

# **Factors for Successful Crowns**

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## LIST OF ABBREVIATIONS

AE	Adverse Event/Adverse Experience
CC	Coordinating Center
CFR	Code of Federal Regulations
CI	Confidence Interval
CDM	Clinical Data Manager
CMP	Clinical Monitoring Plan
CNC	Computer numerical control
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DMP	Data Management Plan
FFR	Federal Financial Report
FWA	Federalwide Assurance
GEE	Generalized Estimating Equations
GPI	Grant Principal Investigator
HIPAA	Health Insurance Portability and Accountability Act
ICC	Intraclass Correlation Coefficient
ICF	Informed Consent Form
IDEA	Instrument Design, Evaluation, and Analysis
IRB	Institutional Review Board
MOP	Manual of Procedures
N	Number (typically refers to participants)
NND	National Network Director
NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
OCTOM	Office of Clinical Trials Operations and Management, NIDCR, NIH
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PBRN	Practice-Based Research Network
pCRF	Paper Case Report Form
PVS	Polyvinyl siloxane

QA	Quality Assurance
QC	Quality Control
RAS	Regional Administrative Site
RC	Regional Coordinator
SAE	Serious Adverse Event/Serious Adverse Experience
SMC	Safety Monitoring Committee
SMS	Survey Management System
SPI	Study Principal Investigator
SOP	Standard Operating Procedure
UAB	University of Alabama
UP	Unanticipated Problems
US	United States
VIF	Variance Inflation Factor

## **STATEMENT OF COMPLIANCE**

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

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## SIGNATURE PAGE

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

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## SIGNATURE PAGE- NETWORK STAFF

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

The signature below constitutes:

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

Signed: \_\_\_\_\_ Date: \_\_\_\_\_

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Title: \_\_\_\_\_

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## PROTOCOL SUMMARY

- Title:** Factors for Successful Crowns
- Précis:** This study examines patient, dentist, and laboratory factors associated with the fabrication of successful crowns. Each year, dentists must re-do hundreds of thousands of crowns that are returned from the dental laboratory but are not clinically acceptable. It is not clear why some of these crowns are unsatisfactory. This study will be conducted in two stages. The first stage is a questionnaire that will document current practices among clinicians making crowns, such as material choices and impression techniques. The second stage is a clinical study that will analyze dentist and clinical variables to find predictors for crown success. Data from dental laboratories will also be collected in the clinical study to determine the prevalence of acceptable impressions, crown preparations and jaw relation records sent to labs for crown fabrication.
- Objectives:**
- Primary:* The primary objective of this study is to estimate the percentage of single-unit crowns deemed acceptable by the practitioner at clinical try-in and identify practice/practitioner-, patient/clinical-, and technique- factors associated with crown success. The primary outcome measures are the practitioner rating of crown acceptability and factors that may be associated with crown success, which are grouped into dentist factors (years in practice, region, gender, training); patient/clinical factors (margin depth, tooth location, history of endodontic treatment, hemostasis during impression, factors associated with opposing arch); and prosthodontic factors (impression technique, crown materials, impression materials, margin design).
- Secondary:* The secondary objectives of this study are to:
- Quantify the prevalence of different methods and procedures utilized with crown preparations and explore whether these methods and procedures are associated with practitioner and practice factors, and
  - Estimate the percentage of single-unit crown preparations, impressions, and opposing casts deemed optimal by the dental laboratory, and examine if this laboratory rating is associated with practitioner acceptability and crown success.
- Secondary outcome measures include the following: 1) Methods and procedures utilized with crown preparations and practice/practitioner factors, and 2) the dental lab technician's assessment and acceptability rating of the crown impression and opposing casts.
- Population:** Stage 1: A total of approximately 2,300 National Dental PBRN dentists who reported on their Enrollment Questionnaire that they routinely perform nonimplant restorative procedures will be invited to complete

the questionnaire with the goal of obtaining at least 1,500 eligible respondents.

Stage 2: The goal is to recruit approximately 200 practitioners who completed the stage 1 questionnaire and perform at least seven crowns per month. Prospective data will be collected as each practitioner performs preparations for and places approximately 20 crowns, for a total of 4000 observations (N=4000).

A geographic distribution of National Dental PBRN practitioners is desirable. Clinicians should be able to enroll approximately 20 patients needing single-unit crowns.

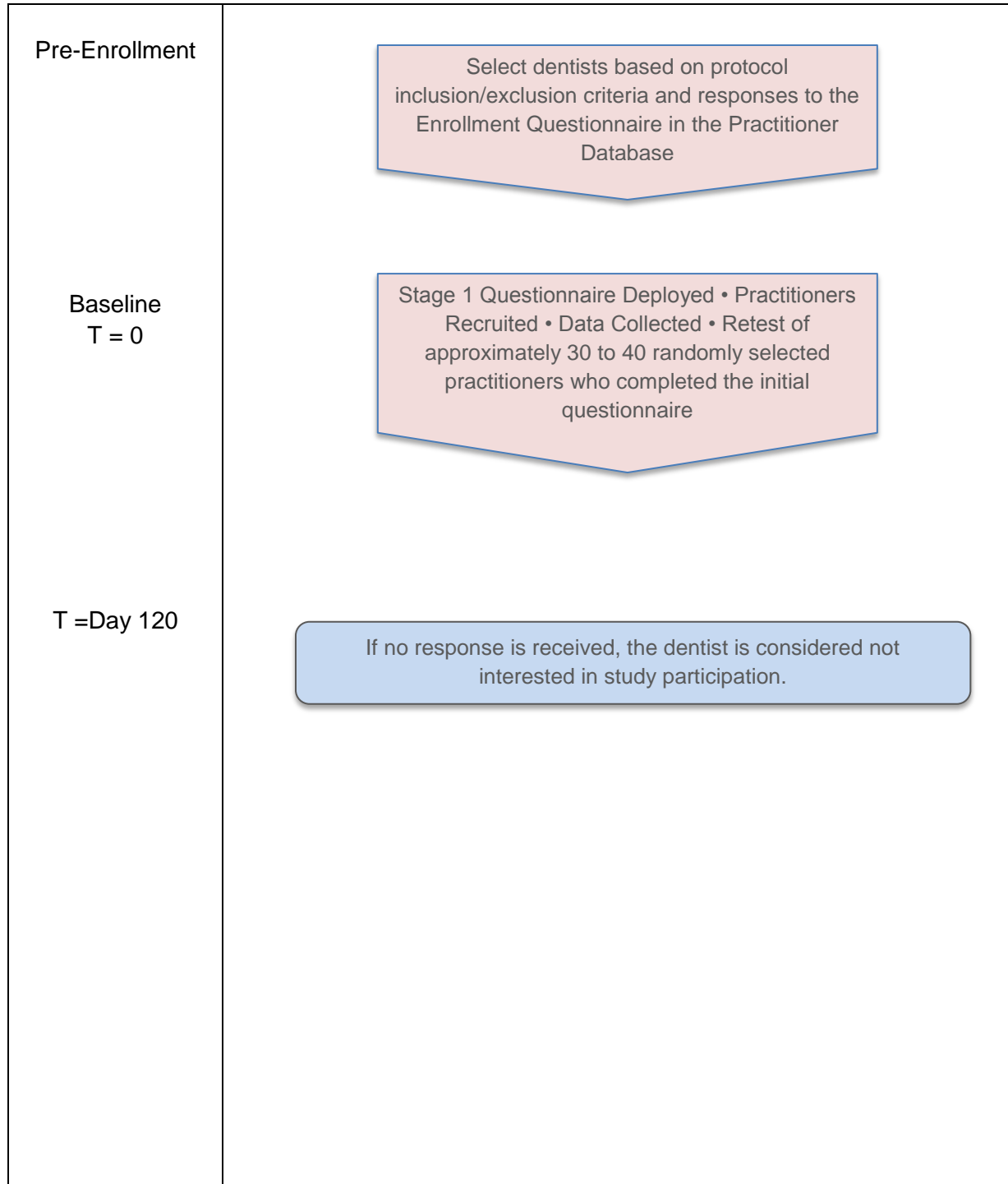
Patients will be recruited from the clinician's family of patients. Adults over the age of 18 needing a single-unit crown on a single natural tooth will be eligible to participate. Implant-supported crowns and fixed bridges are excluded.

Clinicians will be required to identify one or more dental laboratories to also participate in the investigation. Dental laboratories will evaluate technical aspects of the crown preparation (quality of impression, margin finish, occlusal space) and complete a data form on factors about that crown.

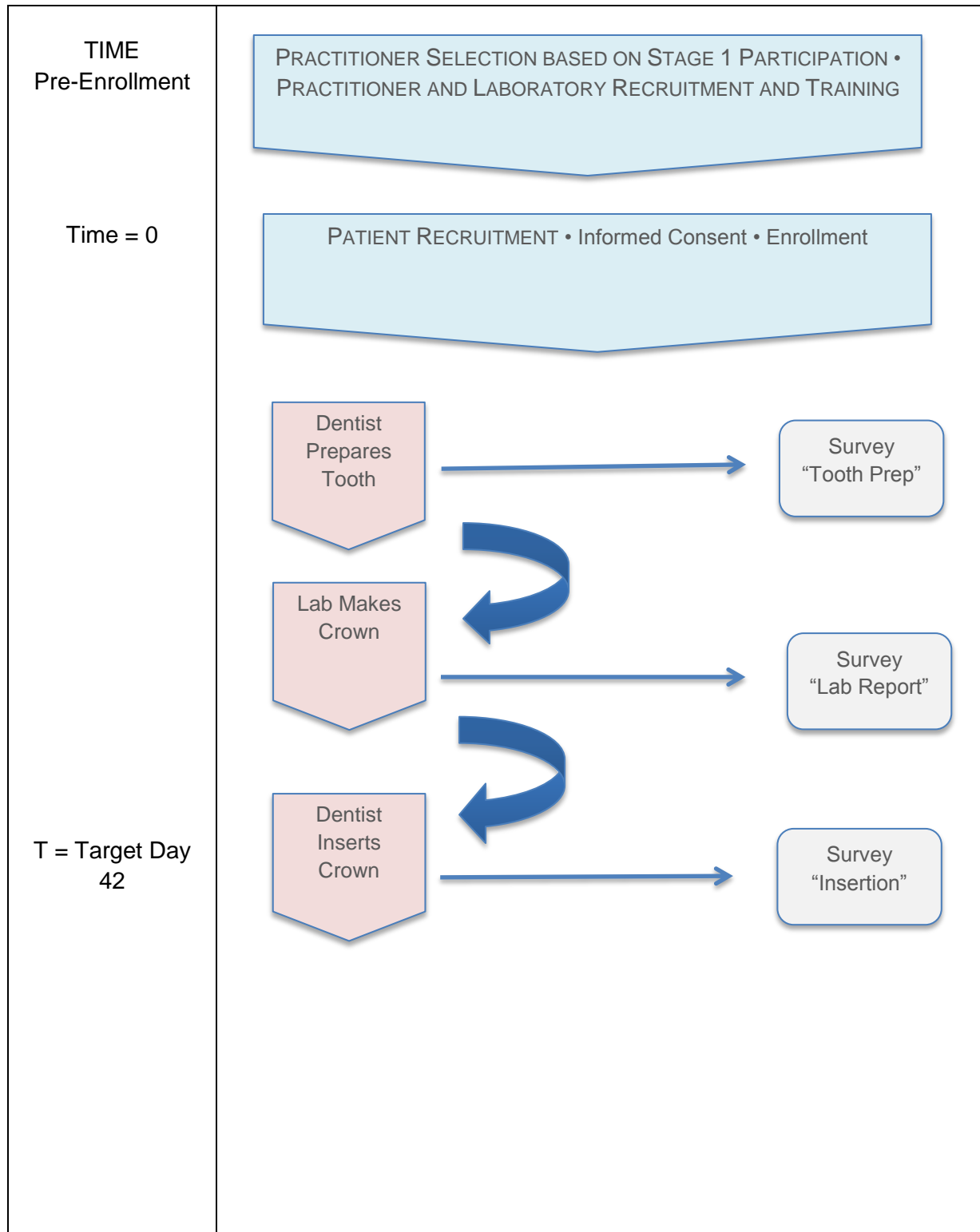
<b>Number of Sites:</b>	Stage 1: N/A Stage 2: 200 National Dental PBRN practitioners
<b>Study Duration:</b>	36 months
<b>Patient Participation Duration:</b>	Stage 2: 1 month
<b>Estimated Time to Complete Enrollment:</b>	Stage 2: 12 months

### Schematic of Study Design:

#### Stage 1: STUDY DEVELOPMENT AND QUESTIONNAIRE ADMINISTRATION



Stage 2: CLINICAL COMPONENT DATA COLLECTION





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## 2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

### 2.1 Background Information

Few things are more clinically frustrating than getting a crown back from the laboratory that is not clinically acceptable. The patient is disappointed, the dentist is disappointed, and the laboratory is disappointed. A new impression must be made, the patient has to wait another three weeks for the crown, and everyone involved is frustrated. Even though we produce 40 million crowns per year in the U.S., many of them must be remade. What are the factors associated with clinical rejection? Is it the fault of the laboratory, or clinician, or somewhere in-between? Can we predict which crowns are more likely to be unacceptable, so clinicians may take more time with them or otherwise improve predictability? Any literature that can reduce our remake rate will be a tremendous benefit to dentists, patients, and laboratories.

The great majority of crowns in the US are made by the indirect method, meaning the clinician makes an impression of the prepared tooth, and sends it to a laboratory to fabricate a crown. Increasingly, a laboratory will scan the model and fabricate a crown using computer numerical control (CNC) milling machines. In other cases, crowns are made by hand, or some combination of machine and technician fabrication.

The process is not perfect. When the crown is returned from the laboratory, the clinician must insert the crown and evaluate the clinical fit. Not only does the crown have to fit well at the edge of the preparation, or margin, but also it has to fit well between the teeth, and the bite must be correct. If any of these aspects are deemed clinically unacceptable, the crown may have to be remade. The remake rate is close to 5%, approximately two million crowns per year, according to proprietary internal data from large commercial laboratories, and from one published article.<sup>(1)</sup>

Common reasons for rejecting a crown are: (1) poor marginal adaptation; (2) poor esthetics; (3) inappropriate contours; (4) unacceptable occlusion (including crown thinness on occlusal surface); (5) poor fit (crown rocks, or won't go on at all); and (6) open proximal contacts.

Common causes for these errors include: (1) inadequate detail in impression; (2) insufficient occlusal reduction; (3) insufficient axial reduction; (4) distorted impressions; (5) poor mounting in laboratory, or incorrect interocclusal record; (6) improper preparation design; (7) poor laboratory work; and (8) unknown factors.

Existing research has focused on one or two aspects of the process of making a crown, rather than a multi-factorial analysis. For example, there are studies comparing impression materials, but they do not control for tooth position or dentist factors.

Cox published a clinical trial evaluating marginal fit of crowns made with double-arch and complete-arch impressions.<sup>(2)</sup> It was a randomized clinical trial, but with only 20 observations. The double-arch technique produced better occlusal accuracy, with no difference in marginal accuracy.<sup>(2)</sup> This was supported by Ceyhan, who analyzed tray type and impression viscosity in vitro using a typodont tooth.<sup>(3)</sup> Another study investigated impression viscosity and tray type clinically, but the outcome was the quality of the impression. The fit of crowns was not

examined.<sup>(4)</sup> Some authors show the dual-arch impression to be clinically acceptable in many circumstances.<sup>(5-7)</sup> Other authors have questioned their accuracy.<sup>(8-10)</sup>

One article examined impressions submitted to a commercial laboratory. It found that 73% were dual-arch impressions, and rated 85% as excellent or good.<sup>(11)</sup> This indicates that much information may be derived from the presentation of impressions in the laboratory and may give insights on why some crowns do not fit.

Another study investigated one- and two-stage impression techniques, but only evaluated the clinical appearance of the impression; the fit of crowns made from these impressions was not investigated.<sup>(12)</sup> One study compared materials (Polyvinyl siloxane (PVS)) using a one-stage impression, finding no difference in the materials tested.<sup>(13)</sup> Another author found a decrease in clinical accuracy using an ultra-light impression material.<sup>(14)</sup>

Factors influencing marginal fit have been well documented. Generally, however, these studies are in vitro. They focus on finish lines,<sup>(15-17)</sup> die spacer,<sup>(18-21)</sup> and cementation techniques.<sup>(20, 22-24)</sup> Also, esthetic outcomes have been investigated clinically.<sup>(25, 26)</sup>

Both the location of the crown margin and marginal fit can influence periodontal health.<sup>(27)</sup> For this reason, clinicians typically reject crowns with “open” margins, or crowns lacking precision of fit at the tooth interface. Marginal fit of crowns can be influenced by the design of the margin. One analysis of extracted teeth shows better marginal adaption of porcelain butt margins compared to feather edge metal margins.<sup>(28)</sup> The location of the margin can be important for acceptable esthetics.<sup>(26)</sup>

One study did examine the incidence of crown remakes in a general dental population.<sup>(1)</sup> After analyzing over 3,000 restorations, the overall remake rate prior to cementation was 4.4%. Of these, 2.8% of remakes were due to color match, 0.8% to misfit, and 0.7% to fractures. This 1% misfit rate seems to be lower than reported by laboratories in general. Color remakes were higher for veneers, as was the overall number of remakes. Neither dentist factors (region, years in practice, gender) nor patient factors (insurance, race, age) were considered in this article.

It is difficult to find any literature relating dentist factors to clinical success of crowns. These would include such items as years of practice, education, and type of practice. Also, patient factors are not well documented in the literature, factors such as gender, socio-economic factors, insurance status, or region. Surprisingly, it is hard to find cohort data even on simple clinical factors leading to crown success, such as tooth position in the arch, type of impression tray used, impression technique, materials, or whether the prepared tooth has adjacent teeth.

## 2.2 Rationale

There is a paucity of clinical literature about factors leading to crown success. Consequently, several critical clinical questions can be answered with further research on this topic. First: does the impression technique used really make a difference in reducing re-makes? Much opinion is expressed on this topic, but it is not based on published evidence. If one impression technique is truly better, it will be an instant practice enhancer for clinicians. Further, if particular situations are associated with crown misfit, clinicians can take care in these situations. For example, the data might show that the most common reason for remakes on second molars is lack of occlusal reduction. Clinicians can then give more attention to this point of preparation and achieve a more predictable outcome. Reducing failure rate and improving the fit of crowns that

are cemented will both have significant impact on oral health. Reducing failure rate may lead to these benefits: (1) reduction in cost of care; (2) reduction in number of visits and time taken off from work or school by patients; (3) reduction in the need to repeat administration of anesthetic during re-preparation of the crown or re-impresion; (4) reduction in need to re-pack gingival retraction cord, with a reduced likelihood of causing gingival attachment loss; and (5) reduction in the length of time that a patient has to wear a temporary crown.

Improving the fit of crowns that are cemented may lead to these benefits: (1) reduction in the likelihood of recurrent dental caries at the interface between the crown margin and the remaining tooth structure; and (2) reduction in the likelihood of localized periodontal disease and its sequelae.

Additionally, this study would be part of an overall network initiative to foster not only research in clinical practice, but also quality improvement. Taking advantage of the fact that the PBRN research context lies in the overlap between research and quality improvement, one means by which the National Dental PBRN seeks to transform clinical practice is to create openness to ongoing self-assessment and quality improvement among dentists. This study should help foster that openness, and may ultimately lead to quality improvement partnerships between dentists and their dental laboratories.

## **2.3 Potential Risks and Benefits**

This is an observational study. Research participants will not receive dental care as a study procedure, but will continue to receive normal clinical care as patients of the participating dentists. Risks of dental procedures provided as part of normal clinical care are not considered to be study-associated.

### **2.3.1 Potential Risks**

Risks for the proposed study are minimal. Practitioners may not feel comfortable answering particular questions on the questionnaire. As such, they will have the option of skipping any question that they do not feel comfortable answering. As with any study, there is the possibility of breach of confidentiality. Appropriate precautions will be taken and procedures will be followed to maintain confidentiality. These include use of unique study codes for participants, encryption of electronic data for transmission to the coordinating center, and password-protected computers for data storage. Compliance with all IRB regulations concerning data collection, data analysis, data storage, and data destruction will be strictly observed.

*Laboratory.* There may be a perceived risk among laboratories in critiquing the clinical work of their practitioners, or a perceived business risk in reporting sensitive data such as remake rates. However, data will only be reported in aggregate, and precautions and procedures will be followed to maintain confidentiality.

### **2.3.2 Potential Benefits**

Participation in the study would provide no direct benefit to participants. Benefits would accrue to society in that information regarding the fuller characterization of crown remakes and treatment outcomes and could enhance care for future patients through evidence-based recommendations for more timely and appropriate interventions.

### 3 OBJECTIVES

#### 3.1 Study Objectives

##### 3.1.1 *Primary Objective*

The primary objective of this study is to estimate the percentage of single-unit crowns deemed acceptable by the practitioner at clinical try-in and identify practice/practitioner-, patient/clinical-, and technique- factors associated with crown success.

##### 3.1.2 *Secondary Objectives*

The secondary objectives of this study are to:

- Quantify the prevalence of different methods and procedures utilized with crown preparations and explore whether these methods and procedures are associated with practitioner and practice factors, and
- Estimate the percentage of single-unit crown preparations, impressions, and opposing casts deemed optimal by the dental laboratory, and examine if this laboratory rating is associated with practitioner acceptability and crown success.

#### 3.2 Study Outcome Measures

##### 3.2.1 *Primary Outcomes*

To estimate the percentage of single-unit crowns deemed acceptable by the practitioner at clinical try-in, the practitioner rating of crown acceptability after being returned from the laboratory for clinical try-in will be ascertained in the Stage 2 portion of the study.

A concern of this outcome measure is that it is not standardized among practitioners. Some practitioners may be very exacting, rating one crown unacceptable that would be accepted by another practitioner. However, the decision about crown acceptability is an important outcome measure for this practice-based research study, regardless of the practitioner's technical ability or clinical bias. Further, each practitioner's "clinical acceptability" level will be ascertained using a question from the questionnaire administered during Stage 1 (before the clinical component) of the study (see Section 7) as well as data from the laboratory CRF analyzing the technical aspects of the crown preparation, impression and bite registration.

To identify factors associated with practitioner acceptability of crowns, the following practice/practitioner, patient/clinical, and prosthodontics technique variables will be ascertained via a Case Report Form (CRF) administered during the crown preparation and impression appointment (during Stage 2), while the practitioner factors will be obtained from the National Dental PBRN enrollment questionnaire:

- **Practice/practitioner factors** (percentage of practice time spent doing fixed prosthodontics; whether or not the practitioner has had prosthodontic, advanced general dentistry residency, or MAGD training; years in practice; network region);
- **Patient/clinical factors** (tooth position; corono-apical position of the crown preparation margin; dentist-assessed quality of hemostasis during the crown impression; endodontic status; whether the crown has proximal contacts; type of tooth opposing the crown); crown preparation design; and

- **Prosthodontic technique factors** (impression technique; impression material; whether the person making the impression is a dentist or a dental assistant; crown preparation design; dentist-assessed quality of the opposing cast and centric jaw relation; material used for the prosthetic crown).

### **3.2.2 Secondary Outcomes**

To quantify the prevalence of different methods and procedures utilized with crown preparations, the following methods and procedures will be ascertained via a practitioner online or printed questionnaire to be completed in the Stage 1 portion of the study:

- Crown preparation techniques;
- Impression techniques and impression materials;
- Materials used to fabricate crowns; and
- Indications for recommending a single-unit crown restoration to a patient.

To explore whether these methods are associated with practitioner and practice factors, the following variables will be collected via the enrollment questionnaire completed by practitioners upon enrolling in the National Dental PBRN or the practitioner online or printed questionnaire:

- Practitioner characteristics: age, gender, race/ethnicity, year of graduation from dental school, specialty status;
- Practice characteristics: Practice size, location, number of patient visits per week, hours of patient care per week, insurance volume;
- The number of different dental laboratories to which the practitioners sends single-unit crowns to be fabricated; and
- Practice busyness. This is a self-reported estimate of the level of patient demand and time available in a practice.

To estimate the percentage of single-unit crown preparations, impressions, and opposing casts deemed optimal by the dental laboratory, the dental lab technician's assessment and acceptability rating of impressions and opposing casts sent to the laboratory will be obtained via a dental laboratory CRF in the Stage 2 portion of the study. The laboratory acceptability rating will be compared with the practitioner acceptability rating.

## 4 STUDY DESIGN

### Stage 1: Questionnaire of approximately 1,500 practitioners.

To be eligible for Stage 1, practitioners must be enrolled in the National Dental PBRN, complete an Enrollment Questionnaire, and report on the enrollment questionnaire that they routinely perform restorative dentistry in their practices.

This practitioner questionnaire component of the study (Stage 1) is a cross-sectional study that is limited to network practitioners who report doing at least some single-unit fixed prosthodontic treatment. A random selection of 2,300 practitioners will be invited to complete an online or printed questionnaire, among all of the estimated 2,785 practitioners who meet inclusion criteria. This questionnaire portion of the study will query use of specific prosthodontics techniques (impression techniques; impression materials; use of digital impressions; materials used for prosthetic crowns, crown preparation techniques; techniques and materials used for hemostasis during impressions; techniques and materials used for bite registration for single-unit crowns; dental cements used for single-unit crowns); clinical scenarios used to describe indications for recommending a single-unit crown restoration to a patient; and the number of different dental laboratories to which the practitioner sends single-unit crowns to be fabricated. Dentists will be informed that the questionnaire may be completed either electronically or on paper.

Development and administration of the questionnaire is detailed in Section 7.1.

### Stage 2. Clinical study of crown fit.

A subset of 200 practitioners will be selected from practitioners who complete the practitioner questionnaire from Stage 1, based upon responses to the questionnaire items. Practitioners will be included from each of the network regions, and region will be included as a stratification variable in all statistical analyses. Data will be collected on practitioner gender, time since graduation, numbers of crowns done each month, remake rates, use of optical impression systems, group vs. solo practitioners, and insurance-based status of the practice. These will be evaluated for possible inclusion in multivariable statistical models for prediction of crown acceptability. Further, practitioners must do at least seven crowns per month to be eligible for the study, pending an adequate distribution of responses to the applicable question on the Stage 1 questionnaire. Each practitioner will be asked to report prospective data about patient/clinical factors during crown preparation and impression and crown insertion appointments and technical aspects of these appointments, with a goal of assessing 20 prepared teeth/crowns. We estimate that approximately 4000 prepared teeth/crowns will be evaluated in this Stage 2 portion of the study. Participating practitioners will be requested to enroll patients until they either 1) reach their enrollment goal of approximately 20 observations, 2) reach the end date for patient enrollment, or 3) decline further participation. They also must confirm the participation of their dental laboratory.

The clinical component is a longitudinal cohort analysis to find associations between practitioner characteristics, patient characteristics, and technical dental factors and crown acceptability rates. Practitioners will complete a case report form (CRF) at the time of tooth preparation, and again at crown insertion. Only single-unit crowns supported by a natural tooth are eligible. The length of participation for each patient will be approximately 3-6 weeks (i.e., the length of time between preparation and crown insertion).

Laboratory evaluation of crowns.

To engage in Stage 2 of the study, practitioners must confirm the participation of their dental laboratories. Practitioners will be asked to contact their lab(s) and explain the study, asking for laboratory participation. Once this is obtained, practitioners will forward their list of participating labs to the Regional Coordinator. The RC will directly confirm (i.e., verbally, email) the participation of the lab and arrange a training session.

Upon receipt of the impression and supporting materials (i.e., bite registration, opposing impression or cast), laboratory technicians will complete a questionnaire about the restoration, in which they will evaluate technical aspects of the impression and preparation. For practitioners using Optical Scanners (e.g. CEREC) along with a commercial laboratory and/or in-office milling, the files will be sent to an independent laboratory technician selected *a priori* for similar evaluation. The questionnaire will be sent directly to the RAS, and the practitioner/practice will not receive information related to individual questionnaire responses.

This portion of the Stage 2 study will attempt to identify factors which may be associated with successful crown fabrication from the perspective of the laboratory technician.



## 5 STUDY ENROLLMENT AND WITHDRAWAL

### 5.1 Inclusion Criteria

#### 5.1.1 Stage 1 (Questionnaire Component) Inclusion Criteria

A practitioner must meet all of the following criteria:

- Is enrolled in the National Dental PBRN as limited or full network members;
- Has completed an Enrollment Questionnaire;
- Is licensed in the U.S. to treat patients, treats patients in the U.S. on a recurring basis and maintains an active practice address at which he or she can be contacted; and
- Performs non-implant restorative (i.e., crowns) procedures routinely in his/her practice as reported on the enrollment questionnaire.

#### 5.1.2 Stage 2 (Clinical Component) Inclusion Criteria

**Patients:** Patients will be recruited from within practitioners' patients. In order to be eligible to participate in this study, patients must meet all of the following criteria:

- Age  $\geq$  18 years old;
- In need of a single - unit crown on a single natural tooth (1 through 32) and willing to have only one crown prepared during the patient's study period; and
- Willing and able to provide informed consent for treatment and return for the crown insertion.

**Practitioner:** In order to be eligible to participate in this study, a practitioner must meet all of the following criteria:

- Is a "Full" participation level member of the National Dental PBRN or willing to change from "limited" to "Full";
- Viewed a National Dental PBRN orientation session or has attended at least one annual regional meeting of practitioners;
- Has completed Stage 1 of the study (clinical crown questionnaire);
- Is a dentist who is licensed in the U.S. to treat patients, treats patients in the U.S. on a recurring basis and maintains an active practice address at which he or she can be contacted;
- Completed all region specific IRB requirements, as needed;
- Performs at least seven crowns per month;
- Affirms that the practice will devote sufficient time to allow for all the study procedures; and
- Confirms the participation of his/her dental laboratory/laboratories. (Practitioners who use optical Scanners (e.g. CEREC) along with a commercial lab and/or in-office milling for either a portion of crown procedures or exclusively are eligible to participate.)

**Laboratories:** Laboratories will be recruited by practitioners. In order to participate, the laboratories must be:

- Willing to complete the assigned evaluations of the crown preparations and other technical aspects of the clinical work;
- Willing to communicate with RCs regarding study expectations, preferably, this communication will occur in English; and

- Willing and able to participate in training with the RC.

## 5.2 Exclusion Criteria

### 5.2.1 Stage 2 (Clinical Component) Exclusion Criteria

**Patients:** Patients meeting the following criteria will be excluded from the study:

- In need of a crown associated with a fixed bridge or supported by a dental implant, without a need for a single-unit crown on a natural tooth.

## 5.3 Strategies for Recruitment and Retention

### 5.3.1 Stage 1 (Questionnaire Component)

Eligible dentists for the Stage 1 questionnaire will be identified based on the criteria noted from their responses on the Enrollment Questionnaire. All eligible dentists will first receive a study invitation email from the CC on behalf of the RC inviting them to participate in the study. The invitation will include a link to the electronic version of the questionnaire. Dentists will have an opportunity to complete an electronic or paper version of the questionnaire in order to increase participation rates. Based on previous regional PBRN questionnaire studies, we anticipate a response rate of approximately 60-70%. Calls will be held as needed with the RCs to review contact information for eligible dentists, discuss recruitment issues and enrollment progress, manage study documentation and procedures, and troubleshoot problems related to enrollment.

Dentists will be reimbursed \$75 for participation in the Stage 1 study. This is a cross-sectional questionnaire study; retention strategies are not applicable.

### 5.3.2 Stage 2 (Clinical Component)

The National Dental PBRN has demonstrated the ability to recruit practitioners and patients for clinical research studies. Since the clinical study is of short duration (approximately three weeks) and there is significant incentive to return (to receive a crown), patient retention is expected to be high. Regardless, the following procedures will be in place to ensure study retention:

- At the time of the crown preparation appointment, a crown insertion appointment will be made within approximately three weeks of the crown preparation appointment.
- If the patient has not returned to the office within four weeks of the crown insertion appointment, the Regional Administrative Site (RAS) will contact the office to investigate the cause of the delay and will work with the dental office to coordinate the follow-up appointment.

Dentists will be reimbursed \$50 for completion of the tooth preparation CRF and another \$25 at crown insertion for the completion of the crown insertion CRF. Dental Laboratory Technicians will be reimbursed \$25 for completion of the Laboratory Evaluation questionnaire. Enrolled patients will not receive any compensation for their participation in the study.

## **5.4 Practitioner and Patient Withdrawal**

### **5.4.1 *Reasons for Withdrawal***

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

### **5.4.2 *Handling of Practitioner and Patient Withdrawals***

Practitioner: Dentists who withdraw from the study will not be replaced.

Patients: Patients who withdraw from the study will not be replaced.

Laboratories: Laboratories who withdraw from the study will not be replaced.

## **5.5 Premature Termination or Suspension of Study**

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party. If the study is prematurely terminated or suspended, the GPI will promptly inform the Institutional Review Board (IRB) and will provide the reason(s) for suspension or termination.

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

- Determination of unexpected, significant, or unacceptable risk to patients.
- Insufficient adherence to protocol requirements.
- Data that are not sufficiently complete and/or evaluable.
- Determination of futility. A power (sensitivity) analysis will be used to track whether loss to follow-up that will occur during the study jeopardizes the validity of the primary outcome measure.

## 6 STUDY SCHEDULE

### 6.1 Stage 1 Questionnaire Component: Enrollment/Baseline

- Eligible practitioners will be identified from responses to National Dental PBRN Enrollment Questionnaire and will be invited to complete an online or printed questionnaire over a period of three to four months.
- Completion of the questionnaire will indicate tacit consent.

### 6.2 Stage 2 Clinical Component: Pre-Enrollment/Screening

#### 6.2.1 Practitioner: Pre-Enrollment

- Practitioner and staff undergo training for the clinical component of the study.
- Practitioner will approach and confirm participation of his/her dental laboratory or laboratories.

#### 6.2.2 Patient: Screening

- Designated office personnel will introduce the study to the potential patient and will verify inclusion/exclusion criteria.

Informed consent, enrollment, examination, and treatment may occur during the same dental visit at which eligibility was confirmed.

#### 6.2.3 Laboratory: Pre-Enrollment

- Participating laboratory technician undergoes training for the clinical component of the study. Completion of the Laboratory Evaluation of Case questionnaire will be conducted.

### 6.3 Stage 2 Clinical Component: Enrollment/Baseline (Time: Day = 0)

#### 6.3.1 Patient: Enrollment

- Verify inclusion/exclusion criteria.
- Initiate consent procedures and document consent from the patient.
- Obtain demographic information on Patient Characteristics CRF.

#### 6.3.2 Practitioner: Baseline

- After the practitioner performs a crown preparation and impression appointment, the CRF "Crown Preparation" is completed by the practitioner for each patient. Practitioners send the crown impression and supporting materials to the lab(s) that have agreed to participate in the study.
- Practitioners using optical scanners (e.g. CEREC) along with a commercial lab and/or in-office milling will send the files to the independent laboratory for review.

## **6.4 Stage 2 Clinical Component: Laboratory Assessment**

### **6.4.1 Laboratory: Baseline**

- Upon receipt and assessment of the crown impression and supporting materials from the practitioner, the dental laboratory technician completes the “Laboratory Evaluation of Case” questionnaire.
- Completion of the questionnaire indicates tacit consent.
- Similarly, technicians at the independent laboratory will complete the questionnaire upon receipt and review of the digital files for practitioners using optical scanners (e.g. CEREC) along with a commercial lab and/or in-office milling.

## **6.5 Stage 2 Clinical Component: Final Study Visit (Time: Target Day 42)**

### **6.5.1 Practitioner: Final Study Visit**

- After the patient returns for the crown try-in appointment, and the crown is either inserted or rejected.
- The practitioner completes the CRF “Crown Insertion”.

## **6.6 Withdrawal**

If a patient decides to withdraw from the study, the date and reason for withdrawal will be recorded on the discontinuation CRF and submitted to the RAS.

## 7 STUDY PROCEDURES/EVALUATIONS

### 7.1 Stage 1 Questionnaire Development and Administration

#### Practitioner Questionnaire Development

This questionnaire was developed by our study team, which had input from dentists, laboratory technicians, and a statistician with content expertise in crown insertions. Following the development of the questionnaire, the instrument was reviewed and evaluated by Instrument Design, Evaluation, and Analysis (IDEA) Services at the CC, a group with expertise in questionnaire development and implementation.

#### Cognitive Interviewing

A pretest was given to eight dentists recruited from a list provided by the National Dental PBRN in the form of cognitive interviews conducted over the telephone. The interviews were conducted by IDEA Services at the CC. Nine practitioners were approached and eight interviews were conducted. General practitioners from five of the six National Dental PRBN regions participated, providing regionally balanced responses. Survey researchers believe that pretesting new surveys can have a substantial positive effect on data quality.<sup>(29-31)</sup> During the interviews, respondents reviewed their responses to a completed questionnaire, and cognitive interviewers probed to assess possible respondent problems in understanding questions, recalling necessary information, and/or reporting accurately. We also asked participating dentists how relevant they think the items in the draft questionnaire were to issues of crown placement, and whether any issues relevant to crown placement were not addressed in the questionnaire. A paper version of the instrument was used during this assessment, because it provided an opportunity to observe if respondents had problems with instructions or any other language in the questionnaire. Results from the pretest resulted in appropriate questionnaire revisions.

#### Questionnaire Testing-Retesting

The online version of the questionnaire will be administered twice to a subset of approximately 30 to 40 practitioners to assess the test-retest reliability of the questionnaire. Practitioners who complete the online version of the initial questionnaire will be sent a second online questionnaire request by email approximately two weeks after receipt of the first completed questionnaire.

Practitioners will be randomly selected for the retest. The selection will be based on the response rate to the initial survey. Each practitioner will be given approximately one week to complete the retest. If the retest is not completed within the timeframe, the link to the retest questionnaire will be disabled. This process will be continued until 30 practitioners complete the retest. The questionnaire will take up to 30 minutes to complete each time.

#### Website and Questionnaire Pilot Testing

The CC's IT team will perform extensive internal testing of the website, including internet browser compatibility. Study team members (e.g., SPI, National Network Director (NND), Regional Directors, Statistician and Regional Coordinators (RC)) will also be given the opportunity to externally test the website prior to administration with study participants.

### Questionnaire Content

The questionnaire includes items to collect the date and assess the outcome measures specified in subsection 3.2. Some information will be collected from the National Dental PBRN Enrollment Questionnaire (e.g., demographics and practice characteristics) and linked to participants' responses to the study questionnaire.

Each practitioner's "clinical acceptability" level will be ranked using a vignette series within the questionnaire. Practitioners will be shown a series of clinical photographs and scenarios of crowns and impressions and asked to rate these as clinically acceptable or unacceptable. As an example, practitioners will be shown a picture of an impression with a small bleb or defect at the finish line, and asked if it is clinically acceptable. These rankings of practitioner exactness will help us interpret the results of the study.

### Questionnaire Administration

Eligible dentists will be identified from their responses to the Enrollment Questionnaire. Although unlikely, responses from dentists who do not meet eligibility criteria but who still are asked to complete the questionnaire will be removed prior to statistical analyses.

A waiver of documentation of signed informed consent for participants who complete the electronic or paper questionnaire will be requested. Consistent with regulations outlined by the University of Alabama (UAB) IRB, information about the study will be provided to all eligible dentists in the postal invitation mailing as well as in the electronic or paper questionnaire prior to the start of the questionnaire questions. Completion of the questionnaire will indicate tacit consent.

The questionnaire will be administered by the CC. An initial study invitation email will be sent to approximately 2,300 eligible practitioners by the CC on behalf of the RCs over a period of three to four months. The invitation will include information regarding the study. A follow-up postal letter on National Dental PBRN stationery will be mailed to inform the dentists that they received an email with a link to the electronic version of the questionnaire to complete. Dentists will be informed that ideally the questionnaire must be completed in one-sitting (although they will be given an option to save and complete the questionnaire at a later time) and that it will take up to 30 minutes to complete. Practitioners will receive multiple reminders to complete the questionnaire. Those who do not respond to email invitations will be mailed paper versions of the questionnaire.

Both electronic and paper versions of the questionnaire will be used to increase participation rates. Practitioners will be encouraged to visit the secure web site to complete the questionnaire. Questionnaires completed on paper will be sent to the CC and entered into the secure web site by CC study personnel.

If no feedback is received or the practitioner does not complete the electronic or paper version of the questionnaire after multiple follow up attempts over a period of three to four months, it is assumed the practitioner is not interested in the study.

## **7.2 Stage 2 Study Procedures/Evaluations**

The practitioner and staff will undergo training for the clinical component of the study. The goals of the study, inclusion/exclusion criteria, CRF and other documentation will be explained. In

addition, the practitioner will approach and confirm the participation of his/her dental laboratory or laboratories.

The laboratory will undergo training for the clinical portion of the study. After participation is confirmed (i.e., email, verbally) by the RC, goals of the study will be explained and training on the study and completion of the Laboratory Evaluation of Case questionnaire will be conducted. Training will detail study goals, provision of tacit consent when completing the questionnaire, and procedures for maintaining confidentiality.

A potential patient may be recruited at any dental visit, not just examination or recall visits. When it is determined that a patient may be eligible for study participation, the designated office personnel trained in human subjects protection will introduce the study to the patient and will ascertain that inclusion criteria are met.

For patients who express interest in participating in the study, a designated office individual trained in human subjects protection will initiate the consent process with the patient and ensure that the consent document has been executed. It is anticipated that in most cases this will be the dentist. At this time patient demographic information will be recorded on the Patient Characteristics CRF and submitted to the RAS.

After entry into the study, a patient will undergo a baseline visit that will involve routine patient care for crown preparation. Data regarding the patient, tooth and clinical environment (after visual assessment of the tooth, supporting structures and occlusion), crown preparation procedure, and impression procedure and materials will be recorded on the “Crown Preparation” CRF for each patient and submitted to the RAS. Then, at the crown insertion appointment, data related to the crown fit and crown adjustments, if warranted, will be recorded. The practitioner completes the CRF “Crown Insertion” and submits it to the RAS.

Practitioners are required to send the crown impression and supporting materials to the lab(s) that have agreed to participate in the study. Upon receipt and assessment of the crown impression and supporting materials (e.g., bite registration, opposing impression or cast), dental laboratory technicians will record data related to technical aspects of the impression and supporting materials on the “Laboratory Evaluation of Case” questionnaire. For practitioners who use Optical Scanners (e.g. CEREC) along with a commercial lab and/or in-office milling, their digital files will be transmitted to an independent laboratory technician to review; this technician will complete the dental laboratory questionnaire. In order to maintain confidentiality of the technicians to allow truthful responses and not intentionally jeopardize the professional/business relationship with the practitioner, the technician (or designee) will mail the completed questionnaire to the RAS.



## 8 ASSESSMENT OF SAFETY

### 8.1 Specification of Safety Parameters

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

#### 8.1.1 *Unanticipated Problems*

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

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

#### 8.1.2 *Serious Adverse Events*

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the patient at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect

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.

### 8.2 Reporting Procedures

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

- Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- A detailed description of the adverse event, incident, experience, or outcome;
- An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an UP;

- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

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

- UPs that are serious adverse events will be reported to the IRB and to NIDCR within 1 week of the practitioner becoming aware of the event.
- Any other UP will be reported to the IRB and to NIDCR within 2 weeks of the practitioner becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the practitioner.

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

- Product Safety Fax Line (US): 1-888-746-3293
- Product Safety Fax Line (International): 919-287-3998
- Product Safety Email: [rho\\_productsafety@rhoworld.com](mailto:rho_productsafety@rhoworld.com)

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

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

## **9 STUDY OVERSIGHT**

Stage 1: The GPI and SPI will be responsible for study oversight, including monitoring safety, ensuring that the study is conducted according to the protocol and ensuring data integrity. The SPI will review the data for safety concerns and data trends at regular intervals, and will promptly report to the IRB and NIDCR any UP, protocol deviation, or any other significant event that arises during the conduct of the study.

Stage 2: In addition to the PI's responsibility for oversight, study oversight will be under the direction of the NIDCR Medical Monitor. The PI will submit a report every 6 months to the NIDCR Medical Monitor for review. This report will include data regarding enrollment and retention, unanticipated problems and protocol deviations, outcome measures, quality management findings and other relevant parameters. If necessary, additional steps may be taken to ensure data integrity and protocol compliance.

## 10 CLINICAL SITE MONITORING

### Stage 1 – Practitioner Questionnaire

Clinical site monitoring will not occur for this survey component of the study. The CC is responsible for launching the survey and collecting data received as part of the survey. Quality assurance (QA)/Quality Control (QC) activities associated with data collection and processing will be outlined in the data management plan (DMP). The CC will ensure that the quality and integrity of study data and data collection are maintained, as detailed in the DMP. The RCs will be responsible for following up with eligible dentists who are considered non-respondents (see Section 6) to encourage study participation.

### Stage 2 – Clinical Component

Clinical site monitoring is conducted to ensure that the rights of human subjects are protected, that the study is implemented in accordance with the protocol and/or other operating procedures, and that the quality and integrity of study data and data collection methods are maintained. The network RAS will be responsible for clinical site monitoring for this study. RCs at each RAS will provide study training to practitioner sites and perform clinical site monitoring activities, to evaluate study processes and documentation based on NIDCR standards and principles of good clinical practice.

Quality management procedures are detailed in the protocol, Section 13 and the National Dental PBRN Manual of General Operations, Section 10. If concerning trends or other issues are identified through quality management activities, For-Cause, in-office clinical monitoring will be conducted. The general guidelines for conducting in-office monitoring for the network's observational clinical studies are documented in the network's Clinical Monitoring Plan in Section 11 of the National Dental PBRN Manual of General Operations. Documentation of monitoring activities and findings will be provided to the practitioner, GPI, and SPI, and aggregate reporting will be provided to NIDCR via [NIDCR\\_Reports@rhoworld.com](mailto:NIDCR_Reports@rhoworld.com). NIDCR reserves the right to conduct independent audits as necessary.

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## 11 STATISTICAL CONSIDERATIONS

### 11.1 Study Hypotheses

Primary objective: (1) Estimate the percentage of single-unit crowns deemed acceptable by the practitioner at clinical try-in, and (2) identify factors associated with crown success.

For this portion of the primary objective, the focus will be on estimation rather than hypothesis testing. We will obtain reliable and precise estimates (as determined by the width of the 95% confidence interval for the estimate) of the percentage of crowns that are deemed acceptable (upon receipt from laboratory and at time of clinical try-in). Second, we will test the hypothesis that there are factors (related to prosthodontic technique, patient/clinical, and practitioner) associated with crown acceptability. The null hypothesis for part (2) of this objective is that there is no association between prosthodontic techniques, patient/clinical characteristics or dentist characteristics and the rating of a crown as acceptable. This hypothesis will be explored using adjusted two-way tables and multivariable statistical models.

Secondary objective: (1) Quantify the prevalence of different methods and procedures utilized with crown preparations, and (2) explore whether these methods are significantly associated with dentist and practice characteristics.

The purpose of quantifying prevalence is for estimation rather than hypothesis testing. We will obtain reliable and precise estimates of the frequency of use of the various methods and procedures listed above. Furthermore, we will examine the relationship between the likelihood of using these methods and the characteristics of the dentist (e.g., age, gender, full-time vs. part-time) and practice (e.g., geographic location, urban vs. rural). The hypothesis is that there are variations in the use of methods and procedures for preparing crowns that are associated with dentist and practice characteristics. The null hypothesis for part (2) of this objective is that differences in dentist and practice characteristics do not explain variation in the use of particular methods and procedures. This hypothesis will be explored using unadjusted two-way tables and multivariable statistical models.

Secondary objective: (3) Estimate the percentage of single-unit crown preparations, impressions, and opposing casts deemed optimal by the dental laboratory, and (4) examine if this laboratory rating is associated with practitioner acceptability.

As the focus for (3) will be on estimate rather than hypothesis testing, estimates of the percentage (and 95% confidence interval) of patients with optimal materials received by the laboratory will be computed. For (4), we will test the hypothesis that the laboratory rating is associated with whether or not the crown is deemed acceptable by the practitioner at clinical try-in. The primary null hypothesis is that there is no association between laboratory rating and whether or not the crown is deemed acceptable by the practitioner at clinical try-in. Additional null hypotheses are that prosthodontic technique factors, patient/clinical factors, and dentist factors are not associated with laboratory ratings of crowns as optimal.

These data will be further analyzed by comparing the prosthodontic technique factors, patient/clinical factors, and dentist factors associated with primary objective (2). We will test the hypothesis that these factors are associated with an increased risk of optimal laboratory ratings.

This hypothesis will be tested using unadjusted two-way tables and multivariable statistical models.

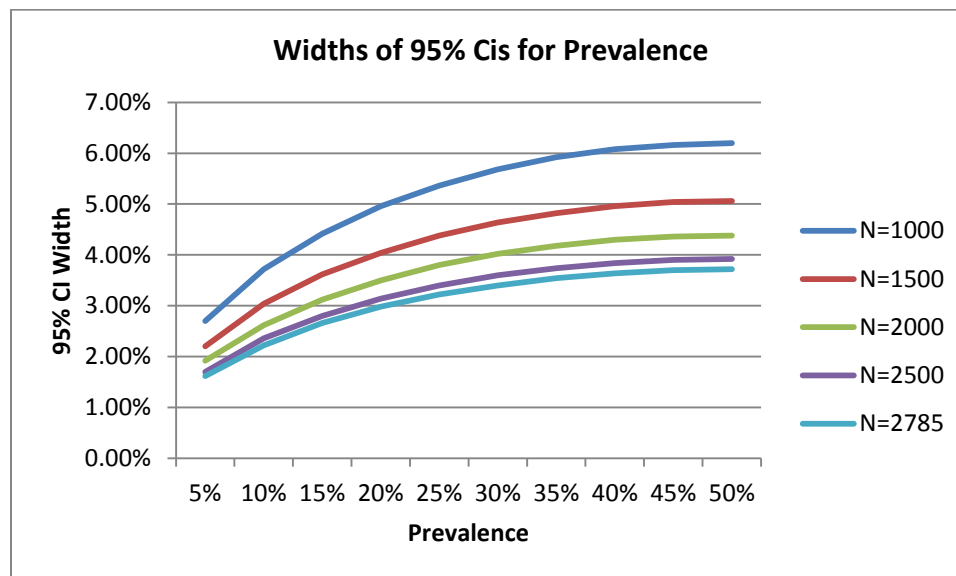
Information collected in Phase 1 of the study on dentist and practice characteristics, methods and procedures used for single-unit crowns and percentage of single-unit crowns deemed acceptable, will be compared between dentists who participate in Phase I only and those who participate in Phase 2. Categorical variables will be compared using the chi-square test, and ordinal or continuous variables will be compared using the t test or Wilcoxon's rank sums test.

## 11.2 Sample Size Considerations

The primary objective (1) and (2) will be addressed using data collected from questionnaires completed by National Dental PBRN practitioners. As of June 2014, there are 2785 practitioners who reported performing nonimplant restorative procedures on the Enrollment Questionnaire. It is anticipated that approximately 1500 practitioners will complete the questionnaire. The primary measures to be calculated are percentages and confidence intervals (CIs) for prevalence of categories of response to the questionnaire items. Precision of estimation for these measures was calculated as the length of 95% CIs for a range of values of prevalence from 5% to 50%. CIs were based on the normal approximation to the binomial distribution. The maximum CI width occurs when prevalence equals 50%, with widths decreasing symmetrically on each side of this value.

Given the anticipated sample size of 1500 questionnaires, the expected total width of the 95% CI would be 5.06%, that is,  $\pm 2.53\%$ . Thus, for any value of prevalence, this sample size would provide sufficient precision to estimate the prevalence within no more than  $\pm 2.53\%$ , at the 95% confidence level. Smaller values of prevalence yield narrower expected CI widths, so that the expected CI widths for prevalence equal to 5% would be  $\pm 1.10\%$  and for prevalence equal to 10%, would be  $\pm 1.52\%$ .

The chart shows the total widths of expected 95% CIs for the proposed sample size of 1500 questionnaires, and for sample sizes of 1000, 2000, 2500 and 2785 questionnaires.



For primary objective (2), power to detect an association between a risk factor and the dichotomous outcome variable indicating an unacceptable crown was estimated using the chi-square statistic. The magnitude of odds ratio that would be detectable with 80% power was calculated for 100, 150 and 200 practitioners, each enrolling 15 or 20 crowns. To account for the reduction in power due to clustering, the effective sample size was used for the calculations. Effective sample size was calculated by dividing the total sample size by a variance inflation factor (VIF), equal to  $1 + (m - 1)\rho$ , where  $m$  is the number of observations (crowns) per cluster (dentist), and  $\rho$  is the intraclass correlation coefficient (ICC). Values of ICC of 0.00, 0.01, 0.02, 0.03, 0.04 and 0.05 were assumed. Prevalence of unacceptable crowns was assumed to be 5%. Prevalence of the potential risk factor in the “unacceptable crown” group was assumed as 50%, in order to provide conservative estimates of power.

Values in the table are odds ratios that would be detectable with 80% power for each combination of numbers of dentists, crowns per dentist and ICC.

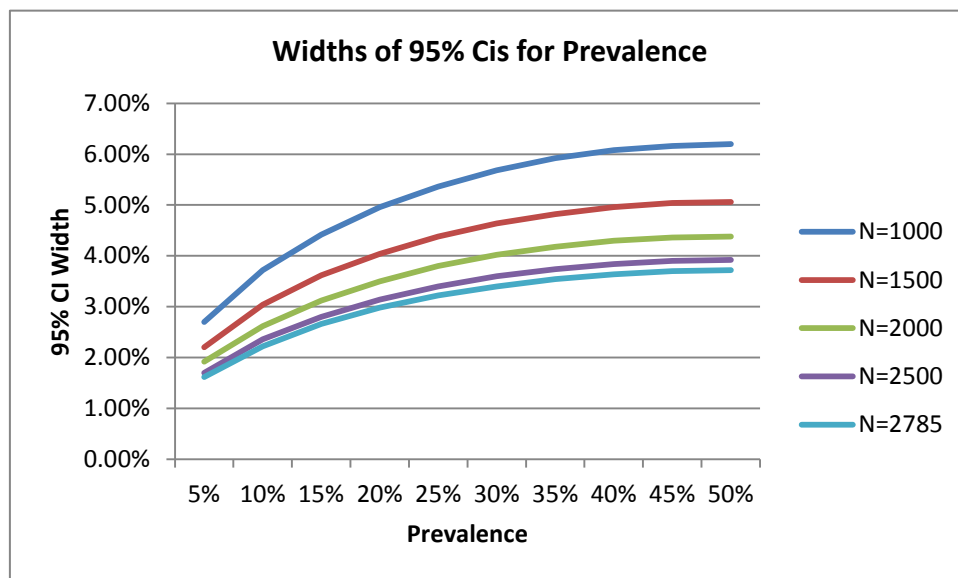
Dentists	Crowns/Dentist	Total Crowns	Intraclass Correlation					
			0	0.01	0.02	0.03	0.04	0.05
100	20	2000	1.78	6.61	1.90	2.08	2.17	2.28
100	15	1500	1.97	2.06	2.13	2.23	2.33	2.39
150	20	3000	1.60	1.69	1.74	1.80	1.90	1.94
150	15	2250	1.72	1.79	1.86	1.92	1.99	2.05
200	20	4000	1.51	1.56	1.62	1.67	1.70	1.78
200	15	3000	1.60	1.67	1.72	1.75	1.82	1.86

The proposed sample size of 200 dentists, each enrolling 20 crowns, would provide approximately 80% power to detect an odds ratio of 1.78 as significantly different from zero, assuming an ICC of 0.05.

The secondary objective (1) and (2) will be addressed using data collected from questionnaires completed by National Dental PBRN practitioners. As of June 2014, there are 2785 practitioners who reported performing nonimplant restorative procedures on the Enrollment Questionnaire. It is anticipated that approximately 1500 practitioners will complete the questionnaire. The primary measures to be calculated are percentages and confidence intervals (CIs) for prevalence of categories of response to the questionnaire items. Precision of estimation for these measures was calculated as the length of 95% CIs for a range of values of prevalence from 5% to 50%. CIs were based on the normal approximation to the binomial distribution. The maximum CI width occurs when prevalence equals 50%, with widths decreasing symmetrically on each side of this value.

Given the anticipated sample size of 1500 questionnaires, the expected total width of the 95% CI would be 5.06%, that is,  $\pm 2.53\%$ . Thus, for any value of prevalence, this sample size would provide sufficient precision to estimate the prevalence within no more than  $\pm 2.53\%$ , at the 95% confidence level. Smaller values of prevalence yield narrower expected CI widths, so that the expected CI widths for prevalence equal to 5% would be  $\pm 1.10\%$  and for prevalence equal to 10%, would be  $\pm 1.52\%$ .

The chart shows the total widths of expected 95% CIs for the proposed sample size of 1500 questionnaires, and for sample sizes of 1000, 2000, 2500 and 2785 questionnaires.



For the secondary objective (3) and (4), precision of estimation of the percentage of crowns rated as unacceptable by the laboratories will depend on the number of laboratories, number of crowns submitted to each laboratory, and the ICC for ratings within the same laboratory. Precision of estimation assumed 200 laboratories, each examining 20 crowns, 5% prevalence of suboptimal ratings, and ICC values of 0.0 to 0.05.

The chart presents half-widths of expected 95% CIs.

ICC	1/2 Width of 95% CI
0	0.68%
0.01	0.74%
0.02	0.79%
0.03	0.85%
0.04	0.90%
0.05	0.94%

The proposed sample size would provide estimation within  $\pm 0.68\%$  to  $\pm 0.94\%$  of a true 5% rate for this range of values of ICC.

Precision of estimation of agreement between ratings by the laboratories and the dentists will be driven by the level of agreement on crowns rated as unacceptable, since this is expected to be only 5% of the total sample. Assuming that 4000 crowns will be evaluated, approximately 200 are expected to be judged unacceptable. Ignoring the effect of clustering, if agreement between dentist and laboratory ratings is 90%, the expected 95% CI would be (85.8%, 94.2%), or estimation within  $\pm 4.16\%$ . For 80% agreement, the expected CI is (74.5%, 85.5%), or estimation



within  $\pm 5.54\%$ . If agreement is 70%, the expected CI is (63.6%,76.4%), or estimation within  $\pm 6.35\%$ .

### 11.3 Final Analysis Plan

**Primary objective:** (1) Estimate the percentage of single-unit crowns deemed acceptable by the practitioner at clinical try-in, and (2) identify factors associated with crown success.

The primary analysis for this aim will utilize generalized linear models to conduct logistic regression analysis, accounting for clustering of observations contributed by the same practitioner. A term representing the individual practitioner will be included as a random effect in the model. Estimation will be conducted using generalized estimating equations (GEE). The outcome variable will be dichotomous, indicating a crown being judged unacceptable by the practitioner.

Blocks of variables representing prosthodontic technique factors, patient/clinical factors and dentist factors will be evaluated as potential predictors of unacceptable crowns. These will be included as fixed effects in the model. Initial analysis will utilize separate models for each of the potential predictor variables. Multivariable models will be constructed using the variables found to be significant in each block and across blocks. These will be evaluated as predictive models for unacceptable crowns.

**Secondary objective:** (1) Quantify the prevalence of different methods and procedures utilized with crown preparations, and (2) explore whether these methods are significantly associated with dentist and practice characteristics.

The methods and procedures that will be included in the questionnaire are (1) crown preparation techniques; (2) impression techniques and impression materials; (3) materials used to fabricate crowns; (4) indications for recommending a single-unit crown restoration to a patient; and (5) the number of different dental laboratories to which the practitioners sends single-unit crowns to be fabricated.

Questionnaire results from approximately 1500 practitioners will be used to estimate frequencies of responses indicating each of the methods and procedures. Point estimates and 95% CIs for percentages of responses for each category will be calculated. The expected numbers of categories for each of the methods and procedures classifications are: three crown preparation techniques; three each impression techniques and impression materials, yielding nine combinations; five crown fabrication materials; and five indications for recommending a single-unit crown restoration to a patient. Additional categories may occur. If substantial numbers of a particular response occur, these will be counted as additional categories. Summary categories including less-commonly-occurring responses may be coded.

The number of different dental laboratories to which a practitioner sends single-unit crowns is expected to range from one to five. The median is expected to be three laboratories. Descriptive statistics will be calculated including the mean and median and corresponding 95% CIs.

Frequencies and percentages of the total responses will be calculated for each category, and 95% CIs will be calculated. A Bonferroni-type adjustment will be applied in order to obtain simultaneous coverage of approximately 95% for all categories of the classification variables.

The associations between use of specific methods and dentist- and practice-level characteristics will be evaluated using contingency tables and multiple logistic regression analysis. Unadjusted odds ratios and chi-squared statistics will be calculated from contingency tables. Logistic regression models including multiple characteristics and adjusting for region will be used to calculate adjusted odds ratios for each of the characteristics.

All valid questionnaire data obtained from the practitioner questionnaire will be utilized in the analyses. Since this is a cross-sectional questionnaire, loss to follow-up is not a consideration. No imputation of missing values will be conducted.

**Secondary objective:** (3) Estimate the percentage of single-unit crown preparations, impressions, and opposing casts that are deemed optimal by the dental laboratory, and (4) examine if this laboratory rating is associated with practitioner acceptability.

This aim will be addressed by calculating the percentage of crowns judged sub-optimal by the dental laboratories. A 95% CI for this percentage will be calculated.

Association with practitioner judgment of acceptability of the crown will be evaluated by including the laboratory rating as a predictor variable in the logistic regression model developed in Primary Objective (1). This will provide an adjusted odds ratio for the laboratory rating, accounting for the other predictive characteristics included in the model. Clustering by practitioner and by laboratory will be accounted for in this model. If the level of agreement between the practitioner and the laboratory is very high, this approach might not be feasible, as the estimation algorithm for the logistic model would be unstable, and would be likely to fail due to lack of convergence. If this occurs, agreement between laboratory and dentist ratings will be calculated separately using Cohen's kappa for each practitioner and a weighted average will be calculated using the number of crown assessments per dentist, in order to obtain a summary measure of agreement.

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## **12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS**

### Stage 1 Practitioner Questionnaire

Source data/documents will be maintained by the CC for this study. The CC will use a survey management system (SMS) to program the electronic questionnaire. Practitioners are sent an email invitation with a direct link to the electronic questionnaire. After a practitioner submits the electronic questionnaire, data will be available in the SMS. Practitioners responding via paper questionnaire will return their completed questionnaires to the CC via a pre-paid, pre-addressed mailing envelope and data entry staff will enter data from the paper questionnaires into the SMS. The system will identify the mode (electronic or paper) of data entry for reporting and tracking purposes.

Only study personnel, i.e., the SPI, NND and CC staff, will have access to these data elements. All research computers and associated study documents will be password-protected. Data files will be kept in a secure, locked file in the SPI's office and at the CC. A copy will also be stored on a password-protected UAB network computer only accessible to the NND.

### Stage 2 Clinical Component

Each participating site will maintain appropriate dental and research records for this study, using the principles of good clinical practice and complying with regulatory and institutional requirements for the protection of confidentiality of subjects. Each site will permit authorized representatives of NIDCR and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity.

The following clinical records will be considered source documents where they are used to complete CRFs: clinical and office charts, memoranda, recorded data from automated instruments, and x-rays.

The following CRFs or portions of CRFs or questionnaire will be considered source documents, as it is not expected that all patients' clinical charts would contain the exact information collected on these CRFs: Patient Demographics CRF, Crown Preparation CRF, Crown Insertion CRF and Laboratory Evaluation of Case questionnaire.

All study source documents must be maintained in a secure manner, and practice personnel and network personnel will have access to source documents. Study source documents may include clinical records and as such are patient to Health Insurance Portability and Accountability Act (HIPAA) regulations. These records will be subject to examination and copying as stated elsewhere in this section.

### **13 QUALITY CONTROL AND QUALITY ASSURANCE**

For the QA/QC activities associated with data collection and processing, the CC will develop a data management plan (DMP) in which the specific data QA/QC procedures will be provided and a Quality Management section in the MOP to further detail the QA/QC process. In the DMP, the procedures will include the development of automatic data quality checks in the database system for both the Stage 1 Practitioner Questionnaire and the patient CRFs and the processes related to the data manual review, discrepancy management, delinquent data handling, data updates, data verification and approval, and database audit.

#### Stage 1 Practitioner Questionnaire

The SPI will work closely with the CC to ensure that the electronic and paper questionnaires are being collected appropriately and confidentially. Conference calls will be held approximately every two weeks during the practitioner questionnaire data collection phase to monitor progress, manage study documentation and procedures, and troubleshoot any problems that may arise. Responses from paper questionnaires will be entered manually by the data entry staff at the CC into the SMS for subsequent data analysis. A 100% review of data entered will be completed, comparing the original paper questionnaire to the SMS data, for accuracy. Discrepancies will be remediated.

#### Stage 2 Case Report Forms

A work instruction will be provided to the RCs at the RAS with the specified tasks, timelines of completing the tasks, roles and responsibilities. The MOP will detail a QA/QC process associated with data collection on pCRFs that will include quality checks at the participating practices, followed by QA/QC review at the RAS prior to and after data entry into the web system. Data entered into the system will be compared against pCRFs. The RAS staff will ensure that discrepancies generated by the system are resolved in a timely fashion based on study requirements. The RAS staff will work with practitioners to clarify any data issues and maintain a tracking log for the data changes. The Data Manager at the CC will work with the RCs to ensure that all procedures are followed and that the data are checked according to the validation requirements specified from the study protocol. At the end of the study, the RCs will ensure that all data collected by the regional offices are entered and cleaned. The Data Manager at the CC will verify the completion of data entry and clarifications by running monitoring reports. Once confirmed that the data entry are complete and the data are verified and approved for accuracy, the database will be locked for final analysis. During the study period, when interim data analysis is needed, the Data Manager will coordinate the activities with the RCs and the Statistician. The interim datasets will be provided with the data collected as of the specified date. The data in those datasets will be cleaned if possible but may contain pending issues, which will be provided to the Statistician if requested. The datasets will be provided to the Statistician via secure data transfer method. The Data Quality Management plan is detailed in Appendix D.

## **14 ETHICS/PROTECTION OF HUMAN SUBJECTS**

### **14.1 Ethical Standard**

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

### **14.2 Institutional Review Board**

This protocol will be reviewed by the National Dental PBRN Central Institutional Review Board (IRB). The UAB IRB for Human Use serves as the National Dental PBRN Central IRB.

Once the local institution has decided to use the National Dental PBRN Central IRB review, the National Dental PBRN Central IRB is the IRB responsible for the review of the protocol. The National Dental PBRN Central IRB then performs all future continuing protocol reviews and amendment (new protocol version) reviews. The Central IRB also reviews unanticipated problems distributed by the Administrative Unit to local institution PIs.

Local institutions have the prerogative to use the National Dental PBRN Central IRB review or conduct their own local review. If an RAS or other local institution elects not to use the National Dental PBRN Central IRB, the protocol, consent form(s) if warranted, recruitment materials and all participant materials will be submitted to the RAS or other local institution IRB for review and approval.

Approval (either centrally for those regions who agree to central approval, or regionally for those who do not) of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

### **14.3 Informed Consent Process**

#### Stage 1 – Practitioner Questionnaire:

A waiver of documentation of signed informed consent for practitioners who complete the electronic or paper questionnaire will be requested. Consistent with regulations outlined by the UAB IRB, information about the study will be provided to eligible practitioners in an initial study invitation letter as well as in the electronic or paper questionnaire prior to the start of the questionnaire questions. Completion of the questionnaire will provide tacit consent.

#### Stage 2 – Clinical Component:

##### Patients

Participating practices will designate who will execute consent procedures for the study. In most cases this will be the dentist practitioner(s). Any personnel who will be assigned to obtain consent will be defined as study personnel and will complete required IRB training. Consent procedures will be obtained in the practice prior to performing any study-related assessments or procedures.

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. The practitioner or designee will explain the research study to the patient, answer any questions that may arise, and discuss risks and possible benefits of study participation, if applicable. If required by the responsible IRB, a consent form describing in detail the study procedures and risks will be given to the patient to read and review or have the document read to him or her. The participant will sign the informed consent document or give verbal approval of the consent process (depending upon central or regional IRB requirements), and a copy of the consent document will be given to the participant for his/her records, if applicable. The consent process will be documented in the clinical or research record. Participants may withdraw consent at any time throughout the course of the study.

#### Dental Laboratory technician

A waiver of documentation of signed informed consent for who complete “Laboratory Evaluation of Case” survey will be requested. Consistent with regulations outlined by the UAB IRB, information about the study will be provided to dental laboratory technicians in a study letter that accompanies the “Laboratory Evaluation of Case” questionnaire, crown impression and supporting materials from the practitioner. Completion of the survey will provide tacit consent.

Laboratories will be assured that all of their responses are confidential, and will not be linked to any particular practitioner. All data will be reported in aggregate.

#### **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 dentist’s patient population. Individuals of any gender or racial/ethnic group may participate. Patients 18 years of age and older will be included in this study. Additionally, pregnant women will not be excluded.

#### **14.5 Participant Confidentiality**

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

Patients will be assigned a unique identification number, which will be used to maintain study records and organize data transcripts. The study monitor or other authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the practitioner, including but not limited to, dental/medical records (office, clinic, or hospital) for the study participants. The clinical study site will permit access to such records.

## **15 DATA HANDLING AND RECORD KEEPING**

The practitioners are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. The practitioners will maintain adequate case histories of study participants, including accurate CRFs, and source documentation. The DMP is detailed in Appendix D.

Only study personnel (i.e., GPI, SPI, Co-I's, RCs, CC personnel) and clinical site monitors will have access to the study data elements in the study database as described in Section 15.3 Types of Data. Study personnel will include those who are on the approved IRB study protocol. All study personnel will have completed the required training elements for human subjects research certification.

### **15.1 Data Management Responsibilities**

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the practitioner. All source documents must be reviewed by the study staff, and data entry staff that will ensure that they are accurate and complete. Unanticipated problems must be reviewed by the practitioner or designee.

#### Stage 2 Case Report Forms

Staff at the RAS will receive paper CRFs (pCRFs) from practitioners and will enter data into the web system. For the pCRFs that are to be used as source documents (see Section 12), the RAS staff will ensure the signature is complete and copies of the forms are maintained at practitioner or regional sites. The RAS staff will ensure the data are entered and the discrepancies generated by the system are resolved in a timely manner based on study requirements. The RAS staff will work with practitioners to clarify any data issues and maintain a tracking log for the data changes. To aid the data collection and data entry activities, the CC will provide pCRF completion and electronic data entry guidelines. Some or all of the pCRFs may also be sent to the CC for data entry by CC staff.

### **15.2 Data Capture Methods**

#### Stage 1 Practitioner Questionnaire

All eligible network dentists will be invited to participate in this study and can use either the electronic or paper version of the questionnaire.

The SMS will ensure that all required data are collected per protocol requirements, and the data fields in the system are checked for completeness and consistency so that data entered into the web system or paper forms can be validated and data errors be corrected. Edit checks will be programmed into the web survey to correct data issues in real time. Reports or tools will be developed to help monitor the data activities. The reports with the summary of the data completion will be made available on the network web site if requested.

The paper forms will be sent to the CC staff for data entry and maintained at the CC securely. The CC staff will ensure that all paper forms received are entered in the SMS in a timely manner and the data entered are accurate as they are captured on the paper forms.

### Stage 2 Case Report Forms

Patient data will be collected via pCRFs. Study-specific pCRFs will be developed to include fields for all data elements required for participant and laboratory assessments. A Web-based data collection system will ensure that all required data are collected in the study database. Data fields in the database will be programmed to allow only certain values and ranges thus data entered in the web system can be validated and data errors be corrected. Reports and tools will be developed to help monitor the visit and data activities. The reports with the summary of the data completion will be made available on the network web site.

After the paper data collection has been completed for a patient, the study materials for the patient may be placed in the participant's research file. The patient log will be consulted to obtain the name of the patient corresponding to the study ID number printed on the CRF so that the practitioner can cross-check information on the study form with the patient's dental chart. Questions about the data will be resolved by conferring with the staff member(s) who completed the CRF.

### **15.3 Types of Data**

Data for the study consist of the following:

- Practitioner level data from the enrollment questionnaire
- Practitioner responses to the electronic or paper Stage 1 practitioner questionnaire
- Patient demographic information
- Stage 2 practitioner crown preparation/insertion assessments
- Stage 2 laboratory crown impression and insertion assessments

### **15.4 Schedule and Content of Reports**

#### Stage 1 Practitioner Questionnaire

Reports to monitor enrollment will be produced by the CC every two weeks during Stage 1 and will be provided to study team and NIDCR for review. The contents of the report will include a summary of data collected to date by key characteristics and/or regions.

#### Patient Participation

Reports to monitor patient enrollment will be produced by the CC every two weeks during the Stage 2 enrollment period, until all targets are attained and enrollment is closed. These reports will also contain separate sections for each region, with information regarding patient accrual by site and will be provided to study team and NIDCR for review.

Reports to assess study retention will be produced by the CC every two weeks during Stage 2. These reports will provide ongoing monitoring of patient retention. Retention data will be closely monitored, and futility analyses will be performed as needed. In addition, a report will be produced for each individual practice that includes the practice's attrition rate and a comparison to the overall attrition rate for the study. These reports will be provided to study team and NIDCR for review and will be made available to the practitioners.

Study progress and interim analysis reports that address objectives will be produced at the discretion of the CC Statistician, in consultation with the SPI, and other study team members. The content of these reports will be determined by the CC Statistician, in consultation with the SPI, and other study team members.



The procedure for locking the database prior to final analysis will be detailed in Section N of the study DMP, in accordance with the Westat CCs *SOP DSD-001: Development of a Data Management Plan* (see Appendix D) and *SOP DSD-405: Data Lock*. Briefly, the SMS and OC data will be locked and the final SAS datasets will be generated at the end of the study. Prior to locking the database, the Clinical Data Manager (CDM) or designee will ensure all data is complete and clean. Then, the CDM will obtain approval from the Project Manager to proceed with the data lock. The CDM will then direct the Database Development Manager to lock the database. The date and time of database lock will be documented. All team members will receive written notification from the CDM or designee when the database lock is complete. No masking or coding is anticipated for this study.

### **15.5 Study Records Retention**

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

As outlined by IRB regulations, data will be destroyed in an appropriate and safe way after three years from the conclusion of the study. The file connecting subjects' names with their unique identification number will be kept in a password-protected file by the CC and on the GPI's computer for a minimum of three years, in accordance with IRB regulations, before being securely erased.

### **15.6 Protocol Deviations**

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

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

## 16 PUBLICATION POLICY

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

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## **APPENDICES**

- Appendix A: Stage 2 Schedule of Evaluations
- Appendix B: Patient Retention Plan
- Appendix C: Quality Management Plan
- Appendix D: Data Management Plan

### APPENDIX A: Stage 2 Schedule of Events

Procedures	Baseline Study Visit T= Day 0	Dental Laboratory Baseline Visit	Final Study visit T= Target Day 42
Informed Consent of Patient <sub>1</sub>	X		
Assessment of Eligibility Criteria <sub>1</sub>	X		
Obtain or confirm contact information and preferred method of contact <sub>1</sub>	X		
Visual assessment of the tooth, supporting structures and occlusion, crown preparation, impression, possibly bite registration and opposing impression. Completion of the Crown Preparation CRF. <sub>1</sub>	X		
Send crown impression and supporting materials to dental laboratory <sub>1</sub>	X		
Completion of Laboratory Evaluation of Case questionnaire (tacit consent provided by the dental laboratory technician) <sub>2</sub>		X	
Patient returns for crown try-in appointment and the crown is either inserted or rejected. Completion of the Crown Insertion CRF. <sub>1</sub>			X

<sub>1</sub> performed by the practitioner

<sub>2</sub> performed by the dental laboratory technician

## Appendix B: Patient Retention Plan

This Patient Retention Plan provides an outline of the issues associated with patient retention and the procedures for maximizing retention during the course of the Factors for Successful Crowns study. High retention rates increase the validity and generalizability of study data by ensuring that bias due to incomplete follow-up of patients does not affect study findings.

Retention of patients is a multifaceted problem. Difficulties with maintaining complete follow-up can be due to a variety of causes. It is important to identify and delineate the different types of retention issues because the way to address them will depend on the type. The four types of retention issues are:

**Lost:** Patients move and their new location cannot be found.

**Missing Data:** Patients still within the practice but follow-up visit is missed or data are not collected during visit.

**Refused:** Patients decide they no longer want to continue participating in study.

Below the National Dental PBRN describes the plans for addressing each of these retention issues. Also provided are other administrative and design methods that will help to increase retention rates.

### Methods to Minimize “Lost”

- 1) At patient enrollment, emphasize study requirements to patients:
  - a. They are part of study with a follow-up visit.
  - b. Practitioners will contact them by telephone to arrange follow up visit for crown insertion.
  - c. RCs will contact practitioners and patients by telephone to assist in arranging follow-up visits or determine other reason for being lost.
  - d. Entry criteria will include the ability and likelihood of maintaining participation throughout the study.
  - e. Collect information on:
    - i. Home address
    - ii. Home telephone number
    - iii. Cell phone number
    - iv. E-mail address(es)
    - v. Contact information (including cellular telephone and email) of one person who do not live in the same household as the patient and who will know of the patient’s whereabouts.
- 2) During the two study visits, confirm contact information (of patient and a contact person).
- 3) The patient’s preferred method of contact (e.g., postal mail, email, telephone) will be ascertained at the baseline appointment. Experience has shown that it is personal relationships, both between the patients and offices, and the offices and the RCs, that promote successful execution of PBRN studies. In other words, it will be more meaningful for patients to hear from their personal dental offices regarding a reminder

for a study recall appointment. In turn, it will be more meaningful for the office to hear from its RC that it is time for them to contact patients. Experience has shown that it is beneficial for the network to relieve burden on the practices. To that end, the National Dental PBRN will request IRB approval for the RCs to receive the patient contact information and the contact information of one person who does not live in the same household as the patient, so that they can assist the practices with follow-up contacts (e.g. visit reminders, etc), particularly with patients who have had difficulty attending the follow-up visit.

- 4) The process for contacting patients for the final visit will be for the practice to make the initial contact attempts, then inform their RC if there was no response within four weeks of the first contact attempt. Initiating tracking procedures promptly when there is no patient response to contact attempts will minimize missed study visits and also minimize loss to follow-up.

#### Methods to Minimize “Missing Data”

- 1) Ask participating offices to develop a system to flag records of patients in their practices who are participating in the study, as well as to flag study patients in the office schedule. In this way, study personnel will be alerted to the fact that the patient is at the office, and can ensure that data collection takes place if indicated. Flagging the patient in the schedule will help to ensure that patients are not inadvertently scheduled when the practitioner will not be in the office. In the same way, if a patient’s record is requested by another office, study personnel can inform the RC and attempts made to maintain the patient in the study.
- 2) Streamline final visit data collection.
- 3) Ask the practitioners to set aside specific time for final visit assessments.
- 4) Emphasize to practitioners as part of their initial study packages that the dentist has to be the motivational director of the study, especially regarding follow-up appointment, and make sure that the staff understands that the office is committed to taking the study on and seeing it through to completion.

#### Methods to Minimize “Refused”

- 1) The method described in the 1<sup>st</sup> point above under “Lost” will also help reduce the number of patients who refuse to continue participating. At enrollment, patients are informed that they are agreeing/consenting to participate in a follow-up study. Patients who enroll are required to state a willingness to participate throughout the study.
- 2) The method described in the 3<sup>rd</sup> point above under “Lost” (making contact between visits) should also help reduce refusals. The CC has found that retention is increased if patients are kept engaged and interested in the study through the use of periodic newsletters and other study updates, postcards, birthday cards, phone calls, using the patient’s preferred mode of contact. Additionally, follow-up involvement will be kept as light and convenient for the patient as possible.



### Other Administrative and Design Methods To Increase Retention Rates

- 1) IRB/Informed Consent Considerations to Reduce Attrition
  - a. Incorporate into the informed consent form permission for all relevant study personnel, both in the dentist's office as well as the study investigators, and RCs to contact the patient. This will allow communications with the patient by study personnel without having to go through the dental office.
- 2) Financial, but non-coercive incentive to patients to encourage continuing participation.

### Additional Methods for Patients who Miss the Final Study Visit

- 1) The practitioner's office will use the contact information to attempt to contact the patient by telephone (or other preferred means of contact) to schedule the final study visit in a timely fashion, or remind the patient of the visit.
- 2) If successful in contacting the patient, there will be special emphasis on reminding the patient of the importance of his/her participation in the study and the importance of complying with the study visit.
- 3) If the patient cannot be reached, the individual designated as an additional connection to the patient will be contacted to confirm the patient's contact information and/or determine the patient's whereabouts and additional attempts will be made to make contact with the patient.

## Appendix C: Quality Management Plan

This Study Quality Management Plan organizes the plans for QA/QC across the Factors for Successful Crowns Protocol Study Timeline and Study Activities. Some of the planned QA/QC is described in the main text of the protocol. Specifically, the QA/QC for Data Collection and Management is described in Section 13 above. The Patient Retention Plan in Appendix B is also a key component of QA/QC of patient recall visits. The Data Management Plan described in Appendix C below will contain the specific plan for Quality Management of Data Collection and Management.

The following is a summary of the QA/QC activities that are planned for each key study activity:

1. **Practitioner Recruitment, Training, and Enrollment:**
  - a. The RCs who will be recruiting practitioners within each region will work with the practitioners to assure that they understand the expectations of them for the study and assure the quality of practitioner recruitment and enrollment.
  - b. The Study Manager will ensure the proper enrollment of practitioners and their locations' study personnel into the IRB system. Through this activity, the Study Manager will also provide QA/QC of the recruitment across regions according to the protocol and procedures, and will help troubleshoot recruitment/enrollment issues.
2. **Patient screening and enrollment:**
  - a. Proper training of the practitioners and study personnel at the practitioners' locations by the RC on the protocol and procedures as outlined in the study Manual of Procedures (MOP) is a planned QA activity. This will assure that the practitioners are ready to conduct the patient screening and enrollment in accordance with the protocol.
  - b. The RC will be a resource for the practitioners and study personnel to ask questions during patient screening and enrollment. The Study Manager will keep a log of problems encountered and solutions across regions and RCs. This will assure consistency of solutions to problems encountered by practices across RCs and Regions. The RC will also use the log to create a regularly updated 'Frequently Asked Questions' document that will be available to all practices, so that they have a resource for finding information and solutions for commonly encountered problems.
  - c. As the practitioners and each practice are anticipated to be busy dental practices, the study is designed to provide the practitioners with extensive support of the RC, the Study Manager, and the CC. Where possible, QA/QC will be assisted by or performed by the RC, the Study Manager, or the CC to allow the practitioner efforts to be focused on patient enrollment and follow-up.
3. **Patient Follow-up:**
  - a. The QA/QC activity described under 2b above will be continued until all patient follow-up is complete.
  - b. Further QA/QC of patient follow-up is described in the Patient Retention Plan in Appendix B.
4. **Data Collection:**
  - a. The Study Manager will perform a QC review of the data collected on the first patient enrolled by each practitioner after the enrollment visit and provide

feedback to the RC, practitioner, and practice. This early QC is a key component of assuring the quality of data collection at the practice, and data entry at the RAS.

- b. Further details regarding QA/QC of data collection are contained in Section 13 and Appendix D.
5. **Data Analysis and interpretation:**
- a. All data analyses for presentations and publications will be verified by “secondary” programmer/statistician for 1) validity of statistical programming to correspondence with interpretation, and 2) appropriate analytic results (output) are correctly presented in presentation and/or publication.
6. **Manuscript Writing, conference presentations:**
- a. The National Dental PBRN has a Publications and Presentations policy. The SPI will assure that this policy is followed for any manuscripts and conference presentations. This policy assures the quality of all National Dental PBRN manuscripts and presentations through the requirement of specific quality control steps prior to publication of any manuscript or other external publication/presentation. Specifically the policy requires review and approval of manuscripts and presentations by the Publications & Presentations Committee.

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## Appendix D: Data Management Plan

The Study has Standard Operating Procedures (SOPs) which require the development of a DMP for each project for which the CC provides Data Management services. The CC SOPs require that the DMP be developed according to a standard template containing the following sections, where applicable:

- Section A: Protocol Summary, Estimated Time to Complete Enrollment, Study Objectives
- Section B: Definitions And Acronyms
- Section C: Roles/Responsibilities Of Key Organizations
- Section D: Case Report Forms (CRFs)
  - D.1: CRF Development Or Review
  - D.2: CRF Completion Instructions
  - D.3: CRF/ CRF Completion Instructions Revisions
- Section E: Database/Systems Development
  - E.1: Clinical Database
  - E.2: Safety Database
  - E.3: Randomization Database
  - E.4: Imaging System
  - E.5: Electronic Data Loading System
  - E.6: Other Database Or DM System
  - E.7: Database Security/Back Up
- Section F: Training
  - F.1: Paper CRF Completion
  - F.2: Clinical Database/Data Entry
  - F.3: Other Database Or Data Management System
- Section G: Data Processing Of CRF
  - G.1: CRF Receipt And Tracking
  - G.2: Data Entry
  - G.3: Scanning/Imaging
  - G.4: Filing
  - G.5: Data Processing Of Study-Related Documents (Non-CRF)
- Section H: Receipt And Processing Of Electronic Data
- Section I: Medical Coding
- Section J: Data Quality/Data Cleaning
  - J.1: Edit Check Development
  - J.2: Manual Review Development And Process
  - J.3: Discrepancy Management Process
    - J.3.1: Discrepancy Review And Resolution Codes
  - J.4: Study Assumptions/SECS
  - J.5: Delinquent Data
  - J.6: Data Updates
  - J.7: Verification/Approval Functions In OC-RDC
- Section K: Data Reconciliation
  - K.1: Imaging System Reconciliation
  - K.2: Safety Data Reconciliation
  - K.3: Randomization Data Reconciliation

- Section L: Database Audit
- Section M: Reports/Metrics
- Section N: Data Lock
  - N.1: Locking The Data
  - N.2: Unlocking The Data Or Data Updates Post Lock
  - N.3: Data Unblinding
- Section O: Data Transfer
  - O.1: Preparation
  - O.2: Transmission
  - O.3: Schedule
- Section P: Database Close-Out/Archive
- Section Q: Attachments And References