

Selective *versus* Non-Selective Caries Removal in Permanent Teeth

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Study Principal Investigator: Marianne Jurasic, DMD, MPH

Institution: Boston University

NIDCR Program Official: Dena Fischer, DDS, MSD, MS

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STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Council for Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and the 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 US federal regulations and ICH guidelines.

Principal Investigator:

Signed:  Date: 2/5/2021

Name: Marianne Jurasic, DMD, MPH

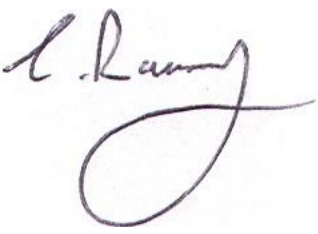
Title: Clinical Professor; Director, Center for Clinical Research

Co-Investigator:

Signed:  Date: 2/9/2021

Name: Janet Clarkson, BDS, PhD

Title: Associate Dean for Research; Co-Director, Dental Health Services Research

Co-Investigator: Signed:  Date: 2/10/2021

Name: Craig Ramsay, PGD, PhD

Title: Director, Health Services Research Unit

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LIST OF ABBREVIATIONS

ADA	American Dental Association
CFR	Code of Federal Regulations
CROMS	Clinical Research Operations and Management Support
EDC	Electronic Data Capture System
DHHS	Department of Health and Human Services
DMP	Data Management Plan
EQ	National Dental PBRN Enrollment Questionnaire
FFR	Federal Financial Report
ICCC	International Caries Consensus Collaboration
ICH	International Council for Harmonisation
IRB	Institutional Review Board
Network	National Dental Practice-Based Research Network (DPBRN)
NCC	Network Coordinating Center
NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PD	Protocol Deviation
PI	Principal Investigator
PID	Practitioner Identification Number
QA	Quality Assurance
QC	Quality Control
RCT	Randomized Clinical Trial
SCRIPT	Selective Caries Removal In Posterior Teeth
US	United States
VA	Department of Veterans Affairs

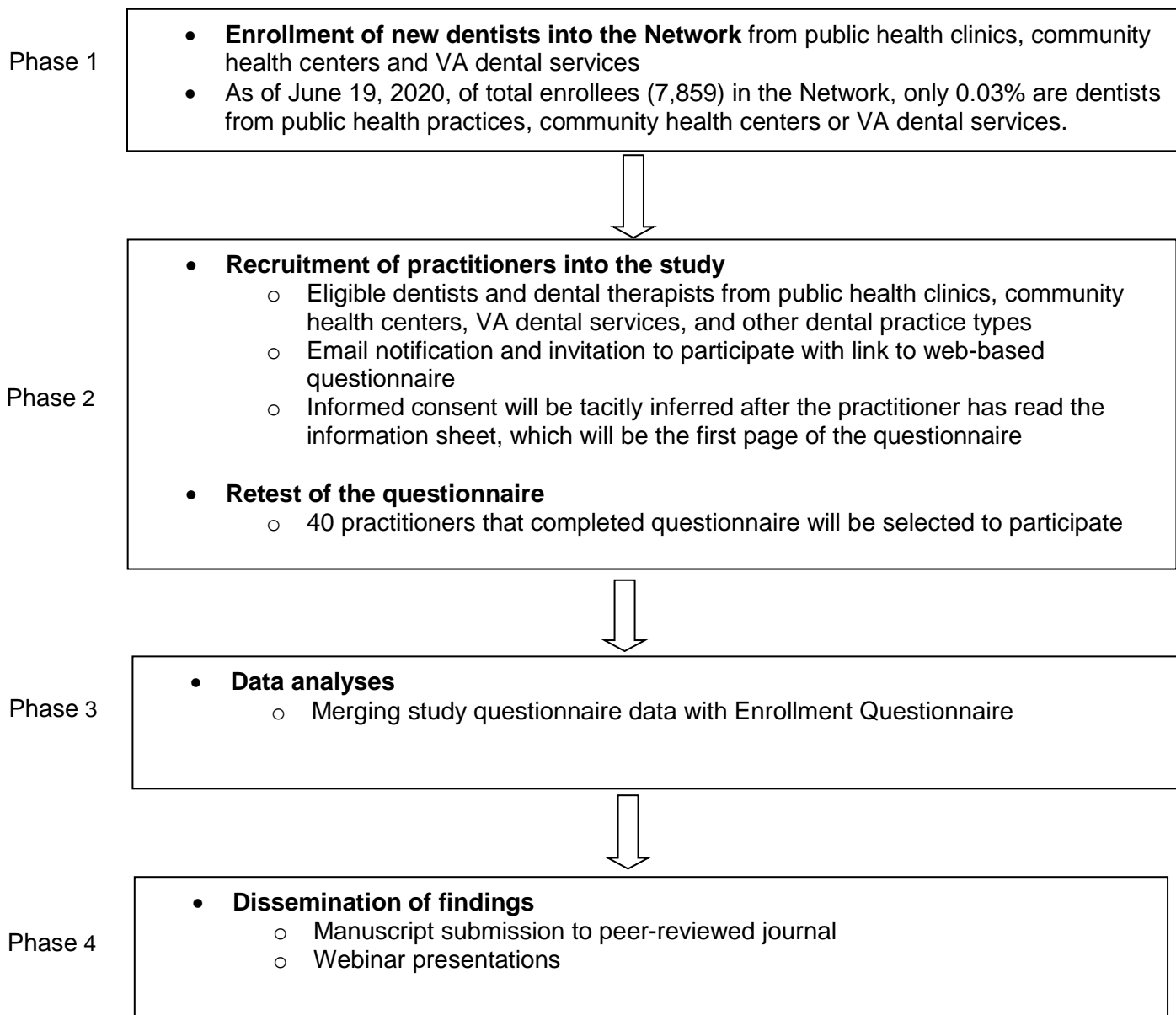
PROTOCOL SUMMARY

- Title:** Selective *versus* Non-Selective Caries Removal in Permanent Teeth
- Précis:** This study is a cross-sectional questionnaire of National Dental Practice-Based Research Network (hereafter, the Network) dentists and dental therapists practicing in public health clinics, community health centers, Department of Veterans Affairs (VA) dental services and other dental practice types, who provide some restorative dental treatment. The purpose is to obtain information regarding their treatment practices for managing deep carious lesions and to assess their ability and willingness to participate in a randomized clinical trial (RCT) evaluating deep caries removal strategies.
- Objectives and Outcome Measures:** The primary objectives are 1) to determine eligible Network dentists' and dental therapists' current use of selective caries removal; and 2) quantify the level of concordance between their reported clinical practice and published recommendations by the International Caries Consensus Collaboration (ICCC).
The secondary objectives are to determine the ability and willingness of eligible Network dentists and dental therapists to participate in a RCT evaluating outcomes of selective *versus* non-selective (complete) caries removal for deep lesions in permanent teeth (adults 18+ years).
Outcome measures will be assessed by an electronic questionnaire regarding current clinical practice when treating deep carious lesions in permanent teeth and the dentists' and dental therapists' ability and willingness to participate in an RCT evaluating outcomes of deep caries removal strategies.
- Population:** The study population will include a stratified random sample. A census of eligible Network dentists and dental therapists practicing in public health clinics, community health centers and VA dental services will be taken. A random sample of eligible Network dentists and dental therapists from other dental practice types will be invited to participate, using a randomized denominator file. A minimum sample size of 385 respondents will be obtained.
- Number of Sites:** NA
- Study Duration:** 9 months

Subject Participation Duration: One-time completion of online questionnaire (approximately 15 minutes). Approximately 40 participants will complete the online questionnaire a second time for the purposes of establishing test-retest reliability.

Estimated Time to Complete Enrollment: 3 months

Schematic of Study Design:



1 KEY ROLES AND CONTACT INFORMATION

Principal Investigator:

Marianne Jurasic, DMD, MPH
Clinical Professor
Director, Center for Clinical Research
Boston University Goldman School of Dental Medicine
560 Harrison Ave, office 327
Boston, MA 02118
Phone: 617-358-1694
Email: mjurasic@bu.edu

NIDCR Program Official:

Dena Fischer, DDS, MSD, MS
Director, Center for Clinical Research
Program Director, Clinical Trials and Practice-Based Research
National Institute of Dental and Craniofacial Research
6701 Democracy Boulevard, MSC 4878
Bethesda, MD 20892-4878
Phone: 301-594-4876
Email: dena.fischer@nih.gov

Co-Investigators:

Janet Clarkson, BDS, Ph. D
Associate Dean for Research
Co-Director, Dental Health Services Research
University of Dundee
Dundee Dental Education Centre
Frankland Building, Small's Wynd
Dundee, GBR: United Kingdom DD14HN
Phone: +44(0)1382 740990
Email: j.e.clarkson@dundee.ac.uk

Craig Ramsay, PGD, Ph. D
Director, Health Services Research Unit
The University Court of The University of Aberdeen
Health Sciences Building, Foresterhill
Aberdeen, GBR: United Kingdom AB243FX
Phone: 0044 (0) 1224 8142
Email: c.r.ramsay@abdn.ac.uk

Consultant: Pina Donaldson
Senior Trial Coordinator (FICTION, REFLECT, BRIGHT)
School of Dentistry, University of Dundee
Dundee, GBR: United Kingdom DD14HN
Phone: +44 (0) 1382 381213
Email: p.z.donaldson@dundee.ac.uk

**ARC
Director/Principal
Node
Director/South
Central Node
Director** Gregg Gilbert, DDS, MBA, FAAHD, FACD, FICD
Distinguished Professor and Chair, Department of Clinical &
Community Sciences
School of Dentistry, University of Alabama at Birmingham
1720 Second Avenue South
Birmingham, AL 35294
Phone: 205-934-5123
E-mail: ghg@uab.edu

**Principal Node
Coordinator** Deborah McEdward, BS, RDH
Research Coordinator 3
National Dental PBRN
University of Florida College of Dentistry
PO Box 100415
Gainesville, FL 32610

Phone: 352-273-5848
Email: dmcedward@dental.ufl.edu

**Network
Coordinating
Center Study
Manager/Data
Manager:**

Suzanne Gillespie, MS
Project Director
Kaiser Permanente Northwest
Center for Health Research
3800 N Interstate Avenue
Portland, OR 97227
Phone: 503-528-3977
Email: suzanne.e.gillespie@kpchr.org

Statistician:

William Vollmer, PhD
Senior Investigator Emeritus
Kaiser Permanente Northwest
Center for Health Research
3800 N Interstate Avenue
Portland, OR 97227
Email: William.Vollmer@kpchr.org

**Midwest Node
Director**

Donald B. Rindal, DDS
Health Partners
2500 Como Ave
Saint Paul, MN 55108-1460
donald.b.rindal@healthpartners.com

**Northeast Node
Director**

Cyril Meyerowitz, DDS, MS
University of Rochester Medical Center
7 Hidden Springs Drive
Pittsford, NY 14534

**South Atlantic
Node Director**

Cyril_Meyerowitz@urmc.rochester.edu
Valeria Gordan, DDS, MS, MS-CI
University of Florida College of Dentistry
PO Box 100415
Gainesville, FL 32610-0415
vgordan@dental.ufl.edu

**Southwest Node
director**

David Cochran, DDS, PhD
University of Texas Health San Antonio Dentistry
8210 Floyd Curl Drive
San Antonio, TX 78229
cochran@uthscsa.edu

**Western Node
Director**

Jeff Fellows, PhD
Kaiser Permanente Northwest Center for Health Research
3800 N Interstate Ave
Portland, OR 97227
jeffrey.fellows@kpchr.org

2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Dental caries remains a significant challenge for older Americans (1,2) and worldwide (3). The Global Burden of Disease 2015 study found a 45% increase in years lived with disability due to untreated caries in permanent teeth from 1990 to 2015 (3). Globally, untreated caries in permanent teeth ranked as the most prevalent condition evaluated (34% age-standardized), affecting 2.5 billion people (3). The expectation is that untreated caries will continue to rise in the US as the aging population increases and the edentulous rate decreases. In treating dental caries, the objective is to control disease activity and preserve hard tissue while restoring the tooth to normal form and function. Current evidence suggests that less invasive treatment should be employed, and the ICCC has published recommendations on carious lesion terminology and recommendations on carious tissue removal (4,5). These recommendations include treating cavitated carious lesions in a manner that preserves hard tissue and retains teeth long-term. The recommended priorities include preserving healthy and remineralizable tissue, achieving good restorative seal, maintaining pulpal health, and maximizing restoration success. Furthermore, the recommendations state that caries removal in shallow lesions should aim to provide a cavity able to support the final restoration, and, in deeper lesions, the priority is to maintain pulpal health (5). Specifically, teeth presenting with shallow or moderately deep cavitated carious lesions should have the carious tissue removed according to *selective removal to firm dentine*, while in deep cavitated lesions, *selective removal to soft dentine* is preferred, with more carious tissue retained selectively over the pulp (5). The FDI World Dental Federation policy on minimally invasive dentistry (2017) supports these recommendations (6). Although the American Dental Association (ADA) recently issued clinical practice guidelines on nonrestorative treatments for carious lesions (7), no clinical practice guidelines have been issued by the ADA regarding selective *versus* complete (non-selective) caries removal.

There is global disparity in the management of deep carious lesions. A survey of dentists in France, Germany and Norway found that 84% of Norwegian dentists employed the more conservative stepwise removal of dental caries from deep lesions, while the majority of French and German dentists (>66%) performed complete caries excavation, even for deep lesions (8). A nationwide survey (9) of US general dentists, pediatric dentists and endodontists showed that most endodontists (68%) and general dentists (47%) practiced complete caries removal, while pediatric dentists (31%) were more likely than both general dentists (12%) and endodontists (4%) to employ partial caries removal. A systematic review of seven randomized controlled trials comparing selective *versus* non-selective caries removal in children and adolescents found the risk of pulpal exposure significantly reduced in the selective caries removal group (OR=0.11, 95% CI: 0.04-0.30); while no significant difference in pulpal symptoms (OR=0.79, 95% CI: 0.30-2.12) and failure (technical or biological complications needing intervention) (OR=1.40, 95% CI: 0.69-2.84) was found between the two groups (10).

2.2 Rationale

Despite the current evidence that supports selective caries removal and that complete (non-selective) caries removal is no longer the standard of care (11-14), dentists are still apprehensive regarding the technique. A systematic review and meta-analysis (15) of dentists' management of deep carious lesions in permanent teeth found that approximately half of dentists rejected evidence-based carious tissue removal strategies. This review found that younger dentists and those in practice settings where professional guidelines were available tended to be more conservative when treating deep carious lesions. This study also noted that male dentists tended to be more invasive with caries removal techniques than female dentists. A recent study exploring teaching practices at US dental schools regarding carious tissue removal during cavity preparations found noticeable differences in management of deep carious lesions (16). An additional complication is that "caries remaining at cavity preparations" is a critical error on US dental licensure exams (16). It is therefore not surprising to observe the reluctance of US dentists to adopt more minimally invasive caries management procedures. A PEARL network study found US dentists tend to prefer nonselective caries removal to hard dentine even in the presence of anticipated pulpal exposure (17).

Dental caries is a preventable disease; however, it still affects large numbers of people globally (3) and in the US (1,2). Data from the US National Health and Nutrition Examination Survey 2011-2012, found that 27% of adults aged 20-64 years old had untreated tooth decay. Variation was observed according to race and ethnicity and higher rates were observed for non-Hispanic blacks (42%) and Hispanics (36%) compared to non-Hispanic whites (22%) and non-Hispanic Asians (17%) (2). Furthermore, rates of untreated dental caries among all age groups (children ages 5 to 18; adults ages 19 to 64; adults ages 65+) are highest for those with the lowest income (<100% federal poverty level) (18). According to a survey conducted by the ADA in 2015, 59% of adults indicated that they forgo dental care due to cost, 22% because they are afraid of the dentist and 19% because they cannot find a convenient location or appointment time (19).

This study is a cross-sectional questionnaire of Network dentists and dental therapists from public health clinics, community health centers, VA dental service and other dental practice types to determine their current use of selective caries removal; quantify the level of concordance between their reported clinical practice and published recommendations by the ICCC; and determine their ability and willingness to participate in a randomized clinical trial that could complement and extend the generalizability of the Selective Caries Removal In Posterior Teeth (SCRIPT) trial currently underway in the United Kingdom (20).

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

This study poses no more than minimal risk to study participants. There are no anticipated physical, psychological, social, legal, economic, or any other anticipated risks to study participants. Study participation is completely voluntary, and participants may discontinue participation at any time without penalty or negative consequences. As

with any study, there is the potential for loss of confidentiality; however, appropriate precautions will be taken to mitigate this risk. These precautions 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 study personnel and will be stored and coded according to OHRP guidelines.

2.3.2 Potential Benefits

There are no direct benefits to the dentists and dental therapists participating in this study; however, this study will contribute to generalizable knowledge concerning selective *versus* non-selective caries removal in permanent teeth. In particular, the data collected will help explore the extent to which dentists and dental therapists are following published recommendations by the ICCC regarding carious tissue removal. Furthermore, analysis of study results will be used to support the decision regarding whether to proceed with a clinical trial. If the decision is to proceed, then it will be determined whether an efficacy trial of the intervention (selective caries removal) or an implementation study should be conducted within the Network.

3 OBJECTIVES AND OUTCOME MEASURES

3.1 Primary

Objective	Brief Description/Justification of Outcome Measure	Outcome Measured By	Time Frame
<p>The primary objectives are to determine participating Network dentists' and dental therapists' current use of selective caries removal and quantify the level of concordance between their reported clinical practice and published recommendations by the ICCC.</p>	<p>Despite current evidence that supports selective caries removal as the standard of care, a recent systematic review and meta-analysis found that approximately half of dentists rejected evidence-based carious tissue removal strategies.</p> <p>Concordance with published recommendations will be assessed as choosing option 1 (remove all caries at the periphery of the cavity and stop before the pulp is exposed) as concordant with guidelines.</p>	<p>The primary outcome measures will be assessed by an electronic questionnaire regarding current clinical practice when treating deep carious lesions in permanent teeth.</p> <p>Level of concordance will be measured as percentage of time option 1 is chosen.</p>	<p>Administration of an electronic questionnaire will be used to measure this outcome.</p>

3.2 Secondary

Objective	Brief Description/Justification of Outcome Measure	Outcome Measured By	Time Frame
<p>The secondary objectives are to determine the ability and willingness of participating Network dentists and dental therapists to participate in a Randomized Clinical Trial (RCT) evaluating outcomes of selective <i>versus</i> non-selective (complete) caries removal for deep lesions in permanent teeth (adults 18+ years).</p>	<p>Currently there is a pragmatic, primary dental care, multi-center, two-arm patient randomized clinical trial underway in the United Kingdom with the aim of comparing the clinical and cost-effectiveness of selective caries removal with complete caries removal in permanent teeth (SCRIPT). An RCT conducted in the Network could complement and extend the generalizability of the SCRIPT trial.</p>	<p>The secondary outcome measures will be assessed by responses provided to an electronic questionnaire regarding the dentists' and dental therapists' ability to recruit patients with deep carious lesions extending to inner 1/3 of dentin; their willingness to participate in an RCT; and their views on outcomes that should be recorded in such a trial.</p>	<p>Administration of an electronic questionnaire will be used to measure this outcome.</p>

4 STUDY DESIGN

This study is a cross-sectional questionnaire of Network dentists and dental therapists practicing in public health clinics, community health centers, VA dental services and other dental practice types across the United States. These practice types were chosen as they are more likely to treat patients with a higher prevalence and incidence of dental caries.

The study population will include a stratified random sample. A census of eligible Network dentists and dental therapists practicing in public health clinics, community health centers and VA dental services will be taken. A random sample of eligible Network dentists and dental therapists from other dental practice types will be invited to participate, using a randomized denominator file. At the end of the first wave of recruitment the study team will review the response rate based on EQ practitioner criteria, and may refine the sampling approach for wave 2 recruitment at that time. A minimum sample size of 385 respondents will be obtained.

Eligible Network dentists and dental therapists as described in the previous paragraph will be sent an email invitation to participate in the questionnaire study. This may be done in two or more waves depending on the numbers of eligible participants and on the response rate. The questionnaire will take approximately 15 minutes to complete and will be administered using the Electronic Data Capture System (EDC) on the Network HUB website, housed at the Network Coordinating Center (NCC).

Following the launch of the questionnaire, approximately 40 of the initial survey responders will be selected to complete the electronic questionnaire again (approximately 2 weeks post initial questionnaire completion) to establish test-retest reliability.

Approximately 3 months are estimated to complete recruitment into the study to obtain the desired sample size.

5 STUDY POPULATION

5.1 Participant Inclusion Criteria

To be eligible to participate in this study, an individual must meet all of the following criteria:

- Is a current limited or full participation member of the Network (EQ Qx 7).
- Practice includes non-implant restorative dentistry (Responds occasionally or routinely to EQ Qx 21).
- Is a practicing dentist or dental therapist in the US (EQ Qx 1: response categories 1-10 or 12).
- For non-VA/CHC dentists, has verified EQ contact information on file since 1-2020 at which he or she can be contacted (EQ contact information).
- Responds to the first item of the study questionnaire that in a typical month, they treat 1 or more adult patients (18+ years) who have at least one deep carious lesion in a posterior tooth, that extends into the inner 1/3 of the dentine.

5.2 Strategies for Recruitment and Retention

Recruitment

As of mid-June 2020, 7,859 members were enrolled in the National PBRN. Of this total, 0.03% are dentists providing care in public health clinics, community health centers and VA dental services, while 45.9% are dentists providing care in other practice types. We will actively recruit new dentists and dental therapists from public health clinics, community health centers and VA dental services to join the Network as practitioners within these practice types treat patients with a higher prevalence and incidence of dental caries.

The study population will include a stratified random sample. A census of eligible Network dentists and dental therapists practicing in public health clinics, community health centers and VA dental services will be taken. A random sample of eligible Network dentists and dental therapists from other dental practice types will be invited to participate, using a randomized denominator file. A minimum sample size of 385 respondents will be obtained. Meetings will be held with Regional Node Coordinators to review recruitment issues and enrollment progress.

Compensation

Participants who wish to receive compensation and are able to accept payment will be remunerated \$50 for completing the electronic questionnaire. If participants complete the test-retest of the electronic questionnaire, they will be remunerated an additional \$50. Payment will be sent to participants following the conclusion of each of the waves of the study.

5.3 Participant Withdrawal

5.3.1 Reasons for Participant Withdrawal

Participants can choose not to participate in the study and are free to withdraw, i.e., not complete the questionnaire, at any time without penalty.

5.3.2 Handling of Participant Withdrawals

It is anticipated that participants will not be replaced since the invitation numbers are based on prior Network recruitment experience.

5.4 Premature Termination or Suspension of Study

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. The PI is responsible for promptly notifying all parties and providing the reason(s) for the termination or suspension.

Circumstances that may warrant termination include, but are not limited to:

- Insufficient adherence to protocol requirements.
- Data that are not sufficiently complete and/or evaluable.
- Determination of futility.

6 STUDY SCHEDULE

6.1 Phase 1 – Enrollment of New Practitioners into the Network

- Dentists practicing in public health clinics, community health centers, and VA dental service clinics will be encouraged to enroll into the Network.
- Dentists in these practice settings tend to treat patients with a higher prevalence and incidence of dental caries and are therefore suited to answer the study questionnaire regarding deep carious lesion treatment strategies.

6.2 Phase 2, Part A – Recruitment of Practitioners into the Study

- Eligible dentists and dental therapists will be identified from responses to the Network Enrollment Questionnaire and will be invited to participate based on inclusion criteria.
- A stratified random sample will be taken. A census of Network dentists and dental therapists practicing in public health clinics, community health centers and VA dental services will be taken. A random sample of eligible dentists and dental therapists from other dental practice types will be invited to participate, using a randomized denominator file.
- Agreement to complete the questionnaire will indicate that study participants have read the consent information, and this will imply tacit consent. A waiver of signed consent will be requested from the IRB.

Phase 2, Part B– Retest of the Questionnaire

- Dentists and dental therapists selected from among those study participants who completed the questionnaire will be emailed a second online questionnaire request approximately two weeks after the receipt of their first completed questionnaire.
- Dentists and dental therapists will be informed they have approximately two weeks to respond to the invitation to complete the retest. If the retest is not completed within the approximate two-week time frame, the link to the retest questionnaire will be disabled. A new potential retest participant will be selected from those having already completed the questionnaire until a total of approximately 40 retests have been completed.
- Completion of the retest questionnaire will indicate implied consent.

6.3 Phase 3 – Merging Study Questionnaire with Enrollment Questionnaire and Completion of Data Analyses

- Study questionnaire and Network enrollment questionnaire 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.
- Data Analyses will be completed as described in Section 11.3 Final Analysis Plan.

7 STUDY PROCEDURES/EVALUATIONS

Questionnaire Development

The study questionnaire was developed by the study team, and contains questions adapted from the United Kingdom's SCRIPT trial and previous Network studies. The questionnaire has undergone review by the NCC to ensure it is psychometrically sound and to ensure the data it collects will allow for adequate evaluation of study objectives. Further, cognitive testing of the questionnaire was completed, in which dentists reviewed their responses to a completed survey and were probed to assess possible respondent problems in understanding questions, recalling necessary information, and/or reporting accurately.

Questionnaire User Testing

The NCC will perform internal testing of the electronic study questionnaire, including internet browser compatibility. Study team members (e.g. SPI, National Network Director, Regional Directors, etc.) will be given the opportunity to externally test the website prior to administration to study participants.

Questionnaire Administration

According to the inclusion criteria, eligible participants, i.e., Network dentists and dental therapists whose practice includes non-implant restorative dentistry will be identified from their responses to the Network's enrollment questionnaire.

Consistent with regulations outlined by the University of Alabama IRB and regional/local IRBs, information about the study will be provided to all eligible participants via an information sheet/questionnaire link in the email invitation.

After the initial invitation and follow-up email reminders, the NCs will systematically contact non-responders, [and participants with incomplete information](#), by email, phone, or fax to encourage questionnaire completion. If no feedback is received or the participant does not complete the questionnaire after these follow-up attempts, it will be assumed the practitioner is not interested in the study. [Node Coordinators may also contact participants as part of data cleaning conducted by the NCC.](#)

8 ASSESSMENT OF SAFETY

8.1 Definitions of Safety Parameters

8.1.1 Unanticipated Problems

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to subjects 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 subject 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 subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.2 Specification of Safety Parameters

Safety monitoring for this study will focus on unanticipated problems involving risks to participants.

8.3 Reporting Procedures

8.3.1 Unanticipated Problem Reporting

Per Network procedures, unanticipated incidents and events will be reported to the PI. After the PI is made aware of the incident/event, the following procedures will be followed.

Incidents or events that meet the OHRP criteria for unanticipated problems require the creation and completion of an unanticipated problem report form. OHRP recommends that investigators include the following information when reporting an adverse event, or any other incident, experience, or outcome as an unanticipated problem 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 adverse event, incident, experience, or outcome;

- an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

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

- Unanticipated problems will be reported to the IRB as soon as possible but in all cases within 10 working days of the investigator becoming aware of the problem.
- All unanticipated problems 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 investigator.

All unanticipated problems will be reported to NIDCR concurrently with reporting to the IRB. These reports will be made to NIDCR's centralized reporting system via the Clinical Research Operations and Management Support (CROMS) contractor:

- Product Safety Fax Line (US): 1-888-746-3293
- Product Safety Fax Line (International): 919-287-3998
- Product Safety Email: rho_productsafety@rhoworld.com

9 STUDY OVERSIGHT

The PI will be responsible for study oversight, including monitoring safety, ensuring that the study is conducted according to the protocol and ensuring data integrity. The NCC will provide the PI with current data summaries, and the PI will review the data for safety concerns and data trends at regular intervals, and will promptly submit reportable events to the IRB and NIDCR that arise during the conduct of the study, per the IRB's reporting time-frame requirements. To ensure data integrity, the PI, NCC, and study team will adhere to data quality management processes (please see Section 13).

10 CLINICAL SITE MONITORING

No outside clinical site monitoring will be employed for this study. The NCC is responsible for launching the study and collecting data received as part of the study. Quality Assurance/Quality Control activities associated with data collection and processing will be outlined in the Data Management Plan. The NCC will ensure that the quality and integrity of the study data and data collection are maintained. The NIDCR reserves the right to conduct independent clinical site monitoring as necessary.

11 STATISTICAL CONSIDERATIONS

11.1 Study Hypotheses

This is a cross-sectional questionnaire of Network dentists and dental therapists assessing their treatment practices regarding the management of deep carious lesions. As such, formal hypothesis testing will not be conducted to achieve the study objectives.

11.2 Sample Size Considerations

The primary aim of the study is descriptive (i.e., to estimate the level of concordance with national guidelines in the sample overall as well as in selected subgroups). As such, sample size calculations are based on the precision with which we can estimate guideline concordance. To a good approximation, if W is the width of the 95% confidence interval (i.e., the confidence interval is of the form $P \pm W/2$) for an estimated proportion P based on N observations, then the N needed to achieve that width is given by

$$N = 16 * P * (1 - P) / (W^2) ,$$

where P and W are expressed on a fractional basis. Thus, a proportion of 20% corresponds to $P=0.20$, and if the width of the conf interval were 10 percentage points then W would be 0.10. For a given value of W , the formula above is symmetric about $P=0.5$ and is largest for $P=0.5$. Hence using $P=0.5$ above will give a conservative value of N that assures a width $\leq W$ regardless of the value of P .

The target N of 385 chosen for this study will enable us to estimate proportions for the population as a whole with a precision (95% confidence interval) of no greater than ± 5 percentage points, ± 7.1 percentage points for subgroups of size $N/2$, ± 8.7 percentage points for subgroups of size $N/3$, and ± 10 percentage points for subgroups of size $N/4$.

11.3 Final Analysis Plan

Primary Objective: Determine the extent to which, for permanent posterior teeth with deep occlusal caries extending to the inner 1/3 of dentin, Network dentists and dental therapists use caries removal strategies that are in concordance with the recommendations of the ICCC.

The primary analysis will be descriptive in nature. The source data for this analysis will be the proportion of the time dentists and dental therapists say they remove all caries at the periphery of the cavity and stop before the pulp is exposed (“selective caries removal”), which will be assessed separately for patients with symptomatic caries and for patients with asymptomatic caries. For each of these two subgroups, we will describe this as a continuous measure using either means and standard deviations (SD) or, if the data are markedly skewed, medians and interquartile ranges.

We will also calculate the percentage of dentists who are “concordant” with guidelines by dichotomizing this measure. Since there is no universally agreed upon definition for how to define concordance based on such data, we plan to use a variety of cut points to document the extent to which concordance varies with the choice of threshold used to define concordance. These cut points will range from a high of selective caries removal 75% of the time, which we feel is a reasonable measure of good concordance, to a low of selective caries removal 25% of the time to allow for comparison with some previous reports in the literature (15,21,22).

As a secondary analysis, we will use logistic regression analysis to determine the extent to which concordance varies according to selected provider characteristics. For the purposes of this analysis, we will define concordance using our upper end threshold of selective caries removal 75% of the time. We will initially look at all candidate variables in a univariate manner and will use those significant based on these analyses to conduct a reverse stepwise multiple logistic regression analysis. As before, separate analyses will be done for patients with symptomatic caries and for patients with asymptomatic caries.

An additional secondary analysis related to this objective will be to assess the relative importance of various factors when making clinical decisions about management of deep carious lesions. Each factor will be graded on a 5-point Likert scale and simple descriptive statistics will be used to summarize the information.

Secondary Objective: Determine the ability and willingness of Network dentists and dental therapists to participate in a randomized clinical trial evaluating outcomes of selective *versus* non-selective (complete) caries removal for deep lesions in permanent teeth in adults (18+ years).

Simple descriptive statistics will be computed as appropriate for data collected from the study questionnaire. The decision whether a clinical trial is warranted will be determined by the proportion of dentists willing to participate in a clinical trial; their ability to recruit the eligible patients for the trial; and their current use of selective caries removal. The thresholds for the decision whether to proceed with a clinical trial are still to be determined.

Missing data. Data from incomplete questionnaires may be included in data analyses. Depending on the extent of missing data and available resources for analyses, the study team may consider statistically appropriate methods for imputing missing information.

12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Source data/documents will be maintained by the NCC for this study. The NCC will program the electronic questionnaire into their EDC. Participants will be sent an email invitation with a direct link to the electronic questionnaire. After completion of the electronic questionnaire, data will be available through the EDC.

Only study personnel (i.e. NCC, PI and designated study team members) will have access to the data. All research computers and associated study documents will be password-protected and maintained in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of subjects. Study staff will permit authorized representatives of NIDCR and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity.

The source documents for this study are:

- Electronic study questionnaire administered through the NCC EDC on the HUB website
- Data collected in the Network Enrollment Questionnaire

13 QUALITY CONTROL AND QUALITY ASSURANCE

For the Quality Control (QC) and Quality Assurance (QA) activities associated with data collection and processing, the NCC will develop a Data Management Plan in which the specific data QC/QA procedures will be provided. These procedures will include the development of automatic data quality checks in the EDC for the questionnaire and the processes related to data accuracy and completeness. The EDC will be programmed with edit checks and response limiters to reduce data response errors.

14 ETHICS/PROTECTION OF HUMAN SUBJECTS

14.1 Ethical Standard

The PI 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 and/or the ICH E6.

14.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials and all participant materials will be submitted to the Network's Central Institutional Review Board (IRB) for review and approval. The UAB IRB for Human Use serves as the Network's Central IRB. Approval of both the protocol and the consent form(s) 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.

For those study investigators requiring IRB approval by their institutions, the study institution PI will submit for IRB approval and provide the Central IRB with the appropriate approved IRB documents.

14.3 Informed Consent Process

The standard waiver of documentation of signed informed consent for internet-based surveys will be requested for this study. Consistent with regulations outlined by the Central IRB, informed consent language will be provided on the entry page to the questionnaire and will indicate that consent is provided if the respondent chooses to enter the questionnaire via the link they have been provided (tacit consent).

14.4 Exclusion of Women, Minorities, and Specific Age Groups

Network dentists and dental therapists of any age, sex/gender or racial/ethnic group may participate if they meet the eligibility criteria.

14.5 Participant Confidentiality

Participant confidentiality is strictly held in trust by the investigators, study staff, and the study sponsor 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 study sponsor.

Practitioners' pre-assigned identification numbers (PIDs) (practitioner IDs assigned by the Network) will be used to maintain study records and organize data files. A file linking participants' names with their unique identification number will be kept in a password-protected file by the NCC.

The study monitor or other authorized representatives of the NIDCR may inspect all study documents and records required to be maintained by the investigator.

The National Program Manager, who will be responsible for ensuring Network dentists completing the questionnaire are remunerated \$50, will be provided the minimum information necessary from the questionnaire to fulfill the responsibility of appropriately directing practitioner payments to their desired address.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical, or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (<https://humansubjects.nih.gov/coc/index>). As set forth in [45 CFR Part 75.303\(a\)](#) and [NIHGPS Chapter 8.3](#), recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

Confidentiality of Data Sharing

As described in section 16, it is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see <https://grants.nih.gov/policy/sharing.htm>). PIs and funding recipient institutions will ensure that all mechanisms used to share data include proper plans and safeguards to protect the rights and privacy of individuals who participate in NIH-sponsored research.

15 DATA HANDLING AND RECORD KEEPING

The study team is responsible for ensuring the accuracy and completeness of the data reported, and for following the data collection procedures as outlined in the DMP. Access to study data will be provided to study team members by NCC staff.

15.1 Data Management Responsibilities

The PI will work closely with the NCC to ensure that the electronic surveys are collected appropriately and completely, and that confidentiality is being maintained according to protocol-specified procedures. Conference calls will be held approximately every month during the data collection phase to monitor progress, manage study documentation and procedures, and troubleshoot any problems.

The NCC will develop and maintain an EDC system including the study questionnaire. The DMP will include details on the EDC and procedures that will be followed to launch and monitor the study. The data reported in the Network's Practitioner Database will be used by the NCC to identify eligible dentists for this study.

15.2 Data Capture Methods

Data from the electronic questionnaire will be captured using REDCap forms in the EDC. The NCC will conduct preliminary testing and review of data fields in the initial programming and online launch of the questionnaire. The NCC will ensure that all required data are collected per protocol requirements and edit checks will be programmed in the web questionnaire 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 data entered in the EDC can be validated and data errors corrected in real time. Reports or tools will be developed to help monitor the data capture activities. The reports with the summary of data completeness and accuracy will be made available to the study team and NIDCR as requested.

15.3 Schedule and Content of Reports

Ongoing reports to monitor enrollment will be produced approximately monthly, or more frequently if desired, for study team and NIDCR review. The contents of the reports will include the summary of data collected and can be developed in separate sections by key characteristics or regions.

Final data analysis reports that address objectives of the study will be produced by the NCC for review by the study team and NIDCR. The content of these reports will be determined by the study team and the NCC and defined in the Statistical Analysis Standard Operating Procedure.

The procedure for locking the database prior to final analysis will be detailed in the study Data Management Plan. Briefly, the EDC data will be locked and final study datasets will be generated at the end of the study. Prior to locking the database, the NCC's Data Manager (DM) or designee will ensure all data are complete and clean as

determined by the study team. Then, the DM will obtain approval from the PI to proceed with the data lock.

No masking or coding is anticipated for this study.

15.4 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 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. The file connecting subjects' names with their unique identification number will be kept in a password-protected file by the NCC and PI, in accordance with IRB regulations, before being securely erased on agreement by the ARC Director, the NCC Director and the PI.

15.5 Protocol Deviations

A protocol deviation (PD) is any change, divergence, or departure from the study procedures described in the IRB-approved clinical study protocol. The deviation may be on the part of the participant, the investigator, or study staff.

Consistent with the investigator obligations in the ICH E6 Guideline for Good Clinical Practice, the PI will document in study source documents and explain any deviation from the IRB-approved protocol. The PI will report to the IRB any deviations or changes made to eliminate immediate hazards to participants and any changes that increase risk to participants and/or significantly affect the conduct of the study.

Protocol deviations will be assessed for their impact on safety, study operations, and data integrity. Appropriate corrective and preventive actions will be implemented if warranted.

16 PUBLICATION/DATA SHARING POLICY

This study will comply with all applicable NIH Data Sharing Policies. See <https://grants.nih.gov/policy/sharing.htm> for policies and resources.

NIH Public Access Policy

The NIH *Public Access Policy* requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to *PubMed Central* immediately upon acceptance for publication. This ensures that the public has access to the published results of NIH funded research.

The Network's "National Dental PBRN Publications, and Presentations Policy" document is available at the network's public web site at <https://www.nationaldentalpbrn.org/publications/> .

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