

Reducing Prescription Opioid Misuse: Dental Provider Intervention Development Survey

NIDCR Protocol Number: 16-019-E

NIDCR Funding Mechanism: U19-DE-22516

NIDCR Grant Principal Investigator (GPI):

Gregg Gilbert, DDS, MBA

Study Principal Investigator (SPI):

Jenna L McCauley, PhD

Institutions:

Medical University of South Carolina

NIDCR Program Officials:

Dena Fischer, DDS, MSD, MS

Version Number: 2.0

23 March 2016

TABLE OF CONTENTS

	PAGE
TABLE OF CONTENTS	2
LIST OF ABBREVIATIONS	4
STATEMENT OF COMPLIANCE	5
SIGNATURE PAGE	6
SIGNATURE PAGE- NETWORK STAFF	8
PROTOCOL SUMMARY	9
1 KEY ROLES AND CONTACT INFORMATION.....	12
2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE.....	15
2.1 Background Information	15
2.2 Rationale	16
2.3 Potential Risks and Benefits	17
3 OBJECTIVES.....	18
3.1 Study Objectives	18
3.2 Study Outcome Measures.....	18
4 STUDY DESIGN	19
5 STUDY ENROLLMENT AND WITHDRAWAL	20
5.1 Inclusion Criteria	20
5.2 Exclusion Criteria	20
5.3 Strategies for Recruitment and Retention	20
5.4 Practitioner and Patient Withdrawal	21
5.5 Premature Termination or Suspension of Study	21
6 STUDY SCHEDULE	22
6.1 Stage 1 Questionnaire Component: Enrollment/Baseline	22
6.2 Stage 2 Retest of the Survey	22
6.3 Stage 3 Merging Practitioner Survey with Enrollment Questionnaire.....	22
7 STUDY PROCEDURES/EVALUATIONS	23
8 ASSESSMENT OF SAFETY.....	25
8.1 Specification of Safety Parameters	25
8.2 Reporting Procedures	25
9 STUDY OVERSIGHT.....	27
10 CLINICAL SITE MONITORING.....	28
11 STATISTICAL CONSIDERATIONS	29
11.1 Study Hypotheses	29
11.2 Sample Size Considerations	29
11.3 Final Analysis Plan.....	29
12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS	31
13 QUALITY CONTROL AND QUALITY ASSURANCE.....	32
14 ETHICS/PROTECTION OF HUMAN SUBJECTS	33
14.1 Ethical Standard.....	33
14.2 Institutional Review Board.....	33

14.3	Informed Consent Process.....	33
14.4	Exclusion of Women, Minorities, and Children (Special Populations).....	33
14.5	Participant Confidentiality.....	33
15	DATA HANDLING AND RECORD KEEPING.....	35
15.1	Data Management Responsibilities.....	35
15.2	Data Capture Methods.....	35
15.3	Types of Data.....	36
15.4	Schedule and Content of Reports.....	36
15.5	Study Records Retention.....	36
15.6	Protocol Deviations.....	36
16	PUBLICATION POLICY.....	37
17	LITERATURE REFERENCES.....	38

LIST OF ABBREVIATIONS

AE	Adverse Event/Adverse Experience
CC	Coordinating Center
CFR	Code of Federal Regulations
CRF	Case Report Form
DHHS	Department of Health and Human Services
DMP	Data Management Plan
FFR	Federal Financial Report
GPI	Grant Principal Investigator
IRB	Institutional Review Board
MOP	Manual of Procedures
MUSC	Medical University of South Carolina
N	Number (typically refers to participants)
NND	National Network Director
NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PBRN	Practice-Based Research Network
QA	Quality Assurance
QC	Quality Control
RAS	Regional Administrative Site
RC	Regional Coordinator
SAE	Serious Adverse Event/Serious Adverse Experience
SMS	Survey Management System
SPI	Study Principal Investigator
SOP	Standard Operating Procedure
UAB	University of Alabama
UP	Unanticipated Problems
US	United States

STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the Code of Federal Regulations (CFR) on the Protection of Human Subjects (45 CFR Part 46), and the National Institute of Dental and Craniofacial Research (NIDCR) Clinical Terms of Award. All personnel involved in the conduct of this study have completed human subjects protection training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable United States (US) federal regulations and guidelines.

Grant Principal Investigator (GPI)/South Central Regional Director

Signed: _____ Date: _____

Name: Gregg H. Gilbert, DDS, MBA

Title: Professor and Chair

Study Principal Investigator (SPI)

Signed: _____ Date: _____

Name: Jenna L McCauley, PhD

Title: Assistant Professor

Regional Directors:

Signed: _____ Date: _____

Name: Jeffrey Fellows, PhD

Title: Regional Director, Western Region

Signed: _____ Date: _____

Name: Brad Rindal, DDS

Title: Regional Director, Midwest Region

Signed: _____ Date: _____

Name: Tom Oates, DMD, PhD

Title: Regional Director, Southwest Region

Signed: _____ Date: _____

Name: Valeria Gordan, DDS, MS

Title: Regional Director, South Atlantic Region

Signed: _____ Date: _____

Name: Cyril Meyerowitz, DDS, MS

Title: Regional Director, Northeast Region

SIGNATURE PAGE- NETWORK STAFF

A copy of this page is to be signed by all Steering Committee members, Regional Coordinators, and other National Dental Practice-Based Research Network (PBRN) staff members responsible for conducting any portion of the study (if not already designated to sign the protocol above). The signature page should be printed, signed, then scanned into a PDF document and submitted to the Coordinating Center (NDPBRN-helpdesk@westat.com) for storage on the Internal Website.

The signature below constitutes:

- 1) acknowledgement of having read this protocol version (as indicated in the upper right corner of this page) and the attachments, and
- 2) an assurance that this individual will conduct all of his or her assigned study tasks according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and guidelines.
- 3) an assurance that this individual will read and follow all study plans applicable to his/her role on the study (e.g. Regional Coordinators will read and follow the Manual of Procedures (MOP), Practice Training Manual, Clinical Monitoring Plan, and other applicable plans developed in the future).

Signed: _____ Date: _____

Name: _____

Title: _____

PROTOCOL SUMMARY

- Title:** Reducing Prescription Opioid Misuse: Dental Provider Intervention Development Survey
- Précis:** This study aims to identify critical training gaps in dental implementation of opioid prescribing risk mitigation strategies. Dentists follow primary care physicians as the second leading prescriber of immediate release opioids. However, dentists typically have limited exposure to addiction training and may not be familiar with recommended opioid prescribing risk mitigation strategies. This study consists of an online survey that will document current knowledge, training experiences, and practice behaviors related to acute dental pain management and opioid analgesic prescribing among member dentists. Data from the survey will be paired with key practice-related enrollment data to identify aforementioned gaps in knowledge and directly inform the development of an educational intervention that provides dentists training in opioid misuse screening and implementation of risk mitigation strategies when prescribing opioids for acute pain management.
- Objectives:** *Primary:* The objective of this study is to conduct a national survey of dentists to assess knowledge and behavior related to opioid prescribing practices.
- Secondary:* The secondary objectives of this study are to:
- Identify practitioner-level and practice-level facilitators of conservative opioid prescribing practices, and
 - Identify practitioner-level and practice-level facilitators of consistent implementation of opioid prescribing risk mitigation strategies (i.e., drug monitoring program use and provision of patient education).
- Outcomes:** Primary outcome measures include: (1) pain management strategies used in practice and frequency of their use; (2) opioid prescribing behaviors; (3) situations/procedures eliciting opioid prescribing in the dental setting; (4) training and continuing education relevant to addictions; (5) opinions/current use of opioid risk mitigation strategies/universal precautions; (6) familiarity with, use and perceived utility of state's prescription drug monitoring program (when available); and (7) effects of prescription drug monitoring program use on practice. All data will be self-reported by consenting, participating dental practitioners.
- Population:** A total of 1,428 National Dental PBRN dentists with completed Enrollment Questionnaire data will be invited to complete the online survey with the goal of obtaining at least 1,000 (70% response rate)

eligible respondents.

Number of Sites: 1: Medical University of South Carolina

Study Duration: 13 months

Practitioner Participation Duration: One time completion of survey (up to 30 minutes). A subsample of approximately 50 participants will complete the survey again at Time 2 for the purposes of establishing test-retest reliability (total duration: up to 60 minutes).

Estimated Time to Complete Enrollment: 14 weeks

Schematic of Study Design:

SURVEY QUESTIONNAIRE ADMINISTRATION AND RETEST ACTIVITIES

Week	Launch Timeline	Retest Activity	Wave 1	Wave 2	Wave 3
0	Wave 1 Launch (N=40)				
1			Email Reminder 1		
2	Wave 2 Launch (N=694)		Email Reminder 2		
3			Email Reminder 3 from RCs	Email Reminder 1	
4	Wave 3 Launch (N=694)	Invite (N=25) W1 & W2 completers for Retest	Non-Responders to RC for multi-mode f/u	Email Reminder 2	
5		Continue Retest invites from W1 & W2 until N=25		Email Reminder 3 from RCs	Email Reminder 1
6		Invite (N=25) W3 completers for Retest		Non-Responders to RC for multi-mode f/u	Email Reminder 2
7		Continue Retest invites from W3 until N=25			Email Reminder 3
8					Non-Responders to RC for multi-mode f/u
9			Final RC Follow-Up with Non-Responders		
10			SURVEY CLOSES		
11				Final RC Follow-Up with Non-Responders	
12				SURVEY CLOSES	
13					Final RC Follow-Up with Non-Responders
14					SURVEY CLOSES

1 KEY ROLES AND CONTACT INFORMATION

GPI:

Gregg H. Gilbert, DDS, MBA
Professor and Chair
University of Alabama at Birmingham
1720 Second Ave. South
School of Dentistry, SDB 109
Birmingham, AL 35924-0007
Phone: 205-975-8886
Fax: 205-975-0603
Email: ghg@uab.edu

SPI:

Jenna L McCauley, PhD
Assistant Professor
Medical University of South Carolina
Department of Psychiatry & Behavioral Sciences
67 President Street, MSC861
Charleston, SC 29425
Phone: 843-792-3922
Fax: 843-792-4817
Email: mccaule@musc.edu

**NIDCR Program
Officials:**

Dena Fischer, DDS, MSD, MS
Phone: 301-594-4876
Email: dena.fischer@nih.gov

NIH/NIDCR/DER
6701 Democracy Boulevard, MSC 4878
Bethesda, MD 20892-4878

**Coordinating
Center (CC):**

Westat
1600 Research Boulevard, WB294
Rockville, MD 20850
Robert Harris, PhD,
Phone: 301-294-4414
Fax: 240-294-4494
Email: BobHarris@Westat.com

Medical University of South Carolina
Department of Psychiatry and Behavioral Sciences
67 President Street, MSC 861
Charleston, SC 29425
Phone: 843-792-3922
Fax: 843-792-4817
Email: mccaule@musc.edu

Institutions:

Western Region (region #1)

Administratively based at the Kaiser Permanente Center for Health
Research, Portland Oregon
Camille Baltuck, Regional Coordinator
Kaiser Permanente Center for Health Research
3800 N. Interstate Ave.
Portland, OR 97227-1110
Office: (503) 335-2454
Fax: (503) 335-6311
Email: camilleb@uw.edu

Midwest Region (region #2)

Administratively based at the HealthPartners Institute for Education
and Research in Minneapolis, MN
Sarah Basile, Regional Coordinator
HealthPartners Institute for Education and Research
8170 33rd Avenue South
MS: 21111R
Minneapolis, MN 55445
Office: (952) 967-7404
Fax: (952) 967-5022
Email: Sarah.M.Basile@HealthPartners.Com

Southwest Region (region #3)

Administratively based at the University of Texas Health Science Center at San Antonio in San Antonio, TX
Stephanie C. Reyes, Regional Coordinator
7703 Floyd Curl Drive, MC 7894
San Antonio, TX 78229
Office: (210) 562-5654
Fax: (210) 562-4136
Email: reyess@uthscsa.edu

South Central Region (region #4)

Administratively based at the University of Alabama at Birmingham in Birmingham, AL
Andrea Mathews, Program Manager
Department of Clinical and Community Sciences
School of Dentistry, SDB 114
1720 2nd Avenue South
Birmingham, AL 35294-0007
Office: (205) 934-2578
Fax: (205) 996-2172
Email: ahmathews@uab.edu

South Atlantic Region (region #5)

Administratively based at the University of Florida in Gainesville, FL
Deborah McEdward, Regional Coordinator
University of Florida
P.O. Box 100415
Gainesville, FL 32610
Office: (352) 273-5848
Fax: (352) 273-7970
Email: dmcedward@dental.ufl.edu

Northeast Region (region #6)

Administratively based at the University of Rochester in Rochester, NY
Christine O'Brien, Regional Coordinator
Eastman Institute for Oral Health
625 Elmwood Avenue, Box 683
Rochester, NY 14620
Phone: (585) 275-5780
Fax: (585) 273-1237
Email: Christine_O'Brien@urmc.rochester.edu

**Other Key
Personnel:**

- Dr. Kathleen T. Brady (Study Co-Investigator)
- Dr. Roger B. Fillingim (Study Co-Investigator)

2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Scope of the Problem: Prescription Opioid Misuse. The appropriate management of pain is critical to quality patient care across medical disciplines. Opioids are an effective tool for the management of acute pain and are the most prescribed medication of any drug category in the U.S., exceeding 250 million prescriptions annually.^{1,2} As the legitimate use of opioids for pain management has increased, so has the incidence of prescription opioid misuse.³ As of 2007, prescription opioids surpassed marijuana as the most commonly initiated drug of abuse.⁴ More than 35 million Americans (≈14% of the total population) report past-year prescription opioid misuse.⁵

Various terms (e.g., non-medical use, aberrant use, abuse, misuse) have been used interchangeably in the literature; however, for the purposes of this project, misuse is defined as “use of a medication other than as directed or indicated, whether willful or unintentional.”⁶ Examples of misuse include taking more than prescribed, combining with other substances (e.g., alcohol, sedatives), taking for reasons other than to reduce physical pain (e.g., to reduce anxiety, increase energy, improve sleep), lending to others, borrowing or diverting from others, multiple requests for early refills, reporting medications lost or stolen, and obtaining medications from multiple sources. The consequences of prescription opioid misuse can be tragic, and include the development of more chronic and severe substance use disorders, overdose, and unintentional fatality.⁷⁻¹¹ Recent surveillance estimates (2013) suggest a plateau in rates of diversion and overdose that escalated from 2000-2010, likely a result of increased public health attention and intervention.¹² However, overdose rates and treatment admission rates related to prescription opioids remain high, particularly in comparison to other substances of abuse¹³.

The majority of prescription opioid misusers (~85%) report receiving medications from a single healthcare provider or friends, the majority of which (~80%) were originally sourced by a healthcare provider.^{5,14-16} In addition to intentional drug diversion for profit, this ‘unintended’ diversion (obtaining the medication from a family member or friend) is a leading source of prescription opioids among the burgeoning population of adolescent abusers.¹⁷ Given their role as the leading prescriber, increasing attention has been given to the prescribing practices of primary care physicians, and has highlighted the need to balance pain management with risk mitigation.^{6,18-21} A universal precautions approach is reflected in the Office of National Drug Control Policy paper¹⁰ and the Food and Drug Administration Risk Evaluation and Mitigation Strategies (REMS) for extended release opioids.²² This approach includes the use of strategies such as universal screening, urine drug testing for high-risk patients, use of prescription monitoring programs prior to prescribing, consideration of alternate pain management strategies when appropriate, and patient education (including patient/provider agreements) regarding the appropriate use of opioids, as well as the potential risks of misuse.^{4,6,23} This project expands focus of provider education efforts to immediate release opioids. Immediate release opioids are deserving of focus because they are: (1) prescribed 10 times more often than extended release opioids and regularly prescribed by dentists to manage acute pain; (2) implicated in the majority of opioid-related overdoses and fatalities; and (3) largely ignored by existing prescriber interventions (e.g., REMS).^{3,24}

Relevance to Dental Providers. Dentists follow primary care physicians as the second leading prescriber of immediate release opioids, accounting for 12% of all immediate release opioids dispensed.²⁵ Acute pain is common following a number of dental procedures, making effective pain management an essential component of dental practice.²⁶ Despite being the second leading group of immediate release opioid prescribers, there is a dearth of research addressing the prescribing practices of dentists and their role in reducing misuse and diversion. Due to the at-risk patient population (adolescents and young adults) and typically short-lived patient-provider relationship, initial research in this area focused on prescribing practices of oral and maxillofacial surgeons (N=563) following third molar extraction, a common dental procedure performed at an estimated annual rate of 3.5 million.^{27,28} Results indicated that the majority (85%) of dentists almost always prescribed an opioid subsequent to extraction, most often hydrocodone with acetaminophen, with instructions to take for pain “as needed.” A subsequent statewide survey of dentists practicing in West Virginia (73% general dentists) indicated similar opioid prescribing practices following third molar extraction and reported that approximately 40% of dentists suspected that patients had leftover opioid medications at the end of treatment.^{25,29} More recently, Ashrafioun and colleagues³⁰ found that two-in-five patients sampled in their university’s dentistry patient emergency and admission services clinic reported some level of prescription opioid misuse within the past 30 days. Of note, the most recent dental practice guidelines recommend conservative use of opioid analgesics for pain management and indicate potentially greater pain management efficacy with use of nonsteroidal anti-inflammatory drugs (NSAIDs).²⁶

Existing literature indicates that although dentists regularly encounter patients with problematic substance use and recognize the importance of screening for substance abuse,³¹ they have limited exposure to addictions training and generally lack systems to aid in screening, intervention, and referral to addictions treatment.³² Germane to opioid misuse, the dearth of data available suggest that dentists do not regularly implement risk mitigation strategies - such as using their state’s prescription drug monitoring program and providing patient education - when prescribing an opioid analgesic.^{33,34} In fact, results from a National Dental Practice-Based Research Network (National Network) Quick Poll, conducted in October 2014,^{35,36} indicated the relevance of and need for training in opioid prescribing risk mitigation strategies. Four of five respondents (80%; n=429) reported monthly opioid prescribing. Among these dentists, the majority (75%) reported misuse concerns for some of their patients and fewer than one-in-ten dentists reported *no concerns* of misuse, abuse or diversion by their patients receiving opioids. Notably, one-in-six dentists (16%) reported concerns of misuse or diversion among half or more of their patients receiving opioids. In spite of these concerns regarding potential patient misuse of opioids, more than half of respondents (52%) reported never using their state’s drug monitoring program and many respondents (25%) did not know that such a resource was available to them. Further, although one-in-ten respondents reported ‘always’ providing education and an additional 12% reported ‘often’ providing education, education was not a regular part of practice for the majority (64%) of respondents.

2.2 Rationale

An expert panel convened by the Tufts Health Care Institute Program on Opioid Risk Management²⁵ highlighted the need for additional research to better understand: (1) practice patterns for pain management and analgesic use among dentists and specialists; (2) dentists’ perceptions of risk and safety of immediate release opioids and awareness of prescription opioid diversion problem; and (3) current practices regarding patient education and use of other risk mitigation strategies to reduce prescription opioid misuse and diversion. To this end, the

current study proposes to conduct a national survey of dental prescribing practices through the National Network. Results of this survey will speak directly to aforementioned gaps in knowledge and could inform the development of an educational intervention that provides dentists training in opioid misuse screening, and implementation of risk mitigation strategies when prescribing opioids for acute pain management.

2.3 Potential Risks and Benefits

This study consists of a cross-sectional, single time point self-report assessment of dental providers. The study (survey) will be applicable to National Network dentists only and will not include patient recruitment. National Network member dentists, both generalist and specialist, who are eligible to participate in Network surveys will be invited to participate without exclusion based on race, ethnicity, or age.

2.3.1 Potential Risks

This study poses minimal risk to subjects. Study participation is completely voluntary and participants may discontinue participation at any time without prejudice. As with any study, there is the potential for loss of confidentiality. Appropriate precautions will be taken to mitigate this risk. These include the use of unique study codes for participants and password-protected computers and secure networks for data storage. Compliance with all Institutional Review Board (IRB) regulations concerning data collection, data storage, and data destruction will be strictly observed. Data will only be accessible to research personnel and will be stored and coded according to guidelines set forth by the overseeing IRB.

2.3.2 Potential Benefits

Participating dentists have the potential to directly benefit from their reflection on their own knowledge of risk mitigation strategies in opioid prescribing as they respond to items on the questionnaire. As an indirect benefit to participation, knowledge obtained from the survey has the potential to guide content development for an educational intervention targeting risk mitigation strategies for opioid prescribing in the dental setting. This survey is intended to provide information regarding existing clinical practices pertinent to addictions screening and opioid prescribing in the dental setting. This data will be combined with information from a state (South Carolina) prescription drug monitoring program regarding prescribing volume, frequencies, and patient characteristics to inform the development of dental provider education intervention.

3 OBJECTIVES

3.1 Study Objectives

3.1.1 Primary Objective

The primary objective of this study is to conduct a national survey of dentists to assess knowledge and behavior related to opioid prescribing practices. Based on previous research and preliminary results of our statewide pilot of the current survey, we postulate that dentists will demonstrate significant knowledge gaps regarding: (1) prescription opioid diversion and abuse; (2) recommended prescribing practices, including risk mitigation strategies; and (3) more broad assessment of addictions. We further postulate that gaps in knowledge will be associated with higher rates of reported opioid prescribing and lower utilization of risk mitigation strategies.

3.1.2 Secondary Objectives

The secondary objectives of this study are to:

- Identify practitioner-level and practice-level facilitators of conservative opioid prescribing practices, and
- Identify practitioner-level and practice-level facilitators of consistent implementation of opioid prescribing risk mitigation strategies (i.e., drug monitoring program use and provision of patient education).

3.2 Study Outcome Measures

3.2.1 Primary Outcomes

To assess knowledge and behavior related to opioid prescribing practices, the online Survey instrument (see *Appendix A*) will ascertain the following primary outcome measures: (1) pain management strategies used in practice and frequency of their use; (2) opioid prescribing behaviors; (3) situations/procedures eliciting opioid prescribing in the dental setting; (4) training and continuing education relevant to addictions; (5) opinions/current use of opioid risk mitigation strategies/universal precautions; (6) familiarity with, use and perceived utility of state's prescription drug monitoring program (when available); and (7) effects of prescription drug monitoring program use on practice. All data will be self-reported by consenting, participating dental practitioners.

3.2.2 Secondary Outcomes

The survey data will be merged with coded National Network enrollment data. Data will include basic practice information and practitioner demographics provided in the National Network Enrollment data (see *Appendix B*).

To identify practitioner-level and practice-level facilitators of: a) conservative opioid prescribing practices (defined by this study as responses of "None" or "Few" to survey questions 3C and 3D, See survey in Appendix A), and b) consistent implementation of opioid prescribing risk mitigation strategies (defined as "Always/Almost Always" response on survey questions 17-22 and 25A-25D), merged data from the practitioner survey and enrollment questionnaire will be evaluated.

4 STUDY DESIGN

Questionnaire recruiting approximately 1,428 dentists. To be eligible for this study, dentists must be enrolled in the National Dental PBRN and have completed an Enrollment Questionnaire.

This survey questionnaire is a cross-sectional study that is limited to dentist members who are currently practicing. A total of approximately 1,428 dentists will be invited to participate. For the purposes of sample selection, specialists more likely to regularly prescribe opioids will be oversampled to ensure adequate representation. All National Network members endorsing a specialty practice in Endodontics, Periodontics, Prosthodontics, Dental Public Health, or Oral/Maxillofacial Surgery will be invited to participate (N~409). A random selection of ~1019 remaining general dentists will also be invited to participate. Westat will be responsible for randomly selecting general dentists from within each Network region, according to quotas presented in Section 11.2 (*See Section 11.2 for a recruitment breakdown by Network Region*). Network regional quotas will help to ensure that each region has adequate representation within the survey. Dentists with a specialty practice **only** in Orthodontics, Oral Pathology, or Pediatrics will **not** be invited to participate, as opioid prescribing is not typically involved in the routine practice of these specialties.

Participation involves the completion of the provider prescribing practices survey. Dentists will complete the questionnaire online through the REDCap survey management system. Based on previous survey research within the Network, we anticipate a 70% completion rate, resulting in approximately 1,000 completed practitioner surveys.

Westat Coordinating Center (CC) will be responsible for providing the SPI with a list of ~1,428 member dentists (based on inclusion/exclusion criteria) for participation. The National Dental PBRN/CC will provide the SPI with contact information (including active email addresses) for dentists randomly selected for participation, as well as key selected Enrollment Questionnaire data (see *Appendix B*) in two separate databases, linked with unique participant IDs. Dentists selected for recruitment will be invited via email. The provider survey data will be collected via an online survey instrument housed in the MUSC REDCap survey management system. The REDCap system allows the SPI to monitor which participants have accessed and completed the survey. Only the SPI and study team members will have access to survey data. Upon completion and close of the survey, the SPI will merge provider survey data with Enrollment Questionnaire data. All survey data and linked enrollment data will be coded in this final merged dataset; to enhance confidentiality, participant responses will be stored using unique participant IDs. The SPI will separately store a document linking participant contact information with unique participant IDs in a password-protected file.

Approximately 50 dentists who complete the online survey will be invited to complete the online survey again (approximately 2 weeks post initial completion) for test-retest reliability purposes.

Development and administration of the questionnaire is detailed in *Section 7*.

5 STUDY ENROLLMENT AND WITHDRAWAL

5.1 Inclusion Criteria

A participant must meet all of the following criteria:

- Is enrolled in the National Dental PBRN as limited or full network member;
- Has completed an Enrollment Questionnaire;
- Is a dentist licensed in the U.S. to treat patients, treats patients in the U.S. on a recurring basis and maintains an active practice email address at which he or she can be contacted; and
- Endorses practicing primarily in a General Dentistry, Endodontic, Periodontic, Dental Public Health, Prosthodontic, or Oral/Maxillofacial Surgery setting.

5.2 Exclusion Criteria

A dentist practitioner meeting the following criteria will be excluded from the study:

- Does not have an email address provided in their Enrollment Questionnaire data; and
- Endorses specialty practice *ONLY* in Orthodontics, Oral Pathology, or Pediatric Dentistry.

5.3 Strategies for Recruitment and Retention

Eligible dentists will be identified based on the criteria noted from their responses on the Enrollment Questionnaire. All eligible dentists will first receive a study invitation email from the SPI explaining the study and inviting them to participate in the study. The invitation will include a unique link to the electronic version of the questionnaire and will clearly state the recommended timeframe for survey completion - single sitting. Based on prior Network survey study response rates, we anticipate a response rate of approximately 70%. Non-responding dentists will be sent 2 additional reminder emails prior to initiation of reminder contact by their designated Regional Coordinators (RCs). Recruited participants who have not responded by week 3 will receive their third reminder email from their designated RC. Recruited participants who have not responded by week 4 (after 3 total reminder emails) will receive reminder contacts (e.g., phone, fax, email, postal mailing, etc.) from their respective RCs to prompt participation coupled with a reminder of their unique survey link. Recruited dentists who have not responded within 10 weeks will be considered non-responders, and their survey links will be deactivated. To reduce time burden on the RCs, dentists will be recruited in 3 waves, detailed in *Section 6.1*. In order to minimize access to survey response data, the SPI will communicate with RCs regarding Non-Responders through the use of password protected excel spreadsheets that do not contain survey response data. The SPI will deliver updated completion reports to RCs on a regular basis to minimize unnecessary contact with invited participants who have already completed the survey. In addition, the SPI will hold regular (at least monthly) Study Team calls to troubleshoot any issues that may arise with study recruitment efforts.

Dentists completing the survey will be remunerated with \$50 gift codes delivered via email to their active email addresses. This is a cross-sectional questionnaire study; retention strategies are not applicable. However, a subsample of 50 participating dentists will be invited to complete the survey at Time 2 to establish test-retest reliability. Dentists completing the survey at Time 2 will be compensated an additional \$50 for their participation.

5.4 Practitioner Withdrawal

5.4.1 *Reasons for Withdrawal*

Dentists are free to withdraw from participation in the study at any time upon request.

5.4.2 *Handling of Practitioner and Patient Withdrawals*

Dentists who withdraw from the study will not be replaced. Dentists who withdraw participation prior to completion of the survey will not receive remuneration.

5.5 Premature Termination or Suspension of Study

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party. If the study is prematurely terminated or suspended, the SPI will promptly inform the Institutional Review Board (IRB) and will provide the reason(s) for suspension or termination. Circumstances that may warrant termination include, but are not limited to:

- Insufficient adherence to protocol requirements.
- Data that is not sufficiently complete and/or evaluable.
- Determination of unexpected, significant, or unacceptable risk to study participants.
- Determination of futility.

6 STUDY SCHEDULE

6.1 Stage 1 Survey Component: Enrollment/Baseline

- Eligible dentists will be identified from responses to National Dental PBRN Enrollment Questionnaire by Westat, will be randomly selected for participation based on inclusion/exclusion criteria, and Westat will deliver contact information and selected Enrollment Questionnaire data to the SPI.
- Over a period of 14 weeks, dentists will be invited to complete an online questionnaire.
- Completion of the questionnaire will indicate that practitioners have read informed consent information and will imply consent. A waiver of signed consent will be sought from the IRB.

6.2 Stage 2 Retest of the Survey

- Dentists participating in Waves 1 and 2 will be sent a second online questionnaire request by email approximately 2 weeks after the receipt of their first completed questionnaire.
- Dentists will be informed that they have one week to respond to the invitation for retest. If a selected retest participant has not completed their retest within the one week timeframe, a new potential retest participant will be selected from those having already completed Time 1 survey questionnaire until a total of approximately 25 retests have been completed by Wave 1 and Wave 2 participants.
- Completion of the retest questionnaire will indicate tacit consent.
- In Week 6, the aforementioned process will repeat among Wave 3 (n~25) recruited dentists, for a total of N~50 test-retest participants.

6.3 Stage 3 Merging Practitioner Survey with Enrollment Questionnaire

- Survey and enrollment data will be linked using participant IDs.
- Contact information will be removed from the final merged dataset and data will be stored/saved using Unique Participant IDs.

7 STUDY PROCEDURES/EVALUATIONS

Practitioner Questionnaire Development

The initial draft of this survey instrument was developed with feedback from the initial study team (including a periodontal practitioner and dental researcher). Items were modeled after previously published surveys of opioid prescribing practices among primary care physicians.¹⁶ This initial draft of the survey instrument was reviewed by a focus group of dental providers (n=10) who provided critical feedback regarding the content, clarity, and presentation of the survey. The finalized survey instrument was then piloted in its current online format using REDCap electronic data capture tool³⁷ for data collection and management. Dental practitioners (n=87) were recruited for the survey pilot through a single Listserv announcement disseminated by the South Carolina Dental Association. Following the statewide pilot, content of the survey was iteratively refined through a series of feedback from the National Dental PBRN Executive Committee, the NIDCR Clinical Studies Group, and the National Dental PBRN RCs. This iterative development and pilot process has maximized dental practitioner input in an effort to increase the relevance of the survey and its findings to dentists.

Questionnaire Testing-Retesting

The online version of the questionnaire will be administered twice to a subset of approximately 50 dentists to assess the test-retest reliability of the questionnaire. Dentists who complete the online version of the initial questionnaire will be sent a second online questionnaire request by email approximately two weeks after receipt of the first completed questionnaire.

Retest participants will be randomly selected from among those participants who have completed the survey within the first two weeks of their survey launch. Approximately two weeks following the launch of Wave 2, dentists completing their initial survey participation will be entered into a randomizer application (randomizer.org). Once randomly ordered, the first listed ~25 dentists will be selected for invitation to the retest. Each dentist will be given approximately one week to complete the retest. If the retest is not completed within the timeframe, the link to the retest questionnaire will be disabled and the next dentist on the randomized list will be contacted. This process will be continued until 25 dentists complete the retest. The questionnaire will take up to 30 minutes to complete each time. The entire process will then be repeated approximately two weeks following the launch of the survey to Wave 3 participants until a total of ~50 participants have completed the retest.

Website and Questionnaire Pilot Testing

The SPI and Study team will perform extensive internal testing of the REDCap survey, including internet browser compatibility. Study team members (e.g., SPI, Drs. Brady and Fillingim) will also externally test the website prior to administration with study participants.

Questionnaire Content

Topical areas addressed in the survey are detailed in Section 3. Some information will be collected from the National Dental PBRN Enrollment Questionnaire (e.g., demographics and practice characteristics) and will be linked to participants' responses to the study questionnaire. The survey questionnaire is included in full in Appendix A. Enrollment data is outlined in Appendix B.

Questionnaire Administration

The questionnaire will be administered by the SPI. An initial study invitation will be sent to eligible dentists via email. The invitation will include information regarding the study and will contain a unique participation link to the survey. Dentists will be informed that the questionnaire would ideally be completed in one-sitting and that it will take up to 30 minutes to complete. However, should participants need multiple sittings to complete the survey, they will be able to do this using the "Save & Return Later" feature within the REDCap survey. Should participants decide to "Save & Return Later," a Return Code is provided to participants by the REDCap system. Dentists re-access the survey using the same unique survey link and will need to enter their Return Code to verify their identity and gain re-entry to their survey. Should dentists lose or misplace their Return Code, they will need to contact the SPI or their designated RC to receive a Return Code reminder. Dentists will receive three email reminders to complete the questionnaire. Those who do not respond to email invitations will be contacted through multiple methods by their respective RCs regarding their interest in study participation.

Dentists will be encouraged to visit the secure web site to complete the questionnaire. If no feedback is received or the dentist does not complete the electronic questionnaire after multiple follow up attempts over a period of 10 weeks post-invitation, it will be assumed the dentist is not interested in the study. (See Schematic of Study Design).

8 ASSESSMENT OF SAFETY

8.1 Specification of Safety Parameters

Safety monitoring for this study will focus on unanticipated problems (UP) involving risks to participants, including unanticipated problems that meet the definition of a serious adverse event (SAE).

8.1.1 Unanticipated Problems

The Office for Human Research Protections (OHRP) considers UPs involving risks to patients or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the patient population being studied;
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places patients or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.2 Reporting Procedures

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. OHRP recommends that investigators include the following information when reporting an adverse event (AE), or any other incident, experience, or outcome as an UP to the IRB:

- Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- A detailed description of the AE, incident, experience, or outcome;
- An explanation of the basis for determining that the AE, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs will be reported to the IRB and to NIDCR within 2 weeks of the SPI becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the SPI.

All UPs will be reported to NIDCR's centralized reporting system via Rho Product Safety:

- Product Safety Fax Line (US): 1-888-746-3293

- Product Safety Fax Line (International): 919-287-3998
- Product Safety Email: rho_productsafety@rhoworld.com

General questions about SAE reporting can be directed to the Rho Product Safety Help Line (available 8:00AM – 5:00PM Eastern Time):

- US: 1-888-746-7231
- International: 919-595-6486

9 STUDY OVERSIGHT

The GPI and SPI will be responsible for study oversight, including monitoring safety, ensuring that the study is conducted according to the protocol and ensuring data integrity. The SPI will review the survey data for safety concerns and data trends at regular (weekly) intervals, and will promptly report to the IRB and NIDCR any UP, protocol deviation, or any other significant event that arises during the conduct of the study.

10 CLINICAL SITE MONITORING

Clinical site monitoring will not occur for this survey study. The SPI is responsible for launching the survey and collecting data received as part of the survey. The SPI will ensure that the quality and integrity of study data and data collection are maintained. The RCs will be responsible for following up with eligible dentists who are considered non-respondents (see *Section 5.3*) to encourage study participation.

NIDCR reserves the right to conduct independent audits as necessary.

11 STATISTICAL CONSIDERATIONS

11.1 Study Hypotheses

The primary objective of this study is to conduct a national survey of dentists to assess knowledge and behavior related to opioid prescribing practices. Based on previous research and preliminary results of our statewide pilot of the current survey, we postulate that dentists will demonstrate significant knowledge gaps regarding: (1) prescription opioid diversion and abuse; (2) recommended prescribing practices, including risk mitigation strategies; and (3) more broad assessment of addictions. We further postulate that gaps in knowledge will be associated with higher rates of reported opioid prescribing and lower utilization of risk mitigation strategies.

The secondary objectives of this study are to:

- Identify practitioner-level and practice-level facilitators of conservative opioid prescribing practice.
- Identify practitioner-level and practice-level facilitators of consistent implementation of opioid prescribing risk mitigation strategies (i.e., drug monitoring program use and provision of patient education).

11.2 Sample Size Considerations

All objectives of the current study are either descriptive or exploratory - rather than hypothesis testing - in nature. Therefore, standard sample size calculations based on anticipated effect sizes do not apply. Instead, sample size was selected to ensure adequate representation of both general and specialist dentists in each National Dental PBRN region. All specialists in a given region will be invited to participate. The table below presents National Dental PBRN enrollment data for each region from August 1, 2015, as well as the number of invited participants and the anticipated number of completing participants.

REGION	GENERAL TOTAL	SPECIALIST TOTAL	GENERAL INVITED	SPECIALIST INVITED	TOTAL INVITED	GENERAL ANTICIPATED COMPLETERS	SPECIALIST ANTICIPATED COMPLETERS	TOTAL ANTICIPATED COMPLETERS
Western	387	38	156	38	194	124	12	136
Midwest	318	55	109	55	164	98	17	115
Southwest	585	96	191	96	287	173	28	201
South Central	593	70	202	70	272	170	21	191
South Atlantic	447	58	153	58	211	132	16	148
Northeast	584	92	208	92	300	180	29	209
TOTAL	2914	409	1019	409	1428	877	123	1000

*Specialists include: Endodontists, Periodontists, Prosthodontists, Dental Public Health, and Oral/maxillofacial Surgeons. ** Numbers are approximate.

11.3 Final Analysis Plan

The survey will produce quantitative, objective, and self-report data regarding prescribing practices, addictions training, as well as current knowledge and use of opioid prescribing risk mitigation strategies. Frequency distributions and descriptive statistics will be computed for all outcome variables of interest. These analyses will assist with identification of violation of assumptions of parametric statistical procedures. If violations are detected, appropriate transformations of data will be applied or alternative non-parametric procedures will be employed. Frequency distributions will also be critical in describing the sample with respect

to key outcomes delineated above. Planned contrasts (e.g., gaps in knowledge will covary with less consistent implementation of risk mitigation strategies) will be conducted with significance defined a priori as $p < .05$, controlling for Type I error inflation. Correlation matrices will also be created amongst variables of interest (e.g., provider addictions training, frequency of prescribing opioid analgesics, and use of risk mitigation strategies). When appropriate, chi-square and logistic regression analyses will be used to examine potential associates (e.g., training history, use of PDMP) of conservative opioid prescribing practices. Statistical differences in key outcome variables between National Network Quick Poll participants (Question 41) and non-participants will be assessed. 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.

Two forms of missing data will be addressed by our analysis of main outcomes. First, we anticipate some degree (approximately 30%) of *total non-response*: dentists sent a unique survey participation link who do not respond/initiate the survey within the study period for a variety reasons including refusal, non-contact, illness, death, or some other barrier preventing participation. Data missing due to total non-response will be addressed by the following approach: (1) We will describe characteristics of dentists who did not respond to the survey using data from their NDPBRN Enrollment Questionnaire; (2) We will then examine and report potential demographic (age, gender, ethnicity) and practice (specialty, practice location, primary practice setting) characteristic differences between respondents and total non-respondents; (3) If significant demographic differences emerge between respondents and non-respondents, sample-weighting adjustments will be applied to the data;³⁸ and (4) Main outcomes will be analyzed using both non-weighted and weighted datasets.

Second, we anticipate missing data due to *item non-response*: dentists participating in the survey who fail to provide acceptable responses to one or more of the survey items. Item non-response may occur as a result of a participant refusing to answer a specific item on grounds that it is too sensitive, they do not know the answer to the item, or they overlook the item by accident. Items skipped due to planned skip-logic will not be coded as missing data. In instances where the non-response rate for an item is low (<5% of respondent sample missing for given item), pairwise deletion will be applied given that the amount of potential bias in univariate and bivariate analyses for that item will be small.³⁸ Also, in instances where the non-response rate for an item is non-negligible but the missing data is deemed missing completely at random (MCAR)^{39,40}, pairwise deletion will be applied. However, in instances of non-negligible item non-response where the MCAR assumption is not valid and data are missing at random (MAR), multiple imputation procedures will be applied.^{41,42}

12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Only study personnel (i.e., NND, SPI, Co-I's, RCs, CC personnel) will have access to the study data elements in the study databases (as described below). Data for the study consist of the following: (1) Practitioner level data from the enrollment questionnaire; and (2) Practitioner responses to the electronic practitioner survey.

Enrollment Questionnaire Data. Enrollment questionnaire data will be provided to the SPI by the National Dental PBRN Coordinating Center (Westat; CC). Enrollment questionnaire data will be provided in a separate file from identifying/contact information. The contact information file and the Enrollment Questionnaire data file will be linked by the use of unique participant IDs. A file linking participant IDs with identifying information will be stored electronically in a password protected file on the MUSC secure server network. The contact information file will be used as the basis for communication of study completion status between the SPI and the RCs. Password protected recruitment logs will be shared with RCs via the secure MUSC file sharing service (Box) on a regular (approximately weekly) basis.

REDCap Practitioner Survey. Dentist participants will directly enter all practitioner survey data into the REDCap Survey Management System (SMS). REDCap survey data will be stored in a coded dataset through the use of unique participant IDs.

Survey Closeout. Following close of survey enrollment, a cleaned and completed survey dataset will be merged with dental participants' selected Enrollment Questionnaire data provided by the CC at the outset of study implementation. A final, merged, cleaned, and coded dataset will be delivered to the CC for archival following the closeout of the study. In addition, the SPI will deliver a Study Participation report to the CC documenting the completion status (e.g., complete, incomplete, refused, ineligible) of participants.

13 QUALITY CONTROL AND QUALITY ASSURANCE

For the QA/QC activities associated with data collection and processing, the SPI will develop a data management plan (DMP) in which the specific data QA/QC procedures will be provided. In the DMP, the procedures will include the development of automatic data quality checks in the SMS for the survey and the processes related to the data manual review, discrepancy management, data verification and approval, and database audit.

The SPI will ensure that the electronic surveys are being collected appropriately and confidentially and will ensure completeness of data collected. Conference calls with the Study Team (and relevant RCs) will be held at least monthly (more often if deemed necessary) during the practitioner questionnaire data collection phase to monitor recruitment progress and data completeness and troubleshoot any problems that may arise.

14 ETHICS/PROTECTION OF HUMAN SUBJECTS

14.1 Ethical Standard

The GPI, SPI, and Co-Investigators will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46.

14.2 Institutional Review Board

The UAB IRB for Human Use serves as the National Dental PBRN Central IRB and will review this protocol. If the local institution has decided to use the National Dental PBRN Central IRB review, the National Dental PBRN Central IRB is the IRB responsible for the review of the protocol. The National Dental PBRN Central IRB would then perform all future continuing protocol reviews and amendment (new protocol version) reviews. The Central IRB would also review unanticipated problems distributed by the Administrative Unit to local institution PIs.

Local institutions have the prerogative to use the National Dental PBRN Central IRB review or conduct their own local review. If an RAS or other local institution elects not to use the National Dental PBRN Central IRB, the protocol, consent form(s) or waiver if warranted, recruitment materials and all participant materials will be submitted to the RAS or other local institution IRB (Medical University of South Carolina; MUSC) for review and approval. Approval (either centrally for those regions who agree to central approval, or regionally for those who do not) of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

14.3 Informed Consent Process

A waiver of documentation of signed informed consent for practitioners who complete the electronic survey questionnaire will be requested. Consistent with regulations outlined by the National Dental PBRN Central IRB and Medical University of South Carolina (MUSC) IRB, information about the study will be provided to eligible practitioners in an initial study invitation email as well as in the electronic questionnaire prior to the start of the survey questions. Completion of the survey will provide a record of tacit consent.

14.4 Exclusion of Women, Minorities, and Children (Special Populations)

Racial and ethnic minorities invited to participate in the study at least proportional to the composition in National Network dental practitioner membership. Individuals of any gender or racial/ethnic group may participate.

14.5 Participant Confidentiality

Practitioner confidentiality is strictly held in trust by the study investigators, study staff, and the sponsor(s) and their agents. The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

Participants will be assigned a unique identification number, which will be used to maintain study records and organize data transcripts. The study monitor or other authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the study site.

15 DATA HANDLING AND RECORD KEEPING

The study team is responsible for ensuring the accuracy and completeness of the data collected, which is detailed in the DMP. Only study personnel (i.e., GPI, SPI, Co-I's, RCs, CC personnel) will have access to the study data elements in the study database as described in *Section 15.3 Types of Data*. Study personnel will include those who are on the approved IRB study protocol. All study personnel will have completed the required training elements for human subjects research certification.

15.1 Data Management Responsibilities

Data collection and accurate documentation are the responsibility of the study staff. Dentist participants will directly enter all entered data into the REDCap SMS. The MUSC data center in which the REDCap servers are housed has strict access control; only authorized core personnel may access the facility un-escorted. Only authorized users are allowed to connect to the network, and the security of the network is actively monitored. Power and environmental controls have several layers of backups, from uninterruptible power supplies to alternate and redundant feeds to the local utility company. The REDCap system administrator contributes to the maintenance of institutional disaster recovery and business continuity plans. Load balancers and a highly fault tolerant SAN infrastructure contribute to high availability. The physical security of the data center is actively monitored 24x7 by security personnel using closed-circuit video. The institution actively logs and monitors all communication to the application server (multiple firewall layers prevent direct external communication to the database server), and the system owner is alerted to any unusual activity. If warranted, the institution will immediately as well as automatically ban offending IP addresses at the perimeter before they reach the application server. The application itself also rejects and bans IP addresses of anything it considers abnormal access. All transactions are securely delivered to the application using SSL (SHA-1 with RSA Encryption; 2048-bits). It is then transmitted internally (behind the firewall) to the database server. All transactions are logged at the server layer (http logging), application layer (REDCap logs activity to a database table), and the database layer (using both query and binary logging). Access to the data is managed by institutionally sponsored login IDs. All personnel must pass an employment background check before being issued an ID. Access to individual REDCap projects (and their data) is managed by the owner of the project. The REDCap system relies upon the institution's identity and access management infrastructure. Password complexity, history and expiration standards are implemented at the institutional level.

While REDCap provides the capacity to program response limiters (to prevent impossible responses, reduce typos), study personnel will review data weekly to identify impossible values, outliers, and missing data. Following close of survey enrollment, a cleaned and completed survey dataset will be merged with dental participants' selected Enrollment Questionnaire data provided by the CC at the outset of study implementation.

15.2 Data Capture Methods

The SMS will ensure that all required data are collected per protocol requirements, and edit checks will be programmed into the web survey to correct data issues in real time. The study team will ensure that data fields in the system are checked for completeness and accuracy so that data entered into the web system can be validated and data errors be corrected. Reports or

tools will be developed to help monitor the data activities. The reports with the summary of the data completeness and accuracy will be made available to the GPI, study team, and NIDCR as requested.

15.3 Types of Data

Data for the study consist of the following:

- Practitioner level data from the enrollment survey
- Practitioner responses to the electronic practitioner survey

15.4 Schedule and Content of Reports

Reports to monitor enrollment will be produced by the SPI bi-monthly and upon request and will be provided to study team, GPI, RCs, and NIDCR for review. The contents of the report will include a summary of respondents and non-respondents to date by region. Regular monitoring of responses and tracking of response patterns by region will also be communicated to RCs to assist with their communication efforts.

15.5 Study Records Retention

Study records will be maintained for at least three years from the date that the grant federal financial report (FFR) is submitted to the National Institutes of Health (NIH) or longer as dictated by local IRB or state laws/regulations.

As outlined by IRB regulations, data will be destroyed in an appropriate and safe way after three years from the date the grant FFR is submitted to the NIH. The file connecting subjects' names with their unique identification number will be kept in a password-protected file by the SPI for a minimum of three years, in accordance with IRB regulations, before being securely erased.

15.6 Protocol Deviations

A protocol deviation (PD) is any noncompliance with the clinical study protocol or good clinical practice principles. The noncompliance may be on the part of the patient, the practitioner, or study staff. As a result of deviations, corrective actions may be developed by the study staff and should be implemented promptly. All deviations from the protocol must be addressed in study patient source documents and reported to NIDCR and the local IRB, according to their requirements.

Any PD that is reportable to an IRB must also be reported to NIDCR. NIDCR defers to the IRB for reporting time-frame requirements. Once a PD has been reported to an IRB, action must be taken to report the deviation to NIDCR. If the IRB overseeing the study protocol requires annual reporting of PDs to their IRB, that reporting frequency is acceptable to NIDCR.

16 PUBLICATION POLICY

This study will comply with the [NIH Public Access Policy](#), which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive [PubMed Central](#) upon acceptance for publication. All study personnel are required to read in its entirety and agree to abide by the network's "Data Analysis, Publications, and Presentations Policies" document. The current version of this policy is always kept at the network's public web site at <http://nationaldentalpbrn.org/publication.php>.

17 LITERATURE REFERENCES

1. Kuen B.M. (2007). Opioid prescriptions soar: increase in legitimate use as well as abuse. *Journal of the American Medical Association*, 297, 249-251.
2. Volkow, N.D., McLellan, T.A., Cotto, J.H., Karithanom, M., & Weiss, S.R.B. (2011). Characteristics of opioid prescriptions in 2009. *Journal of the American Medical Association*, 305(13), 1299-1301. PMID: PMC3187622
3. Manchikanti, L., Helm, S., Fellows, B., Janata, J.W., Pampati, V., Grider, J.S., Boswell, M.V. (2012). Opioid epidemic in the United States. *Pain Physician*, 15, ES9-ES38. PMID: 22786464
4. Gudín, J. A. (2012). The changing landscape of opioid prescribing: long-acting and extended-release opioid class-wide Risk Evaluation and Mitigation Strategy. *Journal of Therapeutics and Clinical Risk Management*, 8, 209-217. doi: 10.2147/tcrm.s28764. PMID: PMC3346202
5. Substance Abuse and Mental Health Services Administration (2010). *National Survey on Drug Use and Health: National Findings*. Office of Applied Studies. Rockville, MD. Retrieved from: <http://oas.samhsa.gov/NSDUH/2k20NSDUH/tabs/Sect7peTabs1to21.pdf>.
6. Webster, L., Roller, R., Pixton, G., & Sommerville, K. (2011). Oxycodone HCl/niacin tablets may reduce abuse potential vs dose-equivalent oxycodone HCl in non-dependent recreational opioid users. *The Journal of Pain*, 12(4), P68.
7. Back, S.E., Payne, R.A., Simpson, A.N., & Brady, K.T. (2010). Gender and prescription opioids: Findings from the National Survey on Drug Use and Health. *Addictive Behaviors*, 35, 1001-1007. PMID: PMC2919630.
8. Bohnert, A.S., Valenstein, M., Bair, M.J., Ganoczy, D., McCarthy, J. F., Ilgen, M.A., & Blow, F.C. (2011). Association between opioid prescribing patterns and opioid overdose-related deaths. *Journal of the American Medical Association*, 305(13), 1315-1321. PMID: 21467284
9. Cicero, T.J., Inciardi, J.A., & Munoz, A. (2005). Trends in the abuse of Oxycontin and other opioidanalgesics in the United States: 2002-2004. *Journal of Pain*, 6, 662-672.
10. Cicero, T.J., Surratt, H., Inciardi, J.A., Munoz, A. (2007). Relationship between therapeutic use and abuse of opioid analgesics in rural, suburban, and urban locations in the United States. *Pharmacoepidemiology and Drug Safety*, 16(8), S27-S40.
11. Compton, W. M., & Volkow, N. D. (2006). Major increases in opioid analgesic abuse in the United States: Concerns and strategies. *Drug and Alcohol Dependence*, 81(2), 103-107.
12. Dart, R.C., Surratt, H.L., Cicero, T.J., Parrino, M.W., Severtson, G., Bucher-Bartelson, B., & Green, J.L. (2015). Trends in opioid analgesic abuse and mortality in the United States. *New England Journal of Medicine*, 372, 241-248.
13. Substance Abuse and Mental Health Services Administration, & Center for Behavioral Health Statistics and Quality (2014). Treatment Episode Data Set (TEDS): 2000-2012. National admissions to substance abuse treatment services. BHSIS Series S-71, HHS Publication No. (SMA) 14-4850. Rockville, MD: Substance Abuse and Mental Health Services Administration.
14. Back, S.E., Lawson, K.M., Singleton, L.M., & Brady, K.T. (2011). Characteristics and correlates of men and women with prescription opioid dependence. *Addictive Behaviors*, 36, 829-834. PMID: PMC3164361.
15. Paulozzi, L.J., Weisler, R.H., & Patkar, A.A. (2011). A national epidemic of unintentional prescription opioid overdose deaths: How physicians can help control it. *Journal of Clinical Psychiatry*, 72(5), 589-592. PMID: 21536000.

16. National Center on Addiction and Substance Abuse at Columbia University. (July, 2005). *Under the counter: The diversion and abuse of controlled prescription drugs in the U.S.* New York: NY.
17. Johnston, L.D., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E. (2010). Secondary School Students: 2009. Bethesda, Md.: National Institute on Drug Abuse; 2010:6. National Institutes of Health publication 10- 7584. Monitoring the Future: National Results on Drug Use, 1975-2009, Vol. 1.
18. Bedson, J., Belcher, J., Martino, O. I., Ndlovu, M., Rathod, T., Walters, K., Dunn, K.M., Jordan, K. P. (2012). The effectiveness of national guidance in changing analgesic prescribing in primary care from 2002 to 2009: An observational database study. *European Journal of Pain*. E-pub ahead of print available at: doi: 10.1002/j.1532-2149.2012.00189.x
19. Chiauzzi, E., Trudeau, K. J., Zacharoff, K., & Bond, K. (2011). Identifying primary care skills and competencies in opioid risk management. *Journal of Continuing Education for Health Professionals*, 31(4), 231-240. doi: 10.1002/chp.20135. PMID: 22189986
20. Keller, C. E., Ashrafioun, L., Neumann, A. M., Van Klein, J., Fox, C. H., & Blondell, R. D. (2012). Practices, perceptions, and concerns of primary care physicians about opioid dependence associated with the treatment of chronic pain. *Substance Abuse*, 33(2), 103-113. doi: 10.1080/08897077.2011.630944. PMID: 22489582
21. Brown, J., Setnik, B., Lee, K., Wase, L., Roland, C. L., Cleveland, J. M., Siegel, S., Katz, N. (2011). Assessment, stratification, and monitoring of the risk for prescription opioid misuse and abuse in the primary care setting. *Journal of Opioid Management*, 7(6), 467-483. PMID: 22320029
22. Food and Drug Administration. (2012). *FDA acts to reduce harm from opioid drugs.* Washington DC: U.S. Food and Drug Administration: Consumer Health Information. Retrieved from <http://www.fda.gov/ForConsumers/ConsumerUpdates>.
23. Srivastava, A., Kahan, M., & Jiwa, A. (2012). Prescription opioid use and misuse: piloting an educational strategy for rural primary care physicians. *Canadian Family Physician*, 58(4), e210-216. PMID: PMC3325473
24. Curro, F. A. (2013). FDA advisory panel assesses hydrocodone prescription writing: every dentist's responsibility. *Journal of the American Dental Association*, 144(5), 462-464.
25. Denisco, R. A., Kenna, G. A., O'Neil, G. O., Kulich, R. J., Moore, P. A., Kane, W. T., Mehta, N.R., Hersh, E.V., Katz, N. P. (2011). Prevention of prescription opioid abuse: The role of the dentist. *The Journal of the American Dental Association*, 142(7), 800-810. PMID: 21719802
26. Hersh, E. V., Kane, W. T., O'Neil, M. G., Kenna, G. A., Katz, N. P., Golubic, S., & Moore, P. A. (2011). Prescribing recommendations for the treatment of acute pain in dentistry. *Compendium of Continuing Education in Dentistry*, 32(3), 22, 24-30. PMID: 21560740
27. Moore, P.A., Nahouraii, H.S., Zovko, J.G., Wisniewski, S.R. (2006a). Dental therapeutic practice patterns in the U.S., II: analgesics, cortico- steroids, and antibiotics. *General Dentistry*, 54(3), 201-207.
28. Moore, P.A., Nahouraii, H.S., Zovko, J.G., Wisniewski, S.R. (2006b). Dental therapeutic practice patterns in the U.S., I: anesthesia and sedation. *General Dentistry*, 54(2), 92-98.
29. O'Neil, M., & Hannah, K. L. (2010). Understanding the cultures of prescription drug abuse, misuse, addiction, and diversion. *West Virginia Medical Journal*, 106(4 Spec No), 64-70. PMID: 20577279
30. Ashrafioun, L., Edwards, P. C., Bohnert, A. S., & Ilgen, M. A. (2014). Nonmedical use of pain medications in dental patients. *Am J Drug Alcohol Abuse*, 40(4), 312-316. doi: 10.3109/00952990.2014.930152
31. Ilgen, M., Edwards, P., Kleinberg, F., Bohnert, A. S., Barry, K., & Blow, F. C. (2012). The

- prevalence of substance use among patients at a dental school clinic in Michigan. *J Am Dent Assoc*, 143(8), 890-896.
32. McNeely, J., Wright, S., Matthews, A. G., Rotrosen, J., Shelley, D., Buchholz, M. P., & Curro, F. A. (2013). Substance-use screening and interventions in dental practices: survey of practice-based research network dentists regarding current practices, policies and barriers. *J Am Dent Assoc*, 144(6), 627-638.
 33. Anderson, C. (2012). Use of SCRIPTS. Presentation for the 2012 South Carolina Clinical and Translational Research/SCOSI Prescription Drug Monitoring Program Retreat. Charleston, SC.
 34. Herman, C. (2011). The Minnesota Prescription Monitoring Program. *Northwestern Dentistry*, 90(2), 33-35.
 35. McCauley, JL, Gordan VV, Riley, JL, Fillingim, RB, Makhija, SK, Brady, KT, & National Dental PBRN Collaborative Group. (2015, June). *Opioid prescribing practices of members of the National Dental Practice Based Research Network*. Accepted for presentation at the 77th annual meeting of the College on Problems of Drug Dependence (CPDD). Phoenix, AZ.
 36. McCauley, JL, Gordan VV, Riley, JL, Fillingim, RB, Makhija, SK, Brady, KT, & National Dental PBRN Collaborative Group. (Under Review, Drug and Alcohol Dependence). Opioid prescribing practices of members of the National Dental Practice Based Research Network.
 37. Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., Conde, J.G. (2009). Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, 42(2), 377-381.
 38. Brick, J.M., Kalton, G. (1996). Handling missing data in survey research. *Statistical Methods in Medical Research*, 5, 215-238.
 39. Rubin, D.B. (1976). Inference and missing data. *Biometrika*, 63, 581-592.
 40. Zarnoch, S.J., Cordell, H.K., Betz, C.J., Bergstrom, J.C. (2010). Multiple imputation: An application to income non-response in the National Survey on Recreation and the Environment. *Research Paper SRS-49*. Ashville, NC: United States Department of Agriculture Forest Service, Southern Research Station.
 41. Rubin, D.B. (1996). Multiple imputation after 18+ years. *Journal of the American Statistical Association*, 91, 473-489.
 42. Pigott, T.D. (2001). A review of methods for missing data. *Educational Research and Evaluation*, 7(4), 353-383.