i.e., on a Secure Socket Layer (SSL) 128-bit encryption server located at MUSC) so as to protect the confidentiality of subject information. Participants in this pilot RCT will be assigned a secure log-in and access code. Log-in information will be associated with PHI (including email address) for the purposes of contacting them at one-month post-intervention for follow-up assessment. All contact information used to recruit and retain study participants will be stored electronically on MUSC's secure network in a password protected file and will be destroyed at the conclusion of the project. Access to research records (paper and computerized) will be restricted to the project staff. Specifically, access to de-identified study data will be limited to named project investigators (including the PI and her Mentorship/Consultation team, NIH audit personnel, and MUSC IRB audit personnel). Data will be maintained per an IRB-approved protocol. When study results are published or presented, only aggregate reports of the results will be used and subjects' identity will not be revealed. All analyses will be conducted on de-identified data only.

*Plans for Interim Analysis of Efficacy Data***.** Given that this is a pilot feasibility trial, recruitment rates are one of the primary outcomes, and *we do not anticipate that results show statistically overwhelming significant differences between groups*; therefore, we do not plan to break the blind for interim analysis of efficacy data.

Responsibility for Data and Safety Monitoring. The PI will be responsible for monitoring the study with regular oversight provided by her primary mentor, Dr. Kathleen Brady. The outcomes database will be examined for missing data, unexpected distributions or responses, and outliers at the close of the trial.

Frequency of DSM Reviews. All AEs will be reviewed weekly by the PI and her mentor team and will be reviewed bi-annually by the Data Safety Monitoring Board (DSMB) during the completion of the pilot.

Content of DSM Report. A DSM Report will be filed with the IRB and NIDA on a *yearly* basis, unless greater than expected problems occur. The report will include subject characteristics, retention and disposition of study subjects, quality assurance issues and reports of AEs, significant/unexpected AEs and serious AEs. We will report results at the end of the pilot trial. Confidentiality will be maintained during all phases of the trial including monitoring, review, and response to monitoring recommendations.

DSM Board Plan. The study PI will create a DSMB to monitor the overall participant safety, the rate and severity of adverse events, and the validity and integrity of the data. The panel will include 3 researchers with experience in addictions research and provider-level interventions, as well as a statistician. The board may be called at any point if needed for unexpected AEs, etc. Modification will be made in the procedures and/or the protocol if necessary based on the recommendations of the board.

14.0 Withdrawal of Subjects

All participation is voluntary and participants may withdraw from the study at any time. Given the low risk for adverse events associated with this study, we do not anticipate many circumstances under which participants would be withdrawn from the study without their consent; however, should it be discovered that a participant does not meet inclusion/exclusion criteria subsequent to their enrollment, they will notified via email that their study participation has been terminated. Should this occur, affected participants will be remunerated for their time spent engaged with the study and a protocol deviation will be completed with the IRB for documentation.

Should a participant contact the study PI and voluntarily withdraw from the study, they will be remunerated consistent with the extent of their participation to that time and will not be contacted for subsequent data collection; however, data provided prior to voluntary withdrawal will be kept for analysis, unless the participant specifically asks for that data to be withdrawn from the study.

15.0 Risks to Subjects

Given the nature of the proposed trial (i.e., not testing a medical intervention), AEs and SAEs (as defined above) are highly unlikely to occur in the context of the current pilot trial. Although also unlikely, two minor risks to participants exist and will be managed. Some participants may become offended when asked questions pertaining to their personal experiences and opinions related to opioid analgesic prescribing practices. Our experience (PI and mentor/consultant team) in previous and ongoing investigations indicates that this risk is minimal. Thus, based on the team's extensive experience, we expect low to non-existent rates of participant distress, and should a participant become offended, they can discontinue participation at any time.

Another potential risk of participation is related to issues of participant privacy and confidentiality. We will implement several previously successful procedures to keep data confidential. Participants will not use their names to log onto the website, nor will they provide any other form of identifying information during their completion of the ROPEs intervention/control. Further, de-identified (log-in coded) data will be collected and stored via a secure server. For participants completing the ROPEs data platform assessments, primary data will be housed on a secure MUSC server using Secure Sockets Layer 128-bit encryption. Further, assessment (pre-intervention, post-intervention, one-month follow-up) data for this study will be stored electronically in de-identified manner using participant identification numbers (USERID). Only members of the study team will have access to the linkage document associating USERID with identifying and contact information. Identifying information will be used only for the purposes of participant reimbursement, linkage of assessment data from various time-points, and contact for follow-up. Participants' identifying information and linkage to data USERID will be stored on a secure MUSC server in a password protected file and will be destroyed at the conclusion of the study.

16.0 Potential Benefits to Subjects or Others

Participants in the proposed research may benefit from knowledge gained regarding (a) standard prescribing practices of dentists; (b) the safe and appropriate use, storage, and disposal of opioid analgesic medications; and (c) available opioid prescribing risk mitigation tools. Although there is a small reimbursement for participants (i.e., $50 for completion of pre-intervention assessments; $50 for completion of post-intervention assessments; $100 for completion of one-month post intervention follow-up assessment), we do not believe that this reimbursement constitutes a substantial benefit for participation.

Potential benefits to others also exist. The public health implications of this project are significant and the findings will provide empirical evidence to inform policies and programs that address the urgent need for effective interventions targeting opioid misuse and diversion in frontline healthcare settings. Specifically, this project will result in a fully developed and piloted ROPEs intervention to enhance dentists' knowledge, motivation, and skill toward implementing recommended risk mitigation strategies when prescribing POs. The pilot RCT evaluation will result in critical data establishing the feasibility of methods and validation of assessments, as well as produce preliminary data regarding ROPEs potential efficacy in improving dental provider knowledge, motivation, and self-efficacy to implement PO risk mitigation strategies. Finally, the prescriber education and intervention content – while specific to dental practitioners – will provide a template with the potential for adaptation to address the opioid prescribing practices of other frontline healthcare practitioners, such as primary care, emergency medicine, and pain management practices.

17.0 Sharing of Results with Subjects

All data will be analyzed and reported in an aggregate, de-identified manner. Key results will be posted in compliant manner on clinicaltrials.gov. Findings will also be disseminated via peer-reviewed publications, professional presentations, and to practice groups (upon request). Individual participants may request a report of aggregate findings from the PI directly and this option will be noted in the informed consent document.

18.0 Drugs or Devices

Not Applicable to the current study.

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