A Clinic Randomized Trial of Clinical Decision Support System to Improve Dental Provider Delivery of Brief Tobacco Interventions and Quitline Referrals

NIDCR Grant Number: U01 DE026135

Protocol Number: 16-069-E

Principal Investigators:
D Brad Rindal, DDS and Heiko Spallek, DMD, PhD, MSBA

NIDCR Program Official: Melissa Riddle, PhD

NIDCR Medical Monitor: Kevin McBryde MD

Draft or Version Number: 9.0

12 January 2021

STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Conference on Harmonization 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 trial 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 Investigators:

Signed:  Date: 1/25/2021

Name: **D. Brad Rindal, DDS**

Title: Co-Principal Investigator

Signed:  Date: 1/29/2021

Name: **Heiko Spallek, DMD, PhD, MSBA**

Title: Co-Principal Investigator

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Acronym or Abbreviation	Term
5As	Ask, Advise, Assess, Assist, Arrange
AE	Adverse Event/Adverse Experience
AHRQ	Agency for Healthcare Research & Quality
BI	Brief intervention
CDS	Clinical Decision Support
CE	Continuing Education
CFR	Code of Federal Regulations
CI	Contextual Inquiry
DH	Dental Hygiene (e.g., DH students, DH clinics)
DHHS	Department of Health and Human Services
DTA	Data Transfer Agreement
DUA	Data Use Agreement
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
HIT	Health Information Technology
HITECH	Health Information Technology for Economic and Clinical Health Act
HPI	HealthPartners Institute
IOM	Institute of Medicine
IRB	Institutional Review Board
NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
PBRN	Practice-Based Research Network
predoc	Predoctoral (e.g., predoc students, predoc clinics)
REDCap	Research Electronic Data Capture
RT	Referral to treatment
SBIRT	Screening, Brief Intervention, Referral to Treatment
SRC	Survey Research Center
TDQ	Theoretical Domain Questionnaire
US	United States

PROTOCOL SUMMARY

Title:

A Clinic-Randomized Trial of a Clinical Decision Support System to Improve Dental Provider Delivery of Brief Tobacco Interventions and Quitline Referrals

Précis:

Use of clinical decision support (CDS) within electronic health record systems (EHR) holds much potential to improve the translation of current scientific evidence into clinical practice and improve the delivery of optimal, evidence-based, personalized treatment. Health care providers have access to evidence-based guidelines that help patients quit smoking. Translation of that knowledge and awareness into daily practice, however, remains low.

This clinic-randomized trial will examine the rate at which dental providers deliver a smoking intervention and refer to a quitline when their EHR system includes health information technology (HIT)-driven CDS compared with providers in control clinics without assistance from the CDS. Providers include experienced dentists, dental therapists, and dental hygienists in private practices and predoctoral and dental hygiene students in dental schools. The primary outcome is a binary variable indicating whether the provider delivered a brief intervention or referral for treatment, as reported by the patient. Additional outcomes include patient self-reported actions toward quitting, smoking reduction, and smoking cessation. Provider-level barriers, facilitators, and potential mechanisms accounting for the effect of tobacco CDS will be examined. Using EHRs to translate current evidence into dental practice holds much potential yet is unrealized in both clinical training and practice. By leveraging the dental encounter as an opportunity to deliver smoking cessation, we can further decrease smoking rates, leading to improved population health.

Objectives:

Objective 1 (primary): Assess if the CDS increases the frequency of BI (Brief Intervention) delivery and/or RT (Referral to Treatment) at an index dental visit as compared to treatment as usual as reported by patients within 7 days of the index visit.

Objective 2 (secondary): Test the efficacy of the CDS on smokers' initial actions related to cessation (contacting a quitline and/or setting a quit date and/or developing a plan to quit and/or

starting nicotine replacement or other medication to help quit within 7 days) as compared to treatment as usual.

Objective 3 (secondary): Test the efficacy of the CDS on smokers' long term actions related to cessation (quitting smoking and/or reducing their smoking within 6 months) as compared to treatment as usual.

Objective 4 (exploratory): Identify provider-level barriers and facilitators of the effect of the CDS, and test potential mediators and moderators of the CDS.

Population:

- **Practitioners.** Up to 88 dental hygienists and 88 dentists working in up to 22 private practice settings and 360 predoctoral and 65 dental hygiene students in two dental schools will be recruited to the trial.
- **Patients.** 720 adult smokers with routine dental visits in dental school settings and 720 adult smokers with routine dental visits in private practice settings seen by practitioners enrolled in the trial are eligible for enrollment in order to achieve 430 completed surveys in each setting.

Phase: Phase 3 clinical trial

Number of Sites: This study will be conducted in up to 14 clinic modules within two dental school programs and 22 private practice clinics.

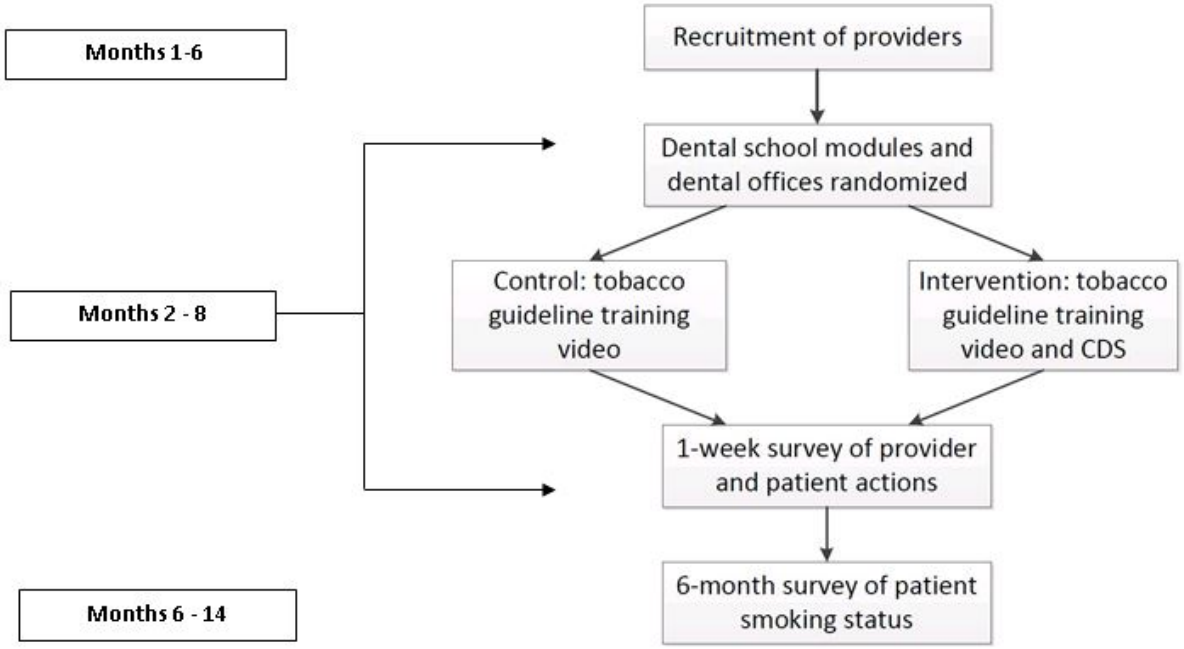
The School of Dental Medicine at the University of Pittsburgh (Pitt) and the Indiana University School of Dentistry (Indiana) have been selected as study sites for this project based on their emphasis on teaching smoking interventions as part of their predoctoral and dental hygiene (predoc/DH) curriculum.

Up to 22 private-practice clinics having 1-5 dentists and 1-10 hygienists will be engaged by recruiting volunteers convenience sampled from dentists and dental hygienists participating in the National Dental PBRN or otherwise recruited through existing relationships with HealthPartners, the University of Pittsburgh, and Indiana University.

Description of The intervention is dental provider exposure to an HIT-driven

Intervention:	CDS tool. The CDS tool generates evidence-based, guideline-driven provider script sets to assist in the delivery of cessation support to smoking patients. A rule-based algorithm personalizes the scripts to account for patients' current smoking status and interest in quitting. A user-centered design approach underpins the CDS tool design that is expected to be delivered in 2 - 5 minutes to remain feasible among the management of multiple priorities in the patient encounter. Provider training will be composed of two components: 1) Clinical practice guideline knowledge (intervention and control clinics) and 2) CDS functionality (intervention clinics only).
Study Duration:	60 months
Subject Participation Duration:	Patients in dental schools and private practices: 7 months. Patient smokers will be surveyed within one week of the index dental visit and 6 months +/-1 week after the dental visit to assess the delivery of tobacco cessation interventions during the dental visit and patient actions related to tobacco use. Dental students, dental hygiene students, dentists, and hygienists: 21 months. Practitioners will be recruited for up to 15 months. Upon randomization of respective clinics or clinic modules, providers will render usual care in either the CDS-supported intervention study arm or the control arm for 21 months.
Estimated Time to Complete Enrollment:	36 months. Initial communication, recruitment, and training of providers will occur on a rolling basis over 15 months. Practices will have 21 months to see up to 45 eligible and willing patients per clinic/clinic module, to complete the provider follow-up study, and to have the intervention in place in the clinic/clinic module setting long enough to plausibly see an effect.

Figure 1. Schematic of Study Design



1 KEY ROLES AND CONTACT INFORMATION

Principal Investigators:

D. Brad Rindal, Co-Principal Investigator
HealthPartners Institute
8170 33rd Avenue South, MS 23301A, Bloomington, MN, 55425
Phone: 952-967-75026 Email: *Donald.B.Rindal@HealthPartners.com*

Heiko Spallek, DMD, PhD, MSBA, Co-Principal Investigator
University of Sydney, Faculty of Dentistry
1 Mons Road, Westmead, NSW, 2145 Australia
Phone: + 61 439 320 490 Email: *heiko.spallek@sydney.edu.au*

Medical Monitor:

Kevin McBryde, MD
Division of Extramural Research, NIDCR, NIH
6701 Democracy Blvd, RM:638, Bethesda MD 20892-4878
Phone: (301) 594-0170 Email: *mcbrydekd@mail.nih.gov*

NIDCR Program Official:

Melissa Riddle, PhD
Behavioral and Social Sciences Research Branch, NIDCR, NIH
6701 Democracy Blvd. RM:650, Bethesda, MD 20892-4878
Phone: (301) 451-3888 Email: *riddleme@mail.nih.gov*

Clinical Site Investigators:

Jean O'Donnell, BSN, MSN, DMD
University of Pittsburgh School of Dental Medicine
Phone: 412-648-8672 Email: *jao4@pitt.edu*

Laura Romito, DDS, MS
Indiana University School of Dentistry
Phone: 317-278-6210 Email: *lromitoc@iu.edu*

Thankam Thyvalikakath, DMD, MDS, PhD
Indiana University School of Dentistry
Phone: 317-274-5460 Email: *tpt@iu.edu*

Tom Kottke, MD, MSPH
HealthPartners Institute
Phone: 651-330-4782
Email: *Thomas.E.Kottke@HealthPartners.Com*

Mark Jurkovich, DDS, BA, MHI
HealthPartners Institute
Phone: 952-967-5016
Email: *Mark.W.Jurkovich@HealthPartners.com*

Institutions:

HealthPartners Institute
8170 33rd Ave. S, MS 23301A, Bloomington, MN, 55425

University of Pittsburgh School of Dental Medicine
3501 Terrace St., Pittsburgh, PA 15261

Indiana University School of Dentistry
1121 West Michigan St., Indianapolis, IN 46202

Other Key Personnel:

Research Methodology and Analysis Team

Jeanette Ziegenfuss, PhD (evaluation)
HealthPartners Institute, Survey Research Center
Phone: 952-967-5020
Email: *Jeanette.Y.Ziegenfuss@HealthPartners.com*

Steve Asche, MA (analysis)
HealthPartners Institute
Phone: 952-967-5018
Email: *Steve.E.Asche@HealthPartners.com*

Tanja Bekhuis, PhD, MS, MLIS, AHIP (methodology)
TCB Research & Indexing LLC
1007 Parkview Boulevard, Suite B
Pittsburgh, PA 15217
Phone: 570-412-2663
Email: *tanja.bekhuis@tcbinfosci.com*

Interoperability Consultant

John Halamka, MD, MS
Beth Israel Deaconess Medical Center
1135 Tremont Street, 6th floor, Boston, MA 02120
Phone: 617-754-8002
Email: jhalamka@bidmc.harvard.edu

Other staff:

Emily Durand RDH, Principal Project Manager
HealthPartners Institute
Phone: 952-967-7404
Email: *Emily.C.Durand@HealthPartners.com*

Chris Enstad, Project Manager
HealthPartners Institute
Phone: 952-967-5007
Email: *Chris.J.Enstad@HealthPartners.com*

2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

Cigarette smoking is a major modifiable risk factor for adverse health outcomes and a major cause of morbidity and mortality (2). Cigarette smoking prevalence among all adults ≥18 years has decreased 42.4% since 1965, but declines in current smoking prevalence have slowed dramatically, from 20.9% in 2005 to 19.3% in 2010 (3). The *Healthy People 2010* objective of reducing smoking among adults to ≤12% has not been achieved, necessitating new strategies to achieve that goal (4). One of the 3 key tobacco use objectives cited is focused on health system changes to increase access, affordability, and the use of smoking cessation services and treatments (5). The National Commission on Prevention Priorities ranking of clinical preventive services identified tobacco-use screening and brief intervention as one of the top 3 most cost-effective preventive services delivered by health care providers, yet rates of delivery remain low (6).

Evidence-based clinical practice guidelines on smoking cessation for health care providers are readily available to clinicians and recommend that different types of providers (i.e., physicians, nurses, *dentists*, psychologists, social workers, cessation counselors, and pharmacists) become involved in smoking cessation because, collectively, they can enhance abstinence rates(7). Despite this, providers are missing opportunities to treat smoking with their patients as recommended (8-10). Limited time during the office visit, lack of expertise, and concern about failure (provider self-efficacy) are often cited as barriers to providing consistent treatment (11). Similar barriers have been identified in the dental setting (12). Previous dissemination and implementation research suggests that simply delivering information to providers rarely changes clinical practice (13-16) and that “available knowledge is too rarely applied to improve the care experience” (17). Passive dissemination of materials, development of clinical guidelines, and knowledge generation through professional continuing education (CE) courses generally have not been effective in demonstrating an impact on provider behavior and clinical outcomes (18-20). Thus, our approach directly activates the provider at the point of care by using HIT-driven CDS to generate scripts for provider use that are personalized on specific smoking attributes.

State quitline services could serve a large percentage of US smokers, yet they are underutilized. Delivery of services is required in order for quitlines to fulfill their potential of improving the health of the US population (21). Increased referral by health care providers, including dental providers, may be part of the solution to fully harness this potential. Ebbert et al determined that dental providers with limited time and resources were able to assist patients who smoke by referring them to a tobacco quitline (22). Various strategies to increase smoking cessation activities in the dental office setting have been investigated (23-25) and have focused on the delivery of brief interventions and quitline referral**.**

2.1 Rationale

By leveraging the dental encounter as an opportunity to deliver a smoking cessation intervention, we will employ an important strategy to decrease smoking rates and improve population health. This clinical trial will determine the degree to which the deployment of health information technology (HIT)-driven clinical decision support (CDS) for smoking interventions in two different dental settings, private practices and dental school, will increase cessation assistance by dental providers. Incorporating smoking-cessation CDS into the clinical curriculum for dental providers (dentists and dental hygienists) can be expected to make smoking cessation counseling part of the accepted routine of dental practice because dental providers initially model care the way they learned it in school (12, 45, 46). Health care providers have access to evidence-based guidelines that help patients quit smoking (47, 48). Translation of that knowledge and awareness into daily practice, however, remains low (26, 49, 50). CDS that reminds and helps providers deliver smoking cessation interventions by providing evidence-based information during care delivery in a clinically relevant format holds the potential to facilitate an evidence-based practice approach (51).

2.2 Potential Risks and Benefits

2.2.1 Potential Risks

Risks to both patients and providers are considered minimal and involve consideration of the risk of violation of confidentiality of study data.

Practitioners. No identifying information on individual provider or student performance with respect to the clinical domains addressed in this study or any other aspect of care gathered as part of this research project will be made available to leaders or managers who make academic, employment, compensation, or disciplinary decisions.

Patients. Potential risks to patients include the possibility that the intervention may provide clinical decision support (CDS) advice to providers on the basis of the national evidence-based guidelines, which may be inappropriate for a given individual patient and, if applied without further checking the clinical status of a given patient, could lead to erroneous therapy, adverse events, disability, or death. However, the clinical recommendations are evidence-based and operationalize current national and regional standards of care and, therefore, the risk of untoward consequences of such clinical actions is considered minimal. Moreover, this potential risk is routinely present in every clinical encounter in the health care system. As with any study, additional risks to patients include principally the risk of violation of confidentiality. Measures to minimize these risks are also discussed below including the use of unique study codes for participants, encryption of data for transmission to the Survey Research Center (SRC), and compliance with Institutional Review Board (IRB) regulations concerning data collection, data analysis, and data storage and destruction.

2.2.2 Potential Benefits

No claim is made in communications with participating providers or patients that they will derive any personal benefit from participating in this project, however study-

associated provider actions that support patients efforts to quit or reduce tobacco is desired and anticipated. Providers will have no defined benefits from participating in this project. However, the CDS designed to encourage smoking cessation conversations in the dental setting may familiarize some providers with new information that can improve the clinical care they deliver in the present or the future. Patients will have no additional direct benefits from participating in this project.

The proposed intervention will modify two existing EHRs to create recommendations for smoking cessation that dentists and dental hygienists can provide for their patients who smoke. Smoking has a major impact on health in general, but it also causes periodontal disease and oral cancer. We will examine if dental providers with this modified EHR will provide more smoking interventions than providers without such an EHR and assess the impact of these interventions on smoking cessation, smoking reduction, and quit attempts. Any reductions in smoking are likely to improve population health in the United States.

3 OBJECTIVES

3.1 Study Objectives

Objective 1 (primary): Assess if the CDS increases the frequency of delivery of BI (Brief Interventions) and/or RT (Referral to Treatment) at an index dental visit as compared to treatment as usual as reported by patients within 7 days of the index visit.

Objective 2 (secondary): Test the efficacy of the CDS on smokers' initial actions related to cessation (contacting a quitline and/or setting a quit date and/or developing a plan to quit and/or starting nicotine replacement or other medication to help quit within 7 days) as compared to treatment as usual.

Objective 3 (secondary): Test the efficacy of the CDS on smokers' long term actions related to cessation (quitting smoking and/or reducing their smoking with 6 months) as compared to treatment as usual.

Objective 4 (exploratory): Identify provider-level barriers and facilitators of the effect of the CDS, and test potential mediators of the CDS.

3.2 Study Outcome Measures

The measurement of outcomes for the primary and secondary objectives will be based on self-reported data from telephone surveys of dental patients 1-7 days following an index dental visit, and 6 months +/- 1 week following the index dental visit. Endpoints from patients are based on patient reports about their first observed index visit (not subsequent visits), where an index visit is a new or established patient visit where an oral evaluation is conducted to determine changes in the patient's medical and dental health status. A detailed description of dependent variables for the primary and secondary objectives is shown in Table 1.

3.2.1 Primary Objective

Aim 1 - Receipt of a brief smoking intervention or referral to a quitline (H1) (Objective 1): The dependent variable for H1 (Objective 1) is a binary indicator of whether the patient reported that their provider 1) delivered a brief smoking intervention: the provider discussed a) developing a quit plan, or b) setting a quit date, or c) using medications to help patients quit or d) discussed strategies for quitting, or 2) referral to a quitline: a) provided information about how to contact a tobacco quitline, or b) arranged for the patient to be contacted by the tobacco quit line, for smoking cessation at the index dental visit. This composite variable is satisfied if the patient reports that any of

the intervention activities or referral was delivered. This information is obtained from the phone survey of patients within 1-7 days of their index dental visit.

3.2.2 Secondary Objectives

Aim 2 – Smoker's cessation actions, within one week of visit (H2.1) (Objective 2): The dependent variable for H2.1 (Objective 2) is a binary indicator of whether the patient reported that they contacted a smoking cessation quitline, set a quit date, developed a plan to quit, or starting nicotine replacement or other medication to help quit. The CDS is designed to provide a more tailored and targeted message that may lead to more tobacco cessation actions by the smoker. This composite variable is satisfied if the patient reports that they have done any of these actions within the 1-7 day period between the index dental visit and date of the first patient survey. This information is obtained from the phone survey of patients within 1-7 days of their index dental visit.

Aim 2 - Smoker's cessation actions, six months after the visit (H2.2) (Objective 3): The dependent variable for H2.2 (Objective 3) is a binary indicator of whether the patient reported that they quit smoking (stopped smoking for more than one day *because they were trying to stop smoking*), or reduced their smoking use (50% reduction in amount smoked at 6 months compared to baseline). This composite variable is satisfied if the patient reports that they have done any of these actions within the 6 month +/- 1 week period between the index dental visit and date of the second patient survey. This information is obtained from the phone survey of patients 6 months +/- 1 week after the index dental visit.

Aim 3 – Barriers, facilitators and mediators of receipt of a brief smoking intervention or referral to a quitline (H3.1, H3.2) (Objective 4):

See the dependent variable for Objective 1.

3.3 Independent variables and descriptive variables

A detailed description of independent and descriptive variables is shown in Table 2.

Table 1. List of Dependent Variables for Primary and Secondary Objectives

Variable	Description	Data source	Variable type
Primary objective, dependent variables			
Percentage of visits with delivery of brief interventions and/or referral to treatment	Composite of provider actions reported by patient	Patient baseline survey (1-7 days)	Binary
Secondary objectives, dependent variables			
Percentage of smokers with initial actions related to cessation	Composite of patient-reported actions	Patient baseline survey (1-7 days)	Binary
Percentage of smokers with long-term actions related to cessation	Composite of patient-reported actions	Patient baseline surveys (1-7 days and 6 months)	Binary

Table 2. List of Independent and Descriptive Variables

Variable	Description	Data source	Variable type
Study arm	Primary independent variable. Coded as control clinic or clinical decision support clinic	Assigned by statistician	Binary
Dental school system	Identifier for the dental school source of the dental school module (Pittsburgh or Indiana)	Administrative	Nominal
Patient age	Years	Patient survey (1-7 days)	Interval
Patient sex	Male or female	Patient survey (1-7 days)	Nominal
Patient race	Standard categories	Patient survey (1-7 days)	Nominal
Patient ethnicity	Hispanic or not	Patient survey (1-7 days)	Nominal
Patient education	Standard categories	Patient survey (1-7 days)	Nominal
Patient income	<12000, 13000-<25000, 25000-<50000, 50000-<75000, >=75000	Patient survey (1-7 days)	Nominal
Visit type	Type of dental visit	EHR	Nominal
Patient smoking status	This used to determine survey eligibility, but not final eligibility.	EHR	Binary
Patient smoking status	Used as a descriptive variable and to select patients as study eligible and analysis eligible	Patient survey (1-7 days)	Binary
Patient amount smoked	Informs script language, functional to CDS	CDS	Interval
Patient amount cigarettes smoked	Patient report of amount of cigarettes smoked in past 30 days. Descriptive variable and covariate.	Patient survey (1-7 days) and at 6 months	Interval
Variable	**Description**	**Data source**	**Variable**

			type
Patient use of other tobacco	Use of cigars, pipes, chewing tobacco, e-cigarettes, hookahs, other	Patient survey (1-7 days) and at 6 months	Binary
Provider age	Years	Provider survey (baseline)	Interval
Provider sex	Male or female	Provider survey (baseline)	Nominal
Provider race	Standard categories	Provider survey (baseline)	Nominal
Provider years in practice	Years	Provider survey (baseline)	Interval
Provider type	Dentist or hygienist	Provider survey (baseline)	Nominal
Provider TDQ individual domain scores	Proposed moderators in Aim 3 (Objective 4) analyses: Theoretical Domain Questionnaire individual domain scores (10 total)	Provider survey (baseline)	Ordinal
Change in provider self-efficacy TDQ individual scores from baseline to 6 months	Proposed mediators in Aim 3 (Objective 4) analyses: Self-efficacy items from Theoretical Domain Questionnaire	Provider survey at baseline and 6 months after intervention	Ordinal
Provider satisfaction with CDS	Provider ratings of satisfaction and usability of CDS	Provider survey 6 months after intervention	Ordinal

4 STUDY DESIGN

The planned study design (see Figure 1) is a group-randomized, controlled, 2-arm trial conducted in two settings: predoctoral dental schools and private-practice clinics participating in the National Dental PBRN. Fourteen modules (12 predoctoral dental school clinic modules, 2 dental hygiene clinic modules) and 22 private practice clinics will be separately randomized using covariate-based constrained randomization. Balancing covariates to be used in each setting are specified in the Final Statistical Analysis Plan.

Each set of dental school modules and set of clinics will be randomly assigned to one of two study arms (CDS or control) using a statistician-prepared randomization table. All consented providers and their patients will be allocated to the study arm to which their clinic is assigned. The participants are dentists, dental therapists, dental hygienists, dental students, dental hygiene students, and patients.

Intervention clinics will receive the CDS that will provide clinical practice guideline-supported, evidence-based, and personalized scripts that are tailored based on patients' self-reported smoking attributes to deliver interventions consistent with the standard of care. Control clinics will continue to provide usual care without CDS support. Both arms receive a training video on how to incorporate the current tobacco cessation guideline. Intervention clinics will receive limited start-up training, demonstrating the technical functionality of the CDS. Clinic modules do not overlap and there is no integration of dental hygiene student and dental student care delivery.

5 STUDY ENROLLMENT AND WITHDRAWAL

5.1 Subject Inclusion Criteria

Dental students and dental hygienists. 3rd and 4th year predoctoral students or dental hygiene students enrolled at selected dental schools.

Private practice dentists and hygienists. General practice dentists or dental hygienists practicing at selected private practice clinics

Adult patients. All consecutive adults (≥ 18 years of age) not yet exposed to the CDS and seen in study-enrolled dental school index visits or study-enrolled private-practice index visits during the clinic-specific implementation period who are current cigarette smokers will be eligible for the study.

Survey-eligible: A subset of patients are contacted by the central Survey Research Center who provide consent to complete the baseline survey.

5.2 Subject Exclusion Criteria

Providers not able or willing to record current tobacco use status in their EHR are not eligible. Private practice providers must not be affiliated with the engaged dental schools (Indiana University or University of Pittsburgh) in a teaching or clinical position.

Patient exclusion criteria applied to the usual care post-index encounter telephone screening include: (a) patients requesting to opt out of research.

5.3 Strategies for Recruitment and Retention

Recruitment and retention of providers: Associated dental hygienists and dentists working in private practice settings, and predoctoral and dental hygiene students will be recruited to the trial using informational handouts and personal communication with study staff. Private practice practitioners will be recruited through existing relationships of the National Dental PBRN or the institutions involved in the project. Dental school students will be recruited through on-site information sessions conducted by non-faculty.

Dental schools: The School of Dental Medicine at the University of Pittsburgh and the Indiana University School of Dentistry will recruit student participants through the dental school predoctoral and DH clinics. Information sessions hosted by the appropriate project staff will be held at each dental school. Information about the study will be presented at that time and any potential questions by students will be answered by study project management staff with no relationship to the students. Study staff with no academic relationship to student providers will administer consent in accordance with IRB-approved site-specific procedures.

Private practices: The study team will recruit private practice clinics through relationships established in the National Dental PBRN and prior studies by the investigators at the academic institutions represented. Midwest Regional Coordinators

who are jointly study staff have relationships with practitioners and can answer questions about the study and about participation in research in general, and further support the involvement of interested practitioners. No additional National Dental PBRN resources will be used. Study staff can use administrative databases and Network enrollment questionnaire data to identify eligible private practice settings.

Provider incentives: Incentives will be provided to students per policy of the school. Private practice providers will receive incentives at the completion of the study. All providers will receive a free CE session with a web-based video course on the current US Department of Health and Human Services: *Treating Tobacco Use and Dependence: 2008 Update— Clinical Practice Guideline.*

Recruitment and retention of patients: We anticipate based on administrative data to achieve cumulative consecutive patient enrollment across sites to total 1,440 in 8 or fewer months (site specific). Patients who have authorized secondary disclosure of their information will be securely transferred to HealthPartners. Only study-eligible patients will be contacted by the SRC. Patient contact data and encounter details will be reported daily using an EHR system routine (to be programmed by vendor).

To facilitate surveys, verbal consent will be obtained for patients contacted by phone within 7 days of their index visit. Consent and surveys will be conducted centrally by SRC professional telephone interviewers trained in human subjects' protection, HIPAA for research and the Responsible Conduct of Research. Patients will be called up to eight times at various times of day, including evenings, and days of the week, including Saturdays, to maximize recruitment and opportunities for follow-up.

Patient participants will be provided an incentive after completion of the baseline and 6-month survey.

5.4 Treatment Assignment Procedures

Dental school predoctoral/dental hygiene clinics in Indiana and Pennsylvania, and private practice clinics will be randomized. All consented providers and their patients will be allocated to the study arm to which their clinic is assigned.

5.4.1 Randomization Procedures

Within the predoctoral and dental hygiene clinics, clinic modules will be randomized to study arm using covariate-based constrained randomization. Balancing covariates will be specified in the final Statistical Analysis Plan. Private practice clinics will be randomized to study arm using covariate-based constrained randomization. Balancing covariates will include factors that are measurable across all clinics in the recruitment pool. Clinic-level factors to be considered include number of patient visits, number of smokers, percentage of patients who are smokers, percentage of patients with public-pay insurance, percentage in specific age groups. The final randomization plan and balancing covariates will be described in the final Statistical Analysis Plan.

5.4.2 Masking Procedures

Neither the CDS- nor the control-study arms in dental school and private practice clinics will be masked. Study staff will know which clinic assignment, and providers will know clinic assignment due to the obvious presence or absence of clinical decision support available within the EHR at each clinic. Some protection from bias occurs due to patients not being aware that a study is occurring until they are contacted by research staff following their index visit. Patients are not made aware of the study arm to which their clinic is assigned. However, provider knowledge of study arm could be relayed by providers during the dental visit. The Survey Research Center interviewers conducting the evaluation interviews will be blind to the patient's clinic assignment.

5.5 Subject Withdrawal

Participants may withdraw voluntarily from the study or the investigator may terminate participation.

5.5.1 Reasons for Withdrawal

Subjects are free to withdraw from participation in the study at any time upon request. Patients or providers may wish not to participate due to the perceived impact on their time or privacy. Incomplete surveys will be counted as withdrawals.

5.5.2 Handling of Subject Withdrawals or Subject Discontinuation of Study Intervention

Patient withdrawal. Within the parameters prescribed by the study protocol, study staff will provide support and encouragement to participants in order to minimize withdrawal and attrition during the intervention. Every effort will be made to undertake protocol-specified safety follow-up procedures and capture adverse events (AEs), serious adverse events (SAEs), and unanticipated problems (UPs).

Patients may elect to withdraw at any time with no impact on their relationship with their provider or the institutions involved on conducting the research. With respect for both patients and providers, refusal conversion will not be attempted. Respondents may actively or passively refuse to participate in the evaluation surveys. Active refusals will not be contacted again by the Survey Research Center. Passive refusals (i.e., a subset of non-responders) will only be contacted up to a maximum number of email (providers) or telephone (patient) attempts (up to 8) to be respectful of participants and within bounds of IRB approval. Withdrawal of providers will be tracked in the provider database by the project manager. Withdrawal of patients will be tracked by the SRC staff in the centralized study database.

Withdrawn patients will not be replaced. In the case of patient withdrawal from the study, staff will only attempt continued follow-up data collection for patients who are withdrawn due to an unanticipated problem (UP). In those cases, only data related to the completion of reporting requirements for the UP will be recorded. Patients withdrawn from the study for any other reason will have the date and reason for withdrawal

recorded (if known), but will not have any additional study data recorded. Although patients withdrawn from the study may continue to receive normal clinical care as patients of the participating dentists, additional study data will not be collected from this continuing clinical care (except as noted above).

Practitioner withdrawal. Withdrawn private practices will be replaced with a suitable alternate clinic until the time of randomization ensuring covariate balance remains intact.

5.6 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 principal investigator will promptly inform the IRB and will provide the reason(s) for suspension or termination.

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

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

6 STUDY INTERVENTION

6.1 Study Behavioral or Social Intervention(s) Description

A user-centered design of the CDS tool is supported by prior multi-method approaches of the study team which have explored tobacco cessation activities and EHR workflows among dentists and dental hygienists. Each patient-specific index visit for the study is defined as the first encounter during the clinic-specific implementation period when the enrolled provider updates that patient's smoking status in the CDS application, cueing contact by the Survey Research Center (SRC). Additional subsequent dental visits may include additional CDS updates by the provider, but these encounters do not result in additional SRC contacts until the 6 month patient survey.

Prior research supports CDS that should not interrupt the providers' usual approach to history taking. Thus a user-centered approach to activation of the CDS will allow for a seamless integration into a variety of practitioner workflows (e.g., dental hygienists' versus dentists' workflow) and visit types. This integration will enable providers to engage the CDS whenever a tobacco cessation is relevant to the patient encounter. Our prior work has shown the merit of this approach (64).

Provider scripts and patient educational materials are based on the current clinical practice guideline endorsed by a consortium of eight Federal Government and nonprofit organizations, AHRQ's evidence-based guidance materials for healthcare providers, and materials available to patients from http://smokefree.gov/. Script flow is based on the 5As model (Ask, Advise, Assess, Assist, Arrange). Supportive motivational intervention messaging is provided for patients not ready to make a quit attempt now.

6.2 Administration of Intervention

The EHR vendors will modify their respective EHR products to integrate the CDS. After pilot testing, this modified EHR product will be installed in all study and control clinic environments and exposed to consented dental providers (dentists, dental students, dental hygiene students).

In the context of the familiar EHR environment, providers in the intervention arm will be exposed to the CDS. Assessment of the patients' reported daily use, previous quit attempts, and interest in quitting drives a CDS rule-based algorithm that displays personalized scripts for that patient. Using the scripts as a jumping off point, the provider is free to adapt the messaging using best clinical judgment and according to patients' individual needs and preferences as well as risk factors for oral disease (see Section 6.3 on observational monitoring of fidelity for details about evaluating standardization of the delivery of the scripts as intended per the clinical guideline). The provider selects scripts and patient resources that were "delivered." Using this information, the tool creates an automated "smart note" to efficiently document the activities for reference in guiding future encounters, as well as for compliance with record keeping requirements.

6.3 Procedures for Training Interventionists and Monitoring the Quality of the Provider Behavior Measures

Procedures for Training Interventionists Providers in private practices in both the intervention and control clinics will participate in a video-cast professional CE course (approximately 30 minutes) on how to implement the current tobacco cessation guideline, specifically in dental practice. The two dental schools participating in this study place a high priority on comprehensive guideline-driven tobacco education. All students are exposed to tobacco cessation training in their curriculum, however it occurs early in the didactic curriculum, so students will also view the video-cast thus standardizing, as much as is practical, their most recent knowledge with practicing providers. All intervention clinics will receive basic training on the functionality of the CDS tool in the form of a video-cast and an interactive session with a project manager who has clinical training experience.

Monitoring Provider Behavior Measures Utilizing Clinic Observations

The outcome measure for Objective 1 relies on patient reporting of the provider actions during the clinical encounter. This measure has the potential for inaccurate recall by the patient. To address this concern we will conduct observations on a subset of the clinical encounters, recording the actions of the provider. These results will be compared to the patient reported results in order to determine the degree of recall bias. The number of observations will be determined after assessing agreement of the two measurements.

6.4 Assessment of Subject Compliance with Study Intervention

The HPI data center will generate reporting tools summarizing patient response rates. These reports will be provided to the study team and reviewed monthly to determine the need for additional training. This report will be reviewed monthly by the study team and by the Medical Monitor as needed.

6.5 Study Procedural Intervention(s) Description

A user-centered design of the CDS tool is supported by prior multi-method approaches of the study team (52) which have explored tobacco cessation activities and EHR workflows among dentists and dental hygienists. Based on this preliminary work and responses to a survey of National Dental PBRN members from across the US, the CDS will be designed to target specific index visits (D0140. Limited oral evaluation; D0150. Comprehensive Oral Evaluation) when it is expected the dentist and/or dental hygienist will routinely update the patient's medical history and smoking status. In the intervention clinics the CDS will be activated when the tobacco status is updated. A flexible approach to accessing the tool will allow for adaptability to a variety of practitioner workflows and visit types and will enable providers to engage the CDS when relevant to the patient encounter.

Provider scripts and patient educational materials are based on the current Clinical Practice Guideline sponsored by a consortium of eight Federal Government and nonprofit organizations (55), AHRQ's evidence-based guidance materials for healthcare providers (56), and materials available to patients from http://smokefree.gov/. Script flow is based on the 5As model (Ask, Advise, Assess, Assist, and Arrange). Supportive motivational intervention messaging (57) is provided for patients not ready to make a quit attempt now.

Figure 1 of the Visualization Appendix (Appendix E) illustrates the three parts of the CDS as it appears within the providers' EHRs. The provider asks a few tobacco questions about smoking status as part of a health history update that triggers the CDS. The interventions delivered by the provider are customized based on the smokers' responses to baseline questions. The provider elects which personalized scripts and patient resources to deliver in the patient encounter by checking the boxes provided. Using this information, the tool creates an automated "smart note" to efficiently document the activities and for use in follow-up during future encounters with the patient. This figure also illustrates the CDS functionality which generates unique script sets based on the patient's smoking status (i.e., reported daily use), previous quit attempts, and interest in quitting.

6.6 Administration of Procedural Intervention

See study Manual of Procedures (MOP) for this detail.

6.7 Procedures for Training of Clinicians on Procedural Intervention

See site-specific training materials (MOP appendix) for this detail.

6.8 Assessment of Clinician and/or Subject Compliance with Study Procedural Intervention

See study MOP monitoring plan for this detail as well as Section 14 on quality control and quality assurance.

7 STUDY SCHEDULE

7.1 Screening

Providers: To ensure students meet inclusion criteria, they will attend a lunch and learn session at which time informed screening, recruitment, and consent procedures will be completed with study staff who do not have a relationship with the students (e.g., no academic oversight).

Patients: Providers will routinely assess patients for tobacco status. Patients who have authorized secondary disclosure of their information will be securely transferred to HealthPartners. Only study-eligible patients will be contacted by the SRC.

7.2 Enrollment/Baseline

Provider baseline enrollment: Providers in private practices may be enrolled in dentist/dental therapist/dental hygienist, as appropriate, since care is delivered as a team. Dental and dental hygiene students will be enrolled as individuals nested within clinic modules that are anticipated to be static for the duration of the study period. Upon enrollment, providers and student providers will be invited to complete the baseline survey.

Patient baseline enrollment: Study enrollment and all follow-up data are driven by the index visit. A system-generated, study specific-encounter ID will ensure patients are only contacted at baseline one time, even if intermediate dental encounters occur and their tobacco status is updated again.

7.3 Intermediate Visits

Patient intermediate visits: Not applicable. Patients may return for non-study related dental visits. These visits will not alter the timeline of the baseline or 6-month follow-up surveys

Provider intermediate visits: Not applicable. Providers are surveyed at baseline and after 6 months of study participation.

7.4 Final Study Visit

Patient final visits: The final patient contact consists of the SRC-administered 6-month survey conducted by phone and tracked in the central REDCap database.

Provider final visits: The final provider visit consists of the 6-month survey administered electronically and tracked in the central REDCap database.

7.5 Withdrawal Visit

Patient withdrawal: Patients may withdraw at any dental visit within the study period. This will be relayed by the dental provider and tracked by the project manager or SRC staff such that follow-up is discontinued. This option will be addressed with providers in

training. Patients may also withdraw while in contact with SRC staff. This will not affect nor be communicated to providers, practices, or schools.

Practice withdrawal: Up to 4 back-up private practices will be recruited to accommodate clinic-level withdrawal. Withdrawn private practices will be replaced with a suitable alternate clinic to ensure clinic randomization remains intact.

7.6 Unscheduled Visit

No unscheduled intervention-related visits are anticipated. Unscheduled contact may occur with the study manager whose contact information will be provided (e.g., patients seeking clarification about incentive payment). This is common and typical in practice-based research which takes a customer-service based approach to ensuring participants have comfort with and ease of accessibility to the researchers.

8 STUDY PROCEDURES /EVALUATIONS

8.1 Study Procedures/Evaluations

Patient Survey procedures: Patient contact data will be sent to the HPI Survey Research Center in keeping with HIPPA authorization procedures and Data Use Agreements approved by the respective sites. In the period between 1-7 days after the index dental visit, a baseline survey will be attempted with each patient. Call attempts continue until either a survey is completed or a patient indicates that they do not want to participate. The outcome disposition of each call attempt is recorded by the interviewer in the centralized study database to ensure accurate calculation of contact, response, cooperation and refusal rates. Upon successful contact with a patient, interviews will be conducted with willing participants in a standardized manner utilizing the IRB approved script and survey questions and responses. Refusal conversion is not attempted. Any study-related patient questions are fielded using a study Frequently Asked Questions document. Survey responses are recorded by the interviewer in real-time in the centralized study database. Interviewers are monitored for script adherence, accuracy of data entry and study knowledge by SRC staff.

Patients that complete a baseline survey become due for a follow-up survey six months after the index visit. In order to maximize response rates, the SRC will begin calling these patients one-week before the six-month mark. Up to eight call attempts will be made in the two-week window spanning the six-month mark. Call attempts, survey administration and documentation follow the same procedure as the baseline survey. Survey questions vary slightly between the baseline and six-month surveys as indicated in the Survey Item Grid (Appendix K).

Interviews will be conducted in English and Spanish. The IRB approved script and questionnaire will be translated, back-translated and reconciled by a professional translation firm. Spanish-speaking trained telephone interviewers, employed by the SRC, will attempt survey completion with Spanish-speaking patients. All interviewers work onsite in a central location. In addition to completion of training in practices of standardized telephone interviewing for research, all interviewers are trained in HIPAA and the responsible conduct of research through CITI.

Provider survey procedures: Upon enrollment in the study, providers will receive their baseline survey. Private practice providers will be asked to complete and return theirs by the completion of the training session. Student providers will be invited to complete theirs in the lunch and learn session where the study is introduced. Survey responses will be collected separately from any identifiers (e.g., provider ID) needed to connect provider data to clinic level data for the purposes of analysis. Six-month surveys (90 days -30/+90 days) will be provided and collected confidentially by the project staff at the respective sites. HealthPartners project managers will deliver and obtain surveys from the private practice settings. Baseline and 6-month surveys will be marked with a common study ID.

8.2 Laboratory Procedures/Evaluations

No laboratory procedures are anticipated in this trial.

9 ASSESSMENT OF SAFETY

9.1 Specification of Safety Parameters

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

(1) 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;

(2) 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

(3) 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.

9.1.1 Adverse Events

An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

9.1.2 Serious Adverse Events

An SAE is one that meets one or more of the following criteria:

(1) Results in death

(2) Is life-threatening (places the subject at immediate risk of death from the event as it occurred)

(3) Results in inpatient hospitalization or prolongation of existing hospitalization

(4) Results in a persistent or significant disability or incapacity

(5) Results in a congenital anomaly or birth defect

(6) An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

9.2 Time Period and Frequency for Event Assessment and Follow-Up

Unanticipated problems will be recorded in the data collection system throughout the study. The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. Since there are no routine research contacts with patients aside from the surveys after the index visit and 6 month survey, we will train providers to solicit and record information about potential AEs. The study coordinator will solicit information from clinicians monthly through electronic communications. Events will be followed by the Study Coordinator for outcome information until the event has resolution or stabilization. Patients will also be referred to their dental or medical provider as appropriate for management and resolution.

9.3 Characteristics of an Adverse Event

9.3.1 Relationship to Study Intervention

All adverse events will have their relationship to study intervention or study participation assessed and documented in the patient research record and will be included in summary reporting to the IRB and the Medical Monitor. Evaluation of relatedness will consider etiologies such as natural history of the underlying disease, concurrent illness, concomitant therapy, study-related procedures, accidents, and other external factors. To assess relationship of an event to study intervention, the following guidelines are used for this study:

1. Related (Possible, Probable, Definite)
    a. The event is known to occur with the study intervention.
    b. There is a temporal relationship between the intervention and event onset.
    c. The event abates when the intervention is discontinued.
    d. The event reappears upon a re-challenge with the intervention.
2. Not Related (Unlikely, Not Related)
    a. There is no temporal relationship between the intervention and event onset.
    b. An alternate etiology has been established.

9.3.2 Expectedness of SAEs

The NIDCR Medical Monitor and the Study PIs will be responsible for determining whether an SAE is expected or unexpected. An adverse event will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention.

9.3.3 Severity of Event

The following scale will be used to grade adverse events:

1. Mild: no intervention required; no impact on activities of daily living (ADL)
2. Moderate: minimal, local, or non-invasive intervention indicated; moderate impact on ADL
3. Severe: significant symptoms requiring invasive intervention; subject seeks medical attention, needs major assistance with ADL.

This will be recorded in the subject's research record and in summary reports of the study.

9.4 Reporting Procedures

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 AE, or any other incident, experience, or outcome as an unanticipated problem to the IRB:

(1) Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number.

(2) A detailed description of the AE, incident, experience, or outcome.

(3) An explanation of the basis for determining that the AE, incident, experience, or outcome represents an unanticipated problem.

(4) 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:

(1) Unanticipated problems that are SAEs will be reported to the IRB and to NIDCR within one week of the investigator becoming aware of the event.

(2) Any other unanticipated problem will be reported to the IRB and to NIDCR within two weeks of the investigator becoming aware of the problem.

(3) All unanticipated problems will 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's centralized reporting system via Rho Product Safety:

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

(2) Product Safety Fax Line (International): 919-287-3998

(3) 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):

(1) US: 1-888-746-7231

(2) International: 919-595-6486

9.5 Halting Rules

Halting rules are not expected to be applicable for this trial involving CDS-supported usual care.

10 STUDY OVERSIGHT

Medical Monitor. In addition to the Grant PI's (GPI) and Study PI's (SPI) responsibility for oversight, external study oversight will be involve Medical Monitor Oversight Reporting. This oversight includes submission of a Medical Monitor Oversight Report to NIDCR at 6 month intervals, beginning approximately 6 months after enrollment begins until data collection is completed.

11 STATISTICAL CONSIDERATIONS

11.1 Primary Objective

Aim 1: Assess the impact of tobacco CDS on the frequency of provider-delivered brief smoking interventions or referral to a quitline for smoking cessation treatment.

Hypothesis 1.1 (Objective 1): Smokers seen in dental clinics using CDS will be more likely to report that their provider delivered a brief smoking intervention or referral to a quitline for smoking cessation at their index encounter than smokers seen in clinics without CDS.

11.2 Secondary Objectives

Aim 2: Assess the impact of tobacco CDS on smokers' cessation and reduction actions.

Hypothesis 2.1 (Objective 2): Smokers seen in dental clinics using CDS will be more likely to report contacting a quitline, setting a quit date, developing a plan to quit or starting nicotine replacement or other medication to help quit within 7 days of their index encounter than smokers seen in clinics without CDS.

Hypothesis 2.2 (Objective 3): Smokers seen in dental clinics using CDS will be more likely to report quitting smoking, or reducing their smoking within 6 months of their index encounter than smokers seen in clinics without CDS.

11.3 Sample Size Considerations

Sample size justification for aim 1 Primary objective):

Dental schools: Based on data extracted from an administrative review of dental visits in 2013 in the two dental school settings, there are 2,800 visits by smokers (by an estimated 2,660 smokers) in a 12-month period in the 14 study dental clinics. A total of 720 smokers will be approached to participate in the study over an 8-month recruitment period. Based on an expected 60% response rate to the 7-day survey of smokers, it is anticipated that 430 patient surveys (215/study arm) will be completed. In our prior study (see section 1.1.2) found that 15-20% of patients in control clinics reported receiving a brief smoking intervention in the dental clinic. The expectation for the endpoint for H1.1 (Objective 1) of receiving a smoking cessation intervention or quitline referral in this study is set at the lower end of that expectation at 15%. The actual sample size of n=430 is reduced to an effective sample size of 230-320 for the power analysis to reflect clinic-level ICCs for receiving a smoking intervention, which ranged from an ICC of 0.01-0.025 for specific intervention endpoints in the prior CATI study. With a sample of 430 patient surveys and a clinic-level ICC for the endpoint of 0.01-0.025, this study will have 80% power (alpha=0.05, two-sided, R^2 with other covariates=0.1) to detect a difference in the H1.1 (Objective 1) endpoint of 15% for patients in control clinics compared to 29%-31% (reflecting ICC of 0.01-0.025) for patients in CDS clinics (delta=14%-16%).

Private practices: There are an estimated 1,475 visits by smokers (by an estimated 1,328 smokers) in a 12-month period in 16 randomly selected study private practice clinics, based on surveys of National Dental PBRN private practices. We will initially recruit 22 practices with the expectation that 20 will remain involved in the study. Patient and sample size calculations are based on 20 private practice clinics. A total of 720 smokers will be approached to participate in the study over an 8-month recruitment period for each clinic. It is assumed that the 60% response rate to the 7-day survey of smokers and ICCs for the endpoint will be the same in this setting as described above for dental schools at 0.01-0.025. It is expected that a lower percentage of smokers in control clinics in this setting will report receiving a brief smoking intervention than in the control dental school setting described above, with an expected rate half that of the dental schools to arrive at 7% in control clinics. The actual sample size of n=430 is reduced to an effective sample size of 288-364 for the power analysis to reflect clinic-level ICCs for receiving a smoking intervention. With these assumptions, this study will have 80% power (alpha=0.05, two-sided, R^2 with other covariates=0.1) to detect a difference in the H1.1 (Objective 1) endpoint of 7% for patients in control clinics compared to 17%-19% for patients in CDS clinics (delta=10%-12%).

All power analysis was conducted with Pass v11(58) with the goal of adequately powering the primary objective. An interim analysis is planned for review by the Medical Monitor if requested. This analysis will be descriptive and will not alter the course of the study. No adjustment is made to alpha for this interim analysis.

11.4 Planned Interim Analyses (if applicable)

11.4.1 Safety Review

We do not expect any safety events because this is a minimal risk intervention. However, the safety review plan will include quarterly reports of patient accrual, enrollment, follow-up, and provider use of CDS.

11.4.2 Efficacy Review

One interim efficacy analysis on short-term outcomes in aims 1 (Objective 1) and 2 (Objective 2) will be conducted when half of the baseline surveys have been conducted. This analysis will be conducted for review by the Medical Monitor and will be descriptive (no statistical testing). There is no initial plan to stop the study early due to futility or exceptional efficacy. Because this is a minimal risk study, it is unlikely that there would be a rationale for stopping the study due to adverse events. However, the Medical Monitor will ultimately make decisions regarding the need for stopping rules.

11.5 Analysis Plan

Overview. This group-randomized trial will randomize up to 14 dental school modules and up to 22 private dentistry practices to receive or not receive tobacco clinical decision support. All 14 dental school modules are selected for study from the two

participating dental schools. A larger number (22) of private practice clinics are included to increase power and balance study arms on key characteristics, both large concerns in a group-randomized design. Also, it is expected that only 20 of 22 clinics will remain in the study. Primary outcomes are obtained from patient surveys and consist of composites reflecting patient reports of actions taken by the dental provider and patient reports of their own actions regarding smoking cessation. Because of the numerous differences in the dental school and private practice settings and the interest in testing generalizability of the intervention in both settings, all analyses are conducted separately within each setting. Sample size justifications and power calculations are estimated separately within setting to ensure adequate data within each setting to address the primary aims. Sample size determinations are based on needs for the primary objective. Secondary objectives, secondary analyses, and subgroup analyses are exploratory and do not determine sample size calculations. A final Statistical Analysis Plan will provide detail on the specific fixed and random effects to be included in each model, as well as relevant covariates.

Analysis plan for aims 1 (Objective 1, primary) **and 2** (Objectives 2,3, secondary)**.** Hypothesis 1.1 (Objective 1) posits that patients seen at clinics randomly assigned to the tobacco CDS intervention will be more likely to report that their provider offered a brief smoking intervention or referral to a tobacco cessation quitline than patients seen at clinics with CDS. Hypothesis 2.1 (Objective 2) posits that patients seen at clinics randomly assigned to the tobacco CDS intervention rather than control clinics will be more likely to report that they have engaged in short-term activities towards cessation of contacting a quitline, setting a quit date, starting nicotine replacement or other medications to quit, or developing a quit plan. Hypothesis 2.2 (Objective 3) posits that patients seen at clinics randomly assigned to the tobacco CDS intervention will be more likely to report that they have engaged in cessation activities of quitting smoking for one day or longer or reducing smoking use. Because clinics are the unit of randomization and the outcome varies at the level of the patient, generalized linear mixed model regression with a logit link and binomial error distribution will be used to test the effect of the intervention on the binary endpoints of Objectives, 1, 2, 3. Adjustment for imbalances across intervention arms for relevant patient-level characteristics will be consideredThe analytic approach described above will be conducted separately in the dental school setting and the private practice setting.

If the count of dental school modules or private practice clinics having completed patient surveys is fewer than 10, or if the mean number of completed patient surveys per randomized unit (dental school module or private practice clinic) is less than 15, an alternative primary analytic strategy will be conducted. This strategy will emphasize descriptive statistics and comparisons across clusters of within-cluster summaries rather than inferential tests of differences by study arm. Specifically, the count and proportion will be reported within each dental school module or private practice clinic for the Objective 1 endpoint: patient report that within 7 days their provider offered a brief smoking intervention or referral to a tobacco cessation quitline, Objective 2 endpoint: patient report within 7 days that they engaged in short-term activites towards cessation or contacted a quitline, and Objective 3 endpoint: patient report at 6 months that they have engaged in cessation activities of quitting smoking for one day or longer or

reducing smoking use. Proportions and exact (Clopper-Pearson) confidence intervals will be computed and plotted by clinic, grouped by study arm. Beyond the grouping or stratification of results by study arm, no other stratification or adjustment will be conducted.

The inferential portion of the alternative analytic strategy will be made secondary due to concerns about biased standard errors (and resulting confidence intervals and p-values) in cluster-randomized studies with a small count of clusters, or few members within each cluster (McNeish & Harring, 2017). However, the planned generalized linear mixed model regression described above will still be used to provide the estimate of the fixed intervention effect (Maas & Hox, 2005) for Objectives 1, 2, and 3. The standard error and p-value for the fixed intervention effect are likely more biased and will be reported but viewed with caution. Due to the small sample size and smaller number of events for Objectives 1, 2 and 3, no further covariate adjustment will be considered in these models. The resulting generalized linear mixed models (logit link, binomial error distribution) will thus consist of a binary endpoint for the specific objective predicted by a fixed effect for study arm, and a random effect for dental school module or private practice clinic. The sample size in this alternative analytic strategy won't allow for adjustment or imputation to address missing surveys or survey items.

The analytic sample for Objectives 1 and 2 consists of patients who have completed constituent items for endpoint composites for Objectives 1 or 2 in the survey completed within 7 days of the index date. Study arm for each patient is based on randomization of the linked dental school module or clinic at which the patient was seen. The analytic sample for Objective 3 consists of patients who have completed constituent items for endpoint composite used in Objective 3 in the survey completed at 6 months following the index date. Study arm for each patient is based on randomization of the linked dental school module or clinic at which the patient was seen.

Handling of missing data in primary aims 1 (Objective 1) and 2 (Objectives 2, 3)

Endpoints for aims 1-3 (Objectives 1-4) are binary indicators from patient surveys. Since the only patients consented for the study are those who complete a baseline survey, it is expected that missing data for the endpoints for H1.1 (Objective 1), H2.1 (Objective 2), H3.1 (Objective 4), H3.2 (Objective 4) will be rare. The endpoint for H2.2 (Objective 3) is binary and will be missing for the estimated 30% not completing the 6 month survey or those who leave the endpoint survey items blank. The approach for handling missing data will depend on the expected mechanism of missingness. Approaches to be considered include conditioning the analysis on characteristic predictive of missing data, and multiple imputation (MI) procedures to accurately estimate parameters across multiply imputed data sets.

12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Study staff will maintain appropriate medical and research records for this study, 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.

13 QUALITY CONTROL AND QUALITY ASSURANCE

Quality Management Plan: The following is a summary of the quality management activities that are planned for each key study activity:

Patient Screening and Enrollment:

Proper screening relies on usual care clinical and administrative EHR data. Follow-up training as need will be conducted for cause or at the request of the providers involved. See Protocol Section 6.10 for detail on how this will be assessed.

Site project managers will be a resource for the EHR managers, vendors, providers and site staff to ask questions during the phases of patient screening and enrollment. The HPI project manager will keep a log of questions and issues encountered and solutions across sites. This will ensure consistency of solutions to problems encountered by providers. The Study Team will also use the log to create a regularly updated 'Frequently Asked Questions' document that will be available to all sites. Quality assurance queries implemented by the vendors and EHR managers to ensure quality data reaches the HPI data store will be developed in the pilot testing phases of the project. Quality management processes and periodic reporting will be continued until all patient and provider follow-up is complete.

Data Collection:

Metrics. All data will be reviewed for completeness and entered electronically within the centralized study database, Accuracy and completeness of the data is maximized through alerts and pop-ups if the data is inconsistent or not entered.

Protocol Deviations. All deviations from protocol will be captured, documented, reviewed and addressed on an ongoing basis to insure integrity of the data.

Monitoring Quality Assurance. Co-Investigator leaders will regularly meet with their site's study staff to discuss study progress and problem solve. The purpose of these meetings is to focus on the day-to-day operations of the project and to assure that all necessary tasks are completed in a timely fashion and strictly according to study protocol. Monthly meetings will include all co-investigators and will address scientific issues, including refinement of conceptual models, strategies to streamline and deploy the interventions efficiently and effectively, and strategies to maximize both recruitment and retention of study subjects, as well as methods to assure uniformity and fidelity to intervention protocols and data collection.

In collaboration with the Survey Research Center and HPI programmer, the HPI project manager and study statistician will develop and provide to the study team and NIDCR regular reports related to subject accrual and data quality to assess the progress of the clinical study, any relevant safety data, and critical efficacy endpoints and provide recommendations to NIDCR.

Data Analysis and Interpretation. All data analyses for presentations and publications will be verified by a "secondary" programmer/statistician for 1) validity of statistical

programming to correspondence with interpretation, and 2) correct and appropriate analytic results (output) presented in presentation and/or publication.

14 ETHICS/PROTECTION OF HUMAN SUBJECTS

14.1 Ethical Standard

The 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 subject materials will be reviewed by the IRB s at the respective involved sites. Approval of both the protocol and the consent forms must be obtained before any provider or patient 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

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to providers and patients

Providers: Consent forms will be mailed and/or emailed or presented in person to potentially eligible providers with contact information provided to allow the prospective subjects to ask questions. Signed provider consents will be obtained and stored by the site-specific project managers per local IRB requirements as well as requirements by the funder.

Patients: Verbal consent will be obtained for patients surveyed by phone by trained HealthPartners Survey Research Center staff.

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

Racial and ethnic minorities will be included in the study at least proportional to the composition in the sites' patient populations. Individuals of any sex or racial/ethnic group may participate. Patients 18 years of age and older will be included in this study. See the Planned Enrollment Table for estimates of the inclusion of racial and ethnic minorities across all sites.

If needed, HealthPartners' Survey Research Center can conduct surveys with monolingual Spanish speakers. Other languages can be accommodated if the need justifies the expansion of Survey Research Center staff.

Other minority groups and special populations are included in this study unless a cognitive or communication disorder prevents completion of the patient telephone consent and survey.

14.5 Subject Confidentiality

Figures 3 of the Visualization Appendix E shows the data flow of the CDS outlining the protective measures to secure patient and provider confidentiality based on a need-to-know principle. Confidentiality will be ensured by assigning an arbitrary and unique subject identification number to each participant. All electronic study data will be maintained in a computerized database residing on a username and password protected-access fileserver to which only the researchers involved in the study will have access. Access privileges will be role-dependent. A crosswalk table linking this code number to a provider and a patient medical record number will be destroyed within 12 months after completion of analyses needed to test study hypotheses. The documented informed consent procedure for providers and student providers will be reviewed in advance, approved, and monitored on an ongoing basis by the 3 participating IRBs. All study related paper documents containing individually identifiable information will be maintained in locked file cabinets within the respective sites secure physically secured research offices.

All recruitment will be conducted in compliance with applicable federal and state laws. Recruitment processes and materials will be approved by each institution's Institutional Review Board (IRB). Each site will oversee the participant protections at each site, which will include compliance with HIPAA regulations.

14.6 Future Use of Identifiable Data

No protected health information (PHI) data will be included in the analytical dataset. Data will be stored within a secure folder on the research server with limited access to project team members for the required timeframe. This study does not involve specimens or genetic testing.

15 DATA HANDLING AND RECORD KEEPING

15.1 Data Management Responsibilities

The investigators in the study will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

15.2 Data Capture Methods

Data Collection. There are four main data instruments for the study: 1. The patient baseline telephone survey conducted 1-7 days after the index dental encounter, 2. The patient 6-month post-baseline telephone survey, 3. The provider survey conducted both pre- and post-implementation, and 4. The instrument used to monitor general adherence to the use of the CDS tool as intended.

Screening. Demographic and tobacco status information verified at the time of the encounter will be used for determining patient eligibility

CDS Data. Tobacco assessment details and documentation of use of SBIRT scripts and patient resources used by providers will be collected electronically at the point of care through a secure web application.

Data collection and accurate documentation will be the responsibility of all study staff under the supervision of Dr. Brad Rindal and Dr. Heiko Spallek, the co-PIs. Unanticipated problems and adverse events will be reviewed by the investigator or designee.

15.3 Types of Data

All provider- and patient-reported outcome measure data will be stored in the secure centralized study database.

15.4 Schedule and Content of Reports

Reports to monitor enrollment rate, adverse events, outcomes, and study conduct will be generated regularly using the centralized study database and discussed at the site meetings, all-investigator meetings and reported to the Medical Monitor and program official as requested.

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 NIH. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

15.6 Protocol Deviations

A protocol deviation is any noncompliance with the clinical study protocol, Good Clinical Practice, or Manual of Procedures requirements. The noncompliance may be on the

part of the subject, the investigator, or study staff. As a result of deviations, corrective actions that address the non-compliance issue have been developed by the study staff and will be implemented promptly. These practices are consistent with investigator and sponsor obligations in ICH E6:

- Compliance with Protocol, Sections 4.5.1, 4.5.2, 4.5.3, and 4.5.4.
- Quality Assurance and Quality Control, Section 5.1.1
- Noncompliance, Sections 5.20.1 and 5.20.2.

All deviations from the protocol will addressed in study subject source documents and promptly reported to NIDCR and the local IRB, according to their requirements.

16 PUBLICATION/DATA SHARING POLICY

Each participating site must execute a data use or data transfer agreement (DUA or DTA) and seek IRB approval at their local site. These steps will ensure that all de-identified data being shared for analysis will be protected. Identifiable data will not be reused, and the de-identified data set will be transferred via a secure file share or encrypted email.

17 LITERATURE REFERENCES

1. Rindal DB, Rush WA, Schleyer TK, Kirshner M, Boyle RG, Thoele MJ, et al. Computer-assisted guidance for dental office tobacco-cessation counseling: A randomized controlled trial. *American Journal of Preventive Medicine* 2013;44(3):260-64.

2. Prevention CfDCa. How tobacco smoke causes disease: the biology and behavioral basis smoking-attributable disease: a report of the Surgeon General. A Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services; 2010.

3. Vital signs: current cigarette smoking among adults aged ≥18 years--United States, 2005-2010. *MMWR Morb Mortal Wkly Rep* 2011;60(35):1207-1212.

4. Services USDoHaH. Healthy People 2010. Washington DC: U.S. Department of Health and Human Services.; 2000.

5. HealthyPeople.gov. Tobacco Use. In: Promotion OoDPaH, editor.

6. Maciosek MV, Coffield AB, Edwards NM, Flottemesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services: results of a systematic review and analysis. *Am J Prev Med* 2006;31(1):52-61.

7. Fiore M, Jaen C, Baker T, al e. Treating tobacco use and dependence: 2008 Update Clinical Practice Guideline. In: Services USDoHaH, editor. Rockville, MD: Public Health Service; 2008.

8. Conroy MB, Majchrzak NE, Regan S, Silverman CB, Schneider LI, Rigotti NA. The association between patient-reported receipt of tobacco intervention at a primary care visit and smokers' satisfaction with their health care. *Nicotine Tob Res* 2005;7 Suppl 1:S29-34.

9. Ferketich AK, Khan Y, Wewers ME. Are physicians asking about tobacco use and assisting with cessation? Results from the 2001-2004 national ambulatory medical care survey (NAMCS). *Prev Med* 2006;43(6):472-6.

10. Quinn VP, Stevens VJ, Hollis JF, Rigotti NA, Solberg LI, Gordon N, et al. Tobacco-cessation services and patient satisfaction in nine nonprofit HMOs. *Am J Prev Med* 2005;29(2):77-84.

11. Shroeder SA. What to do with a patient who smokes. *JAMA* 2005;294(4):482-487.

12. Rindal DB, Rush WA, Boyle RG. Clinical inertia in dentistry: a review of the phenomenon. *J Contemp Dent Pract* 2008;9(1):113-21.

13. Avorn J, Fischer M. 'Bench to behavior': translating comparative effectiveness research into improved clinical practice. *Health Aff (Millwood)* 2010;29(10):1891-900.

14. Schectman JM, Schroth WS, Verme D, Voss JD. Randomized controlled trial of education and feedback for implementation of guidelines for acute low back pain. *J Gen Intern Med* 2003;18(10):773-80.

15. Rohrbach LA, Grana R, Sussman S, Valente TW. Type II translation: transporting prevention interventions from research to real-world settings. *Eval Health Prof* 2006;29(3):302-33.

16. Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* 1993;342(8883):1317-22.

17. Institute of Medicine. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America: Institute of Medicine; 2012.

18. Bandura A. Perceived Self-Efficacy in the Exercise of Control Over AIDS Infection. *Evaluation and Program Planning* 1990;13.

19. Coates TJ, Stall RD, Catania JA, Kegeles SM. Behavioral factors in the spread of HIV infection. *AIDS* 1988;2 Suppl 1:S239-46.

20. Farmer AP, Legare F, Turcot L, Grimshaw J, Harvey E, McGowan JL, et al. Printed educational materials: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2008(3):CD004398.

21. Keller PA, Feltracco A, Bailey LA, Li Z, Niederdeppe J, Baker TB, et al. Changes in tobacco quitlines in the United States, 2005-2006. *Prev Chronic Dis* 2010;7(2):A36.

22. Ebbert JO, Carr AB, Patten CA, Morris RA, Schroeder DR. Tobacco use quitline enrollment through dental practices: a pilot study. *J Am Dent Assoc* 2007;138(5):595-601.

23. Shelley D, Anno J, Tseng TY, Calip G, Wedeles J, Lloyd M, et al. Implementing tobacco use treatment guidelines in public health dental clinics in New York City. *J Dent Educ* 2011;75(4):527-33.

24. Houston TK, Richman JS, Ray MN, Allison JJ, Gilbert GH, Shewchuk RM, et al. Internet delivered support for tobacco control in dental practice: randomized controlled trial. *J Med Internet Res* 2008;10(5):e38.

25. Little SJ, Hollis JF, Fellows JL, Snyder JJ, Dickerson JF. Implementing a tobacco assisted referral program in dental practices. *J Public Health Dent* 2009;69(3):149-55.

26. Babor TF, McRee BG, Kassebaum PA, Grimaldi PL, Ahmed K, Bray J. Screening, Brief Intervention, and Referral to Treatment (SBIRT): toward a public health approach to the management of substance abuse. *Subst Abus* 2007;28(3):7-30.

27. Romito L, Budyn C, Oklak MA, Gotlib J, Eckert GJ. Tobacco use and health risks in two dental clinic populations: Implementation and evaluation of a brief targeted intervention. *Gen Dent* 2012;60(5):e326-34.

28. Gilbert GH, Richman JS, Qvist V, Pihlstrom DJ, Foy PJ, Gordan VV. Change in stated clinical practice associated with participation in the Dental Practice-Based Research Network. *Gen Dent* 2010;58(6):520-8.

29. Lenz BK. Beliefs, knowledge, and self-efficacy of nursing students regarding tobacco cessation. *Am J Prev Med* 2008;35(6 Suppl):S494-500.

30. Schleyer TK, Song M, Gilbert GH, Rindal DB, Fellows JL, Gordan VV, et al. Electronic dental record use and clinical information management patterns among

practitioner-investigators in the Dental Practice-Based Research Network. *Journal of American Dental Association* 2013;144(1).

31. Velly AM, Schiffman EL, Rindal DB, Cunha-Cruz J, Gilbert GH, Lehmann M, et al. The Feasibility of a clinical trial of pain related to temporomandibular muscle and joint disorders: The results of a survey from the collaboration on Networked Dental and Oral Research Dental Pracitice-Based Research Networks. *Journal of American Dental Association* 2013;144(1):e1.

32. Nixdorf DR, Law AS, Look JO, Rindal DB, Durand EU, Kang W, et al. Large-scale clinical endodontic research in the national dental practice-based research network: study overview and methods. *J Endod* 2012;38(11):1470-8.

33. Gilbert GH, Richman J.S., Gordan V. V., Rindal D.B., Fellows J.L., Benjamin P.L., Wallace-Dawson M., Williams O.D. the DPBRN Collaborative Group. Lessons learned during the conduct of clinical studies in The Dental PBRN. *Journal of Dental Education* 2011;75(4).

34. Carr AB, Ebbert JO. Interventions for tobacco cessation in the dental setting. *Cochrane Database Syst Rev* 2006(1):CD005084.

35. Havlicek D, Stafne E, Pronk NP. Tobacco cessation interventions in dental networks: a practice-based evaluation of the impact of education on provider knowledge, referrals, and pharmacotherapy use. *Prev Chronic Dis* 2006;3(3):A96.

36. Kottke TE, Brad Rindal D, Rush WA, Asche SE, Enstad CJ. Persistence of smoking-cessation decision support use in a dental practice. *Am J Prev Med* 2015;48(6):722-8.

37. ADA. 2010 Technology and Social Media Survey; 2010.

38. Atkinson JC, Zeller GG, Shah C. Electronic patient records for dental school clinics: more than paperless systems. *J Dent Educ* 2002;66(5):634-42.

39. Blumenthal D, Tavenner M. The "meaningful use" regulation for electronic health records. *N Engl J Med* 2010;363(6):501-4.

40. Boyle RG, Solberg LI, Fiore M. Use of electronic health records to support smoking cessation (Review). *Cockrane Database of Systematic Reviews* 2011(12).

41. HIT. JASON Task Force Report - Argonaut Project. In; 2014.

42. Corporation JTM. A Robust Health Data Infrastructure. McLean, VA: AHRQ; 2014. Report No.: 14-0041-EF.

43. HealthIT.gov. Nationwide Health Information Network (NwHIN) Power Team.

44. Technology PsCoAoSa. Report to the President and Congress. Designing a Digital Future: Federally Funded Research and Development in Networking and Information Technology; 2010.

45. Kao RT. The challenges of transferring evidence-based dentistry into practice. *J Evid Based Dent Pract* 2006;6(1):125-8.

46. Spallek H, Song M, Polk DE, Bekhuis T, Frantsve-Hawley J, Aravamudhan K. Barriers to implementing evidence-based clinical guidelines: a survey of early adopters. *J Evid Based Dent Pract* 2010;10(4):195-206.

47. Fiore M, Bailey, WC, Cohen, SJ,. Treating tobacco use and dependence: a clinical practice guideline. Rockville, MD: US Dept. of Health and Human Services; 2000.

48. Services UDoHaH. Treating Tobacco Use and Dependence - 2008 Update: Corrections and Additions to the Public Health Service (PHS) Clinical Practice Guideline. In: Services PH, editor. Rockville, md: AHRQ; 2008.

49. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess* 2004;8(6):iii-iv, 1-72.

50. Walker AE, Grimshaw J, Johnston M, Pitts N, Steen N, Eccles M. PRIME--PRocess modelling in ImpleMEntation research: selecting a theoretical basis for interventions to change clinical practice. *BMC Health Serv Res* 2003;3(1):22.

51. Bright TJ, Wong A, Dhurjati R, Bristow E, Bastian L, Coeytaux RR, et al. Effect of clinical decision-support systems: a systematic review. *Ann Intern Med* 2012;157(1):29-43.

52. Thyvalikakath T, Durand E, Spallek H, Enstad C, Asche SE, Rindal DB, et al. Dental hygienists' usage of tobacco-cessation decision support tools in practice: A qualitative study. *International Journal of Evidence-Based Practice for the Dental Hygienist.* 2015;1(1):57-65

53. Rush WA, Schleyer TK, Kirshner M, Boyle R, Thoele MJ, Lenton PA, et al. Integrating tobacco dependence counseling into electronic dental records: a multi-method approach. *J Dent Educ* 2014;78(1):31-9.

54. Irwin JY, Torres-Urquidy MH, Schleyer T, Monaco V. A preliminary model of work during initial examination and treatment planning appointments. *Br Dent J* 2009;206(1):E1; discussion 24-5.

55. AHRQ. Treating Tobacco Use and Dependence. In. Rockville, MD; 2013.

56. AHRQ. Helping Smokers Quit. A Guide for Clinicians. In; 2014.

57. AHRQ. Patients Not Ready to Make a Quit Attenpt Now (the "5 R's"). In; 2012.

58. Hintze J. PASS 11, LLC (using). In. Kaysville, Utah; 2011.

59. MacKinnon DP. Introduction to Statistical Mediation Analysis (Multivariate Appplications Series): Taylor & Francis; 2008.

60. MacKinnon DP, Fairchild AJ, Fritz MS. Mediation analysis. *Annu Rev Psychol* 2007;58:593-614.

61. Ma J, Akhtar-Danesh N, Dolovich L, Thabane L, investigators tC. Imputation strategies for missing binary outcomes in cluster randomized trials. *BMC Medical Research Methodology* 2011;11(1):18.

62. Hennrikus D, Rindal DB, Boyle RG, Stafne E, Lazovich D, Lando HA. How well does the health history form identify adolescent smokers? *J Am Dent Assoc* 2005;136(8):1113-20.

63. Lando HA, Hennrikus D, Boyle RG, Lazovich D, Stafne E, Rindal DB. Promoting tobacco abstinence among older adolescents in dental clinics. *J Smoking Cessation* 2007;2(1):23-30.

64. Thyvalikakath TP, Durand EU, Spallek HS, Enstad CJ, Asche SE, Rindal DB, Rush WA. Dental Hygienists' Usage of Tobacco-Cessation Decision Support Tools in Practice: A Qualitative Study. *International Journal of Evidence-Based Practice for the Dental Hygienist* 2015; 1(1):17-18.
http://www.quintpub.com/journals/ebh/abstract.php?article_id=15410#.WVP7QrnfNk5

SUPPLEMENTAL MATERIALS

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

See Protocol Appendices for relevant supplemental materials.