1) Abstract of the study

This protocol describes activities that are a part of a clinical trial grant (U01) application by the investigators to the National Institute of Dental and Craniofacial Research (NIDCR) examining an internet-based cognitive-behavioral treatment (I-CBT) for patients of the Temple University Kornberg School of Dentistry (TUKSoD) who suffer from significant dental anxiety. This is a 5-year clinical trial that will evaluate the efficacy of a brief I-CBT for the treatment of impairing dental anxiety among those seeking dental care at the clinics of TUKSoD.

The study will be a randomized controlled trial in which patients seeking services at the TUKSoD Faculty Practice Clinic who screen positive for dental anxiety will be provided with I-CBT under the supervision of psychology clinicians highly trained in CBT techniques versus dental assistants with minimal training designed specifically to prepare them to supervise the delivery of the I-CBT protocol to anxious dental patients. Patients (N=550) will be randomized to one of these two arms of the study or to a third (control) arm in which participants will be asked to view a video of nature scenes for a period of time equivalent to the dental anxiety intervention. The dental care provider for all participants will also be informed of their scores on the dental anxiety screening measure. Demonstration of relatively equivalent efficacy of the I-CBT treatment when provided by dental assistants versus more highly trained psychology personnel will facilitate the dissemination of I-CBT for dental anxiety to dental offices in a sustainable way that would allow greater access for a larger number of potential patients with dental anxiety.

Initial assessments will be conducted in the few weeks preceding patients' already-scheduled appointments for dental treatment at TUKSoD. Patients meeting inclusion and exclusion criteria will then be offered I-CBT or the control intervention, to occur immediately prior to their scheduled dental treatment appointment. Efficacy based on primary outcome measures (e.g., reduction from baseline on self-rated and clinician-rated measures of dental anxiety/fear) and secondary outcome measures will be examined at assessments one and three months thereafter. Some additional interview ratings will be gathered from patients after they complete the dental anxiety intervention and after they complete the pursuant dental treatment appointment, and one brief questionnaire will be administered six and twelve months later. Finally, we will examine the impact that the intervention may have on attendance at scheduled dental appointments over the next 12 months.

2) Protocol Title

Efficacy of an Internet-based intervention for dental anxiety

3) Investigators

Marisol Tellez, PhD, Associate Professor, Chair, and Residency Director, Pediatric Dentistry and Community Oral Health Sciences, Maurice H. Kornberg School of Dentistry, Temple University

Eugene Dunne, PhD, Assistant Professor, Department of Oral Health Sciences, Maurice H. Kornberg School of Dentistry, Temple University

4) Objectives

The primary goal of human subjects activities described in this protocol is to evaluate the efficacy of the Internet-based intervention for dental anxiety among patients presenting to the participating clinic(s). To achieve this overall goal, we propose 3 primary objectives:

Objective 1**:** We will compare the efficacy of I-CBT as administered by personnel with training and experience in CBT to the efficacy of the intervention as administered by dental assistants who have undergone a brief but specific training in the administration of the intervention, a goal which would allow the greater dissemination of this intervention. We will also examine within-group reduction of anxiety at assessments one and three months after the administration of the intervention.

Objective 2**:** We will compare the efficacy of the intervention, administered either by CBT personnel or dental staff, to an active control condition, the viewing of the control video and the notification of the dental provider of the patient's score on a measure of dental anxiety before the dental appointment.

Objective 3**:** We will examine the impact that the intervention has on attendance at scheduled dental treatment appointments over the next 12 months.

Secondary Objectives:

We will examine whether I-CBT has similar effects on related measures (pain sensitivity, anxiety sensitivity, distress tolerance, symptoms of specific phobia of dental procedures, blood-injury-injection phobia, sleep disturbance and sleep-related impairment, functional impairment due to dental anxiety, and consumer satisfaction) at one- and three-month follow-ups.

We will also examine whether the Internet-based intervention reduces anticipated and perceived pain and anxiety during dental procedures in immediately pursuant appointments for dental treatment.

We will also examine whether baseline levels of distress tolerance and pain sensitivity moderate the efficacy of the dental anxiety intervention.

5) Rationale and Significance

Dental anxiety (i.e., anxiety related to undergoing dental procedures) is a major public health concern, as it leads to underutilization of dental care and poor oral health. Approximately 10-20% of individuals in the US endorse significant dental anxiety, and 10-50% cancel regular dental care appointments or delay treatment for a painful dental condition due to fears of dental procedures (Sohn & Ismail, 2005). Patients with dental anxiety are more likely to be referred for nitrous oxide sedation (Boyle, Newton, & Milgrom, 2009) and use emergency dental services (Kanegane, Penha, Borsatti, & Rocha, 2003), both of which increase individual and public dental healthcare costs. Dental anxiety has been consistently associated with increased oral health problems and impairment (e.g., more cavities; Armfield, Stewart, & Spencer, 2007). Few studies have examined the efficacy of psychological treatments for dental anxiety (Gordon, Heimberg, Tellez, & Ismail, 2013), and most of the existing empirically supported psychological interventions cannot be easily disseminated within dental healthcare settings, as they must be administered by highly trained clinicians over a number of sessions. Therefore, it is the goal of our ongoing research program to develop a brief online therapy for dental anxiety that could be easily implemented in dental clinics, allowing for broader dissemination.

Dysfunctional thoughts about dental treatment are central to dental anxiety (Armfield & Heaton, 2013). Many anxious patients think that dental treatment will be extremely painful, that something catastrophic will go wrong during treatment, that the dentist will make a mistake, and that the dentist or others will be judgmental about the state of one's oral health (De Jongh, Muris, Schoenmakers, & Horst, 1995; Moore, Brødsgaard, & Rosenberg, 2004). High physiological arousal is also prominent in dental anxiety. Dental anxiety is positively associated with elevated heart rate, blood pressure, and cortisol levels during dental procedures (Brand, Gortzak, & Palmer-Bouva, 1995). Patients with dental anxiety often delay or avoid dental treatment, which can cause dental problems that require invasive treatment, and, in turn, lead to the maintenance or exacerbation of dental anxiety (Armfield et al., 2007).

CBT techniques are efficacious at reducing dental anxiety and avoidance among adult patients acutely and at follow-up (Gordon et al., 2013). Repeated, graduated exposure to feared dental procedures is a key component of CBT for dental anxiety (Gordon et al., 2013). Cognitive techniques, relaxation, and the provision of detailed information about dental procedures meant to increase patients' sense of control over dental care also appear to reduce dental anxiety and avoidance (Gordon et al., 2013). Although CBT has consistently demonstrated efficacy at managing dental anxiety and dental phobia, rates of dental treatment avoidance have seen only a slight reduction, anxiety treatment is underutilized, and the prevalence of dental anxiety remains high (Choy, Fyer, & Lipsitz, 2007). A major reason that CBT for dental anxiety has not been widely disseminated is that most existing therapy protocols require delivery by a highly trained professional (Gordon et al., 2013). The development of brief, easily disseminated CBT interventions is an important step toward combating dental anxiety and reducing its public health costs.

Computerized or online CBT offers promise as a practical, and potentially efficacious, modality for dental anxiety treatment. Computerized CBT protocols have demonstrated efficacy comparable to conventional CBT in the treatment of mood (e.g., Berger,

Hämmerli, & Gubser, 2011; Christensen, Griffiths, & Jorm, 2004) and anxiety disorders (e.g., Hedman, Andersson, Ljótsson, & Andersson, 2011; Wims, Titov, & Andrews, 2010). One recently published randomized controlled trial found that a computerized exposure-based therapy for dental injection fear reduced self-reported injection-specific dental anxiety when compared to a control group receiving a psychoeducational pamphlet (Heaton, Leroux, Ruff, & Coldwell, 2013). However, the intervention only targeted dental injection fear. Therefore, further empirical investigation of computerized/online therapy interventions for dental anxiety, as well as development of interventions that address anxiety related to a broad array of dental procedures, are needed. We have developed such an experimental intervention and hope to continue its evaluation in this clinical trial.

A single-session computer-based 60-minute CBT intervention has been developed by our group over the last few years, which is administered to patients immediately in advance of an appointment for dental care. It consists of psychoeducation, considering the benefits/drawbacks of working on dental anxiety, cognitive restructuring skills, and graduated exposure to feared dental procedures. It begins with the psychoeducation module, during which the patient is provided with basic education about the nature of anxiety, with an emphasis on dental anxiety. The psychoeducation module reviews anxiety-related topics such as understanding the physiological, cognitive, and behavioral (e.g., avoidance) components of anxiety; how anxious thoughts can be reframed into coping thoughts; rating one's subjective level of anxiety; and the rationale behind exposure to feared situations. These topics are specifically connected to anxiety about dental procedures, and patients are also provided with information about the presence and typical manifestation of dental anxiety. Next, patients are guided through a decisional balance exercise that helps them consider the benefits and drawbacks of learning to cope with their dental anxiety.

Thereafter, patients are guided through the exposure exercises, which are supplemented with opportunities to learn and practice cognitive restructuring skills. First, patients are asked to select their three most feared procedures from a list of six types of dental procedures (drilling and having a cavity filled, typical cleaning, anesthetic injection, root canal, oral X-ray, and tooth extraction) and rank the three procedures from least to most anxiety-provoking. Patients then watch videos of their feared procedures, starting with the least anxiety-provoking and working up to the most anxiety-provoking. For each selected procedure, three videos, each about 4 minutes long, are presented: (1) The first video depicts a dentist and/or hygienist simulating the procedure with an actor playing the role of a patient. Animations of aspects of the procedure that occur within the mouth are included, as are close-ups of the dental tools employed. The voiceover explains the basics of the dental procedure, including how the dental tools are used. This video is intended to help the participating patient develop a greater sense of control over what is happening to him/her in the dental chair by providing increased knowledge about the procedure. (2) The second video presents similar visuals of the dental procedure, but is more focused on the patient's face and his/her emotional experience during the procedure. The voiceover presents a dialogue between the narrator and the patient as if it were occurring in the patient's head; they discuss the patient's negative thoughts and the tools of cognitive restructuring applied to these thoughts. This video provides a second exposure to the feared procedure and

basic training in the nature and use of cognitive coping skills. (3) The third video was filmed from the perspective of a patient in the dental chair and provides additional and more intensive exposure to the feared dental procedure. The voiceover is a “dialogue” between the acting patient in the video, who presents cognitive coping from a self-administered/self-help perspective, and the participating patient, who is led through the steps to develop coping thoughts to counter his/her own anxious thoughts. The intervention closes with a brief module providing additional motivational enhancement for attending future dental appointments. Upon completing the intervention, patients attend their scheduled dental appointment and are encouraged to use the skills they learned from the intervention to cope with any anxiety they experience during that appointment.

The computer-based intervention was piloted on a sample of six dental patients from the TUKSoD Clinics (Potter et al., 2016). All patients completed the experimental intervention and attended their appointment for dental care, and 5/6 were contacted and re-assessed after one month. Three patients demonstrated clinically significant reductions in dental anxiety, and the remainder demonstrated lesser improvements. We next conducted a randomized controlled trial of the experimental intervention in comparison to a waitlist control condition (N = 151; Tellez et al., 2015). The computer-based intervention resulted in greater declines in dental anxiety, and clinician ratings of dental fear and avoidance were also markedly reduced. Among those who met criteria for dental phobia at baseline, a larger percentage of treated patients no longer did so after the treatment interval than was the case for patients assigned to the waitlist condition. Patients who received this computerized dental anxiety intervention reported high levels of satisfaction (83% were “very satisfied”).

We have converted this computer-based intervention to one that can be administered online. In terms of content, it is identical to the intervention described above, but it is no longer dependent on its being resident on the hard drive of a specific computer. In our previous R34 planning grant (a smaller grant required by the NIDCR before an investigator can apply for a full-scale clinical trial grant), one of our objectives was to determine the feasibility and acceptability of this more accessible but less tested form. Findings from the planning grant indicated that this online intervention was indeed acceptable and feasible as administered by psychology personnel to patients attending dental appointments at TUKSoD. It was also the case that before the planning grant, the intervention, while efficacious, had only been administered with the assistance of psychology doctoral students or post-baccalaureate research assistants, all of whom were quite knowledgeable about cognitive-behavioral interventions and treatments for anxiety disorders more generally and who were highly trained in the administration of this protocol. We saw this as a barrier to the intervention’s ultimate adoption or dissemination into dental offices. Findings from the planning grant suggested that the online intervention was equally efficacious when in the hands of dental assistants who were trained for the specific task but who lacked the depth of background knowledge about psychological treatments in general.

In the current trial, we aim to extend these findings by examining the efficacy of I-CBT as administered by psychology personnel compared with dental personnel in a larger sample of 550 patients. We also aim to evaluate whether the I-CBT, as administered by

both psychology and dental personnel, is better than an active control condition. We hypothesize that I-CBT will have a stronger impact on dental anxiety than the active control condition. We also hypothesize that the intervention will be as efficacious when delivered by dental assistants who have undergone a brief but specific training in the administration of the intervention as it is when administered by personnel with experience in CBT based upon prior research on Internet-based interventions for other disorders (Shandley et al., 2008) and our small-scale open trial conducted as part of the R34 project.

6) Resources and Setting

The human subjects activities for this clinical trial will take place at TUKSoD. Patients with dental anxiety will be recruited from the TUKSoD Faculty Practice Clinic (If it appears that we will fall short of enrollment milestones, additional patients will be recruited from among those receiving dental treatment at the Graduate Clinics of TUKSoD: Endodontology, Periodontology, and Advanced Education General Dentistry. See attached letters from the Directors of these clinics.). The administration of the online dental anxiety intervention will take place in the Center for Public Health Research (CPHR) of TUKSoD, which is the research laboratory of one of the study investigators, Dr. Tellez. This is precisely the arrangement that was utilized in the conduct of the randomized controlled trial (Tellez et al., 2015) and in the R34 planning grant described above.

Beyond CITI training, all psychology personnel involved in the human subjects aspects of the current protocol will be highly trained in the relevant activities, which involve the administration of the online dental anxiety intervention, administration of interviews and questionnaires, conducting screening/assessment/follow-up phone calls, and the management of data. Psychology personnel will either (1) have been members of the research team for the previous clinical trial, for which most procedures will be quite similar and will have received training and practice with non-patient research assistants acting as patients in the specific details of the operation of the program, or (2) they will be persons of similar levels of training (postdoctoral fellows in clinical psychology, staff psychologists, or advanced clinical psychology doctoral students). Most of the treatment in service of the first objective will be administered by a postdoctoral fellow or clinical psychology doctoral student. Other research assistants who currently conduct solicitation calls for ongoing studies of dental anxiety will do so for the proposed protocol as well.

A post-baccalaureate study coordinator with a background in psychology or a related field will perform many important tasks for the U01 project. After appropriate training, the study coordinator will conduct the bulk of the initial telephone screening interviews. He/she will also conduct diagnostic interviews at baseline and one-month and three-month follow-up assessments and track attendance at scheduled dental appointments for the 12-month period following the dental anxiety intervention. He/she will also complete reliability ratings for diagnostic interviews conducted by other study staff, providing full coverage of this activity with the graduate student. The study coordinator will also be charged with the rating of treatment fidelity/adherence of a portion of the

interventions completed during the U01 project. The study coordinator will also conduct a range of data entry and management activities.

The dental staff for the proposed U01 will be two or more part-time dental assistants or expanded function dental assistants as defined in the State of Pennsylvania working with Dr. Tellez at TUKSoD (one full-time equivalent). They will be trained in the administration of the Internet-based dental anxiety intervention by a psychologist, postdoctoral fellow, or doctoral student highly trained in CBT and the specific online intervention, and they will administer the dental anxiety intervention to those patients randomly assigned to the arm of the trial in which the intervention is delivered by dental staff. They will also assist in the payment of study subjects and other day-to-day tasks when these activities cannot be performed by the post-baccalaureate study coordinator.

7) Prior Approvals

See attached letters of support from the Directors of the Faculty Practice Clinic and the Graduate Clinics of TUKSoD.

8) Study Design

a) Recruitment Methods

Approximately 550 patients will participate in this research, roughly evenly divided between the three arms of the study.

Participants will be patients who have scheduled an appointment for non-emergent dental care at the Faculty Practice Clinic at TUKSoD (recruitment will be expanded to include the Graduate Clinics if needed to meet recruitment milestones). All such persons' names and telephone numbers will be entered into the Faculty Practice Clinic's scheduling software as part of standard operating procedure, and the study coordinator will have access to this information. Potential participants will be contacted by telephone and asked if they would be willing to be screened for dental anxiety and, if so, if they would be interested in the possibility of participating in a study of the treatment of dental anxiety (See attached "Guidelines for Introducing the Study"). In addition to contacting patients who are already in the dental school scheduling software, we will also display study materials in the waiting area of the clinic. Fliers containing contact information and a brief description of the study will be displayed on waiting area tables and posted at available locations within the clinic. Small cards with a brief description and contact information will also be available for patients to take with them. This will provide the opportunity for patients to reach out to research staff directly to express interest in participating. Recruitment materials will also be made available within the clinic offices where patients receive their dental care. Dental care providers may hand a patient an information card, but will not explain the study or actively recruit the patient. Providers will be instructed to direct any patients questions to the study coordinator or other research study staff. Approved study staff will periodically make rounds through the waiting areas of clinics that are being actively recruited from. They will greet participants

and follow an approved script to gauge interest and provide a brief overview of the research study. If interested in participating, patients can reach out to study staff directly via phone or email. Additionally, if participants prefer to be contacted directly, they can provide their information via a contact form. Information will be collected on a separate form for each patient, rather than a running list, to maintain the privacy and personal information of interested patients. All recruitment methods will utilize the same screening process and eligibility requirements for study enrollment.

If the potential patient responds that they would not be interested, the interviewer will thank the patient for his/her time and terminate the call. If the patient responds affirmatively (i.e., gives verbal consent for the brief screening), the interviewer will first ask one screening question (age) and then administer the Modified Dental Anxiety Scale (Humphris et al., 1995), which is the primary screening measure of dental anxiety employed in this study (see attached measures file for specific questions). The interviewer will also ask whether the patient experiences impairment as a result of dental anxiety. If the patient fails to meet these screening criteria or appears to be insufficiently fluent in English, the interviewer will thank the patient for his/her time and terminate the call. If the patient meets criteria for dental anxiety and impairment, the interviewer will then administer the Medical Screening Interview, and if the patient meets any exclusion criterion based on that interview, the call will be similarly terminated. If not, the interviewer will provide more extensive information about the study and the risks and benefits of study participation (see attached “Summary Consent Script to be Read During Screening Phone Call”), and verbal consent for full study participation will be obtained. If the patient is still willing and appears to meet inclusion/exclusion criteria as outlined above, he/she will be scheduled for a second (“pre-intervention” or “baseline”) interview and questionnaire administration. Patients will be randomized to one of three arms as described above.

To assist in recruitment and retention, we will focus on strategies that we utilized in our recently completed randomized controlled trial for the computer-based version of the intervention and others that we believe to be useful based on that experience with the same patient population. These will include reminder calls and text messages the week before, the day before, and the day of appointments as well as patient payments for completion of assessments ($75 for completion of screening/baseline assessments and initiation of the in-clinic visit, $50 for completing each of the follow-up assessments). We will coordinate closely with the front office staff of the Faculty Practice Clinic in assuring that we are fully aware of patient-initiated schedule changes and to minimize the likelihood that the dental treatment appointment will not be pushed back or rescheduled by the dental treatment staff without advance notice (an issue that arose at times in the conduct of the trial of the computer-based version of the intervention).

Inclusion and Exclusion Criteria

Inclusion criteria will require that the patient endorse high dental anxiety (a total score of 19 or a score of 4-5 on at least 2 of the 5 items) on the Modified Dental Anxiety Scale (Humphris et al., 1995), endorse at least mild impairment as a result of that anxiety at the screening interview, be between 18 and 75 years of age, and be sufficiently fluent in

written and spoken English in the judgment of project staff that the patient would be able to benefit from the intervention and validly complete the assessments.

Exclusion criteria are the following: (a) a self-reported currently uncontrolled medical condition (e.g., heart attack, seizure disorder) that might make exposure to anxiety-evoking stimuli inadvisable; or (b) inability to give informed consent. Participants will not be excluded on the basis of gender, ethnicity/race, or other demographic characteristics, nor will they be required to meet criteria for a formal diagnosis of dental phobia.

b) Study Timelines

- This clinical trial will last for a period of 5 years
- The first 6 months will be devoted to recruitment and training of staff.
- Patient recruitment is estimated to take up to 45 months, with the final enrollee completing follow-ups 3 months later (and monitoring of their attendance at dental appointments continuing for 9 additional months).
- Participants will complete assessments at baseline, day of intervention, and at 1-month, 3-month, 6-month, and 12-month follow-ups. Total participation time for each patient is approximately 12 to 13 months but could be slightly longer pending the interval between screening/baseline and the scheduled date of the dental anxiety intervention/dental appointment. Only brief (5-item) assessments will be conducted at 6- and 12-month follow-ups.
- The last six months will be devoted to major data analyses and the preparation of manuscripts in addition to the ongoing monitoring of attendance at dental appointments.
- The date of the award was August 1, 2018, and we hope to have completed all activities by July 31, 2023.

c) Study Procedures and Data Analysis

Study Schedule

Screening (Time 0)

Until we have ascertained our sample, all patients who have scheduled appointments for non-emergent dental procedures through the TUKSoD Faculty Practice Clinic will be contacted by research staff, who will briefly explain the purpose of the study and obtain verbal consent to conduct a brief dental anxiety and medical screening (See attached "Guidelines for Introducing the Study"). If the potential patient responds that they would not be interested, the interviewer will thank the patient for his/her time and terminate the call. If the patient responds affirmatively, the interviewer will first ask one screening question (age) and then administer the Modified Dental Anxiety Scale (Humphris et al., 1995) and ask whether the patient experiences impairment as a result of dental anxiety. If the patient fails to meet these screening criteria or appears to be insufficiently fluent in English, the interviewer will thank the patient for his/her time and terminate the call. If the patient meets criteria for dental anxiety and impairment, the interviewer will then

administer the Medical Screening Interview, and if the patient meets any of the exclusion criteria based on that interview, the call will be similarly terminated. If not, the interviewer will provide more extensive information about the study and the risks and benefits of study participation (see attached "Summary Consent Script to be Read During Screening Phone Call"), and verbal consent for full study participation will be obtained. If the patient remains interested, he/she will then be offered the opportunity to schedule an appointment for the pre-intervention assessment session. Note that recruitment will be expanded to include the TUKSoD Graduate Clinics [Endodontology, Periodontology, Advanced Education General Dentistry] if needed to achieve enrollment milestones.

Enrollment/Baseline (Time 1)

The interviewer will administer the specific phobia module of the Anxiety and Related Disorders Interview Schedule for DSM-5 (ADIS-5) - Adult Version (Brown & Barlow, 2014). Questionnaires specified in Table 1 (Measures and Timing of Their Administration) will also be administered by the interviewer over the phone. Alternatively, for those patients with Internet access and who prefer to use it, the questionnaires can be completed online through the use of an online data collection service.

Senior research staff will administer the randomization of participants (computer generated). The file will be secured and restricted to the time of randomization. Randomization will be done after the patient has received the consent summary, all baseline assessments are completed, and there are no further concerns about exclusion criteria. At that time, the study coordinator will be instructed to make an appointment for the Clinic Visit (Time 2), but the patient's randomization condition will not be revealed until the patient has arrived at the clinic and in-person informed consent procedures are completed.

Intermediate Visits (Times 2 and 3)

A more thoroughly detailed version of the consent form used during the initial telephone contact will be given to the patient on his/her arrival for the Time 2 appointment, any further questions will be addressed. Electronic informed consent will be obtained at that time using Adobe Acrobat. An electronically signed copy of the consent form will be provided to the patient via email, and another signed copy will be placed in the patient's research record. The dental anxiety intervention will then be administered (or filler activities will be completed for active control participants). Immediately upon the completion of the intervention and immediately after the completion of the following scheduled dental appointment (Times 2 and 3, respectively), debriefing interviews will be administered. These are described in the section on Study Procedures/Evaluations below.

Follow-up Visits (Times 4 and 5)

Time 4 is the follow-up contact one month (i.e., 4-5 weeks) after the day of the dental anxiety intervention and the scheduled dental appointment. This is the first opportunity for an in-depth follow-up assessment, and the full list of assessments administered at

the pre-intervention assessment session will be re-administered. This includes the ADIS-5 interview, amended to include some debriefing questions as described above, and all questionnaires including the Client Satisfaction Questionnaire (CSQ-8). This session will be scheduled as an in-person visit, with both interview and questionnaires completed in the research offices. However, if logistical barriers or scheduling difficulties arise, the session may be conducted by telephone. In that circumstance, questionnaires may be administered over the phone or online.

Time 5 is the follow-up contact three months (12-15 weeks) after the day of the dental anxiety intervention and the scheduled dental appointment. The full list of assessments administered at the pre-intervention assessment session will be re-administered. This includes the ADIS-5 interview, amended to include some debriefing questions as described above, and all questionnaires including the CSQ-8. This session will be scheduled as an in-person visit, with both interview and questionnaires completed in the research offices. However, if logistical barriers or scheduling difficulties arise, the session may be conducted by telephone. In that circumstance, questionnaires may be administered over the phone or online. This assessment is identical to the one at Time 4. Brief (5-item) assessments will also be conducted by phone or online at 6- and 12-month follow-ups. Attendance at dental appointments will continue to be monitored until 12 months have passed since the day of the dental anxiety intervention.

Study Procedures/Evaluations

A table is provided below which lists the measures to be administered and the timing of their administration:

Table 1. Measures and Timing of Their Administration

Measure	Initial Screen	Baseline Assess-ment	Dental Anxiety Intervention/ Index Dental Appointment	1-mo Follow-up	3-mo Follow-up	6-mo Follow-up	12-mo Follow-up
Modified Dental Anxiety Scale	X	X		X	X	X	X
Medical Screening Interview	X						
Anxiety and Related Disorders Interview Schedule-5 Specific Phobia Module		X		X	X		
Post-Dental Anxiety Intervention Debriefing Interview			X				
Post-Dental Appointment Debriefing Interview			X				
Pain Intensity Numeric Rating Scale			X				
Pain Sensitivity Index		X		X	X		
Anxiety Sensitivity Index-3		X		X	X		
Distress Tolerance Scale		X		X	X		
Fear Questionnaire Blood-Injury-Injection Subscale		X		X	X		
PROMIS-Sleep Disturbance-Short Form		X		X	X		

PROMIS-Sleep-Related Impairment-Short Form		X		X	X		
Sheehan Disability Scale		X		X	X		
Client Satisfaction Questionnaire-8			X	X	X		

Initial Screening Measures

Modified Dental Anxiety Scale (MDAS; Humphris et al., 1995). The MDAS is a widely used 5-item measure assessing fear of dental procedures, including cleaning, drilling, and local anesthetic injections; for example, "If you were about to have your tooth drilled, how would you feel?" Items are rated on a 5-point Likert-type scale ranging from 1 (not anxious) to 5 (extremely anxious). The total score ranges from 5 to 25; a score of 19 or above indicates high anxiety based on receiver operating characteristic analyses from two studies. The MDAS has demonstrated good internal consistency (α = .89 in Humphries et al., 1995; α = .91 in our pilot work) and test-retest reliability (r = .82). The MDAS will be administered at several occasions throughout the study. We will also briefly contact patients and ask them to complete the MDAS by phone or online at 6-month and 12-month follow-ups as well.

Medical Screening Interview. During the initial telephone screening, we will administer a medical screening interview that has been used in previous research by former PI Heimberg at Temple University. This medical screening interview assesses a number of medical conditions that may make it inadvisable for the potential participant to be exposed to anxiety-evoking materials unless well-controlled. If the potential participant meets criteria for any of these medical conditions and does not report that they are controlled by medication or other appropriate means, that potential participant will be excluded. It is also important to note that the Faculty Practice Clinic (the clinic in which the trial will be conducted) also conducts it own medical screening and will not schedule a patient for an appointment for dental care if the patient scores positive for any of the listed conditions on their form unless it is medically controlled (patient will be first referred out for appropriate medical care before coming back to the dental clinic when the medical condition is controlled). Although the routine clinical procedures of Faculty Practice Clinic are not a formal part of our protocol, they are thorough and suggest that our procedures are conservative, as we are recruiting only from the population of patients for whom an appointment for dental care has already been scheduled.

Other Self-Report Questionnaires
Note: we will modify the instructions for some questionnaires to refer to the present time or the time since the last assessment, depending on when the scale is administered, so that the relevant time interval is examined.

Client Satisfaction Questionnaire (CSQ-8; Larsen et al., 1979). The CSQ-8 is used in the measurement of client/patient assessment of satisfaction with services and clinical care. It consists of 8 items rated on a 1-to-4 scale. Higher scores indicate greater satisfaction with services, with a maximum score of 32. The CSQ-8 will be administered

on treatment day and at the 1-month and 3-month follow-ups to patients who received the online dental anxiety intervention only.

Anxiety Sensitivity Index-3 (ASI-3: Taylor et al., 2007). The ASI-3 is an 18-item measure which assesses the extent to which individuals are concerned about the potential negative consequences of anxiety-related symptoms and sensations. The ASI-3 has demonstrated high internal consistency (α = .95) and convergent validity with a wide range of established anxiety-related measures (Gonzalez et al., 2011). Anxiety sensitivity is significantly correlated with fear of pain, and fear of pain predicts increased pain, expectation of pain, and avoidance of potentially painful experiences (Ocañez et al., 2010). The ASI-3 will be administered at baseline and the 1-month and 3-month follow-ups.

Pain Sensitivity Index (PSI; Gross, 1992a). The PSI is a 16-item self-report measure that assesses the fearful appraisal of pain and the expected physical, psychological, and social consequences of pain. Items are rated on a scale ranging from 0 (not at all) to 7 (very much) reflecting the degree to which the item applies to the respondent. Higher scores indicate higher levels of pain sensitivity. The scale has demonstrated high internal consistency in previous studies with dental patients (α = 0.92) (Klages et al., 2004). It was found to measure a construct distinct from dental phobia and health concerns (Gross, 1992a). Pain sensitivity is considered a stable characteristic that can influence the development of situational fears (Gross, 1992b). It has been related to dental anxiety and expectation of pain before dental procedures (Klages et al., 2004). The PSI will play a dual role in this study, as a secondary outcome measure and as a hypothesized moderator of the efficacy of the Internet-based dental anxiety intervention compared to the active control condition. It will be administered at baseline and the 1-month and 3-month follow-ups.

Distress Tolerance Scale (DTS; Simons & Gaher, 2005). The DTS is a 15-item self-report measure assessing one's perceived ability to experience and tolerate negative emotional states. This scale measures four dimensions of distress tolerance: subjective appraisal of distress, ability to tolerate emotional distress, absorption of attention by negative emotions, and regulation efforts to alleviate distress. Items are rated on a scale ranging from 1 (strongly agree) to 5 (strongly disagree). Total score range from 15 to 75, with higher scores reflecting higher levels of distress tolerance. This scale has high internal consistency (α = .89), appropriate convergence with other self-report ratings of affective distress and regulation, and adequate six-month test-retest reliability (r =.61). The DTS will also play a dual role in this study, as a secondary outcome measure and as a hypothesized moderator of the efficacy of the Internet-based dental anxiety intervention compared to the active control condition. It will be administered at baseline and the 1-month and 3-month follow-ups.

Fear Questionnaire Blood-Injury-Injection Subscale (FQ-BII; Marks & Mathews, 1979). The FQ-BII is a 5-item subscale of the complete FQ. It assesses the degree to which an individual avoids situations involving blood-injury-injection because of fear, including in the context of dental procedures. Items are rated on a scale ranging from 0 (would not

avoid it) to 8 (would always avoid it). Total scores range from 0-40 with higher scores indicating greater phobic avoidance. The FQ is sensitive to treatment-induced improvements in phobic responding, demonstrates adequate psychometric properties, and is a commonly used measure for research on phobias. The FQ-BII is included here because of evidence that suggests a modest but significant overlap between dental phobia and BII fears (van Houtem et al., 2014). It will be administered at baseline and the 1-month and 3-month follow-ups.

PROMIS-Sleep Disturbance-Short Form (PROMIS-SD-S; Yu, Buysse, & Germain, 2011). The PROMIS Sleep Disturbance Short Form is an 8-item measure that is part of the National Institute of Health's Patient-Reported Outcome Measurement Information System (PROMIS) and derived from its original longer version (Buysse et al., 2010). The PROMIS-SD-S assesses sleep disturbance over the previous 7 days. All items are rated on a 5-point scale. Total raw scores range from 8-40 (which are then converted to T-scores), with higher scores indicating greater sleep disturbance. The measure has demonstrated good psychometric properties and greater precision than other commonly used measures of sleep quality (Yu, Buysse & Germain, 2011). This measure, as well as the measure described below, are included here due to evidence that dental anxiety is associated with sleep disturbance (Almoznino et al., 2015); we hope to assess the association of dental anxiety and sleep-related difficulties in the current study and track potential improvements in sleep outcomes following dental anxiety treatment. This measure and the measure described below will be administered at baseline and the 1-month and 3-month follow-ups.

PROMIS-Sleep-related Impairment-Short Form (PROMIS-SRI-S; Yu, Buysse, & Germain, 2011). The PROMIS-Sleep-related Impairment-Short Form is an 8-item measure that is also part of the PROMIS initiative and derived from its original longer version (Buysse et al., 2010). The PROMIS-SRI-S assesses daytime impairment due to sleep difficulties over the previous 7 days. All items are rated on a 5-point scale. Total raw scores range from 8-40 (which are then converted to T-scores), with higher scores indicating greater sleep-related impairment. Like the PROMIS-SD-S, this measure has demonstrated good psychometric properties and greater precision than other commonly used measures of sleep quality (Yu, Buysse & Germain, 2011).

Sheehan Disability Scale (SDS; Sheehan,1983). The SDS is a 3-item measure of functional impairment due to one's illness in 1) work, 2) social life, and 3) family/home life. Three items assessing each of these domains are rated on a 0 (no impairment) to 10 (extreme impairment) scale which are then summed and used to assess overall current levels of disability due to illness. In the current study, we modified the scale to specifically assess the current impact of participants' *dental anxiety* symptoms on work/school, social life/leisure activities, and family life/home responsibilities. The validity and reliability of the SDS has been previously demonstrated among individuals with panic disorder (Leon et al, 1992) and social anxiety disorder (Hambrick et al., 2004). The SDS will be utilized as a secondary outcome measure in the current study to assess the degree of functional impairment associated with dental anxiety as well as

improvements in functional impairment following the intervention. This measure will be administered at baseline and the 1-month and 3-month follow-ups.

Clinician-Administered Interviews

Anxiety and Related Disorders Interview Schedule for DSM-5 (ADIS-5) - Adult Version (Brown & Barlow, 2014). The ADIS-5 is a semi-structured interview designed to establish reliable diagnoses of the DSM-5 anxiety, mood, somatoform, and substance use disorders. The ADIS has been utilized in former PI Dr. Heimberg's research on anxiety disorders since it was originally created at the Center for Stress and Anxiety Disorders, University at Albany, SUNY, where he was on staff, and he has overseen the training of many doctoral students in clinical psychology in its use in the last 30 years. To minimize participant burden, this study will utilize only the dental procedure-related section of the specific phobia module of the interview. This module includes ratings of fear and avoidance of dental procedures as well as resultant interference (the latter being used to operationalize one of the inclusion criteria). For the dental phobia diagnosis, a dimensional clinical severity rating, ranging from 0 = none to 8 = very severely disturbing/disabling, will be assigned, with scores of 4 or above denoting clinical significance. All interviews will be audio-recorded. A 20% sample will be randomly selected for assessment of inter-rater agreement on the presence of dental phobia and clinical severity. Interviewers have demonstrated excellent inter-rater agreement for the principal diagnosis of specific phobia in a mixed sample of anxiety disorder patients ($\kappa = .86$; Brown et al., 2001). The ADIS-5 module will be administered at baseline and the 1-month and 3-month follow-ups.

Post-Appointment Debriefing Ratings. Two separate sets of interview questions will be administered, one after the completion of the dental anxiety intervention and the other after completion of the following dental appointment. The debriefing interview after the dental anxiety intervention will ask the patient to rate the perceived helpfulness of each component of the intervention, the degree to which any of the components were hard to understand, and the degree of difficulty they experienced watching each set of videos of dental procedures. It will also include an open-ended probe of patients' reactions to any aspect of the dental anxiety intervention. These questions will be asked for the purpose of collecting qualitative data on patients' reactions to the intervention, to determine whether there are differences between patients assisted by psychology versus dental staff, and to gather information to inform future modifications of the intervention. Questions will also be asked to determine the degree of pain and the degree of anxiety patients expect to experience in the dental treatment appointment they will have immediately following the dental anxiety intervention. Because this interview will not be administered to patients randomized to the active control condition, the ratings of expected pain and anxiety will be administered to them after they watch the control video.

Ratings after the dental appointment will assess the degree of pain and anxiety experienced during the appointment, the degree of pain and anxiety in comparison to past dental appointments, how much the dental anxiety intervention helped the patient

to get through the dental procedure (for the full intervention and the major components), and the likelihood of scheduling a dental appointment in the future. The debriefing interview after the dental appointment will also include an open-ended probe of patients' thoughts about the impact that any aspect of the dental anxiety intervention may have had on their reactions to the dental procedure. An abbreviated version of this interview will be administered to active control patients, asking about pain and anxiety, and omitting any questions related to the dental anxiety intervention.

Pain Intensity Numeric Rating Scale (PI-NRS). The PI-NRS is a widely utilized 11-point measure that assesses physical pain intensity on a scale ranging from 0 (no pain) to 10 (worst possible pain). The PI-NRS has been used to assess pain intensity in several studies conducted in medical settings (Farrar et al., 2001, 2010; Rowbotham et al., 2004; van der Roer, 2006). Anxiety increases subjective pain experience, and therefore this scale will be used to assess the intensity of dental related pain that participants experienced during their scheduled dental appointment and expect to experience at their next dental appointment. The PI-NRS will be administered as part of the post-dental-appointment debriefing interview.

Attendance at Dental Appointments

Given that avoidance of dental appointments is strongly connected to dental anxiety, we will also assess whether the Internet-based dental anxiety intervention increases attendance at future dental appointments. We will utilize TUKSoD's automated scheduling system (axiUm, http://www.axiumdental.com/) to do so. It is acknowledged that attendance may be influenced by factors unrelated to dental anxiety, but it is a reasonable hypothesis that anxious avoidance plays a role in attendance, and individuals with dental phobia are less likely to visit a dentist at least once a year than persons without. Thus, it is of interest to determine whether attendance at appointments scheduled prospectively after the index appointment is affected by treatment, and we will monitor this for the following 12-month interval. These data will not be collected for active control patients, who will be offered the intervention to be administered before their first scheduled dental appointment after the completion of the 3-month follow-up.

Planned Analyses

We propose general statistical analyses and sample size considerations for the U01 trial. Initial analyses will be conducted to determine normality of distributions of the continuous variables, and any necessary transformations will be conducted. Primary outcomes will be the MDAS (score ranging from 5 to 25) and the rating of fear of dental procedures from the ADIS-5 (0=no fear to 8=very severe fear). All eligible patients will be randomly assigned to one of the three conditions described above. Although randomization should provide relatively comparable groups, demographic variables that differ between groups and are correlated with the primary outcomes will be used as covariates. Patients will receive a full battery assessment of outcome measures at baseline and 1 and 3 months after the day of their index dental appointment (as well as assessments on the day of their index dental appointment).

Preliminary statistical analysis will include measures of central tendency and dispersion, as well as an examination of the bivariate relationships among the primary and secondary outcome variables (e.g., client satisfaction, blood-injury-injection phobia), potential moderators (e.g., distress tolerance and pain sensitivity), and demographic characteristics.

Differences between the groups on baseline demographic, clinical and psychological measures will be examined using χ^2 (Pearson) or Student's *t*-tests, as appropriate. Moreover, differences on the variables listed above among completers and drop-outs will also be explored. Both per protocol and intention to treat (ITT) analyses will then be conducted.

Specific Aim 1

Aim 1 will test the equivalence hypothesis (Ho: the two intervention conditions are not equivalent). MDAS and ADIS fear scores will be the primary outcomes to be compared between two intervention conditions for equivalence. The two one-sided tests (TOST) procedure of Schuirmann (1987) will be used to conduct the equivalence test. Linear mixed-effects models for repeated measures will be used to assess differences between intervention groups using the MDAS and ADIS fear rating as continuous outcome variables. Linear mixed-effects models will also investigate the treatment effect on dental anxiety or fear after accounting for other confounding factors. Similar analyses will be conducted for secondary outcome measures (pain sensitivity index, anxiety sensitivity index, sleep disturbance and sleep-related impairment scales, disability scale, distress tolerance scale, client satisfaction and blood-injury-injection phobia). Statistical significance will be set at $p < 0.05$. Multiple imputation (MI) will be used to handle missing follow-up data as described below.

Aim 1 will also determine whether the Internet-based intervention reduces dental anxiety/fear as determined by self-ratings or assessor ratings at one month and three months post-intervention. Initially, we will assess within-group change of anxiety or fear scores for each condition separately using paired *t*-tests. Linear mixed-effects models will be used to estimate within-group reduction of anxiety/fear at assessments one and three months after the administration of the intervention adjusting for other covariates.

Specific Aim 2

Aim 2 will assess the superiority hypothesis (Ho: there are no significant differences between the interventions and control). MDAS and ADIS-5 fear scores will be the primary outcomes to be compared. Initially, we will assess the differences between the interventions and control using two-sample *t*-tests. The main analysis will be based on linear mixed-effects models for repeated measures (using the MDAS score and ADIS-5 fear rating as continuous outcome variables) to assess differences between intervention and control groups. Linear mixed models will also investigate the treatment effect on dental anxiety or fear after accounting for other confounding factors. Similar analyses will be conducted for secondary outcome measures (e.g., client satisfaction and blood-

injury-injection phobia). Statistical significance will be set at $p < .05$. MI will be used to handle missing follow-up data as described below.

Specific Aim 3

Aim 3 examines the impact of the intervention on attendance at scheduled dental appointments over the following 12-month period to determine whether the intervention affects avoidance of dental procedures. First, we will examine whether the overall attendance rate is changed from pre- to post-intervention using a one-sample Chi-square test comparing the 12-month periods immediately before and immediately after the delivery of the intervention. The two intervention groups combined will be used for this analysis. We will also use a Chi-square test to compare post-intervention attendance rates between the two intervention groups. We expect the attendance rates will be similar for the two groups. Finally, we will conduct logistic regression analyses predicting attendance/nonattendance among intervention patients who did or did not demonstrate reduction in dental anxiety at 3-month follow-up. Relevant demographic characteristics and other potential confounding variables or moderators will be included in the final logistic models.

Missing Data

MI will be used to handle missing follow-up data when conducting ITT analysis for Specific Aims 1 and 2. There will be three steps in the MI procedure: 1) The missing follow-up data will be filled in 100 times to generate 100 complete datasets; 2) The 100 datasets will be analyzed by analyses of covariance with follow up scores at 1-month or 3-month as outcomes and treatment groups as the independent variable (Tr1 vs. Tr2 for Specific Aim 1, or Tr1 + Tr2 vs. AC for Specific Aim 2), controlling for baseline scores; 3) The results from the 100 complete datasets will be combined for the MI inference (Rubin 1987). SAS PROC MI and PROC MIANALYZE will be used for multiple imputation analysis using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Analysis of Secondary Objectives

To determine whether primary objectives 1 and 2 are reflected in measures of other related constructs such as pain sensitivity, distress tolerance, anxiety sensitivity, and anticipated and perceived pain and anxiety, the statistical methods described above will be used. The moderating role of distress tolerance and pain sensitivity as expressed in the secondary objectives will be assessed as well. We will examine whether baseline levels of distress tolerance and pain sensitivity moderate the efficacy of the dental anxiety intervention. We will examine the moderating effect of these factors on the intervention and the reduction in dental anxiety at the 1-month and 3-month follow-ups. For moderation analyses, we will include a dummy variable for randomization arm, the potential moderator variable (distress tolerance or pain sensitivity), and an interaction term between the two (i.e. dummy variable multiplied by the mean-centered moderator variable). To maintain power to detect moderation, we will explore moderators

separately. We will also use linear-mixed effects models in which we include potential confounding variables, as well as main effects and interaction terms of interest.

d) Withdrawal of Subjects

We do not expect that there will be much in the way of withdrawal during the dental anxiety intervention itself, although it is not entirely out of the realm of possibility. We expect that the major concerns will have to do with the assessments over time, and in that case, concerns over withdrawal are really concerns over retention. However, we note a few issues below.

Reasons for Withdrawal related to the Intervention
First, patients may become highly distressed during the dental anxiety intervention. This is most likely to occur because of their high level of distress in anticipation of either the dental anxiety intervention or the dental appointment itself, and it will be most likely to show itself when, as part of the intervention, patients are asked to view video recordings of dental procedures (described earlier in this document). This level of distress is common, but in running a large number of patients through the study of the computer-based version of the intervention, it never reached a level at which the patient asked to be withdrawn or clinical staff thought it necessary. Although one patient stated that the dental anxiety intervention made her so anxious that she was going to cancel her following dental appointment, she did not do so, and during the debriefing interview thereafter, she noted that she was able to use some of what she learned in the dental anxiety intervention to ease herself through the actual dental procedures. Nevertheless, the possibility exists that some patient(s) will become so distressed by the dental anxiety intervention or display some other negative psychological state that they must be withdrawn.

The second reason for withdrawal is if the patient does not attend the scheduled dental appointment after the dental anxiety intervention, as we consider the dental appointment to be an integral part of the intervention, an opportunity to practice skills learned in the dental anxiety intervention immediately in a “real-world” context. Note that this circumstance may also arise if the dental clinic staff unilaterally reschedules the patient’s dental appointment.

The third reason for withdrawal is failure to appear for the dental anxiety intervention.

The fourth reason is for failure to comply with the required assessments, either at baseline or at the follow-up assessments.

Handling of Subject Withdrawals or Subject Discontinuation of Study Intervention
For the first reason (patient distress during the dental anxiety intervention), if the study clinician judges it appropriate, he/she will stop the intervention and provide supportive counseling as needed. He/she may assist the patient in rescheduling the following dental appointment if it appears that the patient intends to cancel or remains too distressed to follow through with it on that day. He/she will provide referrals for

individualized treatment as needed. During this time, to the extent that clinical circumstances allow, he/she will attempt to ascertain whether specific portions of the intervention contributed to the patient's distress (that is, to the extent possible, he/she will attempt to conduct the post-intervention debriefing interview or gather as much of that type of information as the patient will tolerate). Dr. Tellez or Dr. Dunne will be available by cell phone to consult as needed in this process.

For the second reason (failure to attend the following dental appointment), the patient will be withdrawn from study consideration unless the dental appointment can be rescheduled within 72 hours. We will attempt to help patients do so, because it is likely that they would still benefit from the dental anxiety intervention if the dental appointment can be rescheduled more or less immediately; research staff will interact with dental clinic staff to facilitate this as much as possible.

For the third reason (failure to attend the dental anxiety intervention), the patient will be withdrawn after reasonable attempts to reschedule have failed or if there is a rescheduled appointment and the patient fails to appear.

For the fourth reason (failure to complete assessments), the circumstances will be different depending on the timing of the problematic assessment. If the patient does not complete the pre-intervention assessments, the intervention will not be delivered, and thus the patient will be effectively withdrawn. The patient will be called no less than 3 times to facilitate such completion, but a number of patients may not complete because of this issue. They will be replaced so that we reach our enrollment target. If the patient fails to complete assessments at follow-up, no less than 3 calls will be made, but the patient will be considered lost to follow-up rather than withdrawn. In our recent randomized trial (Tellez et al., 2015), which included only a one-month follow-up, only 2 of 46 intervention patients were lost to follow-up in this way.

e) Privacy & Confidentiality

As in any type of treatment or clinical research program, patients' privacy must be carefully guarded and respected. All identifying information (e.g., contact information) and audio recordings of interviews or video recordings of the I-CBT session will be stored in locked files or digitally on a HIPAA-compliant network. Remaining data will be stored in password-protected computer files on a HIPAA-compliant network. One file will contain patient names, contact information, and associated subject codes; at the end of the study, this file will be destroyed. All other data will reside in a file identified by subject codes and from which other identifying information will have been removed, so the link between these data and subject identifiers will have been severed.

All assistants and others working on the project will be educated about the importance of strictly respecting patients' rights to confidentiality and will have completed training concerning proper practice in accordance with HIPAA regulations.

Data files will be accessible only to the investigators, study coordinator, postdoctoral fellow, doctoral student, and research assistants directly connected with the study. Only members of the research team will review the data. To help patients feel at ease, the study coordinator and other staff will emphasize their right to ask questions throughout the study and to abstain from any aspect of the research which makes them uncomfortable.

No data will be shared with persons unassociated with the project without prior written release from the patient. When the results of this protocol are published, no participant will be identified by name.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. A Certificate of Confidentiality helps protect identifiable information and biological samples. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify participants in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless a participant has consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if a participant has consented to the disclosure, including medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Dental and Craniofacial Research (NIDCR) which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). Participants should understand that a Certificate of Confidentiality does not prevent the voluntary release of information about themselves or their involvement in this research. If a participant wants their research information released to an insurer, medical care provider, or any other person not connected with the research, they must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect, or harm to self or others. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose a participant has consented to in this informed consent document (their baseline dental anxiety score will be reported to the dentist prior to the scheduled dental appointment).

9) Risks to Subjects

Risks Associated with Intervention Procedures:

Internet-based dental anxiety treatment intervention: Based on our experience with the computer-based version of this intervention and our pilot of the online version as part of the R34 project, there are few significant risks. It is certainly possible, and will undoubtedly be the case for a subset of the sample, that the patient could experience elevated anxiety while interacting with the intervention materials, as these involve exposure to descriptions or videos of dental procedures selected specifically because they induce anxiety or are avoided in real life. In our earlier acceptability trial of the computer-based version, some patients did note elevations of anxiety and accompanying physiological symptoms, and some reported annoyance about it, but none asked to stop the intervention midway, and none chose to cancel their immediately following appointments for dental treatment. This experience was replicated in the randomized controlled trial and the piloting that occurred as part of the R34 grant.

Active Control Condition**:** This comparison condition will have patients pursue their scheduled dental appointment as usual, with the exception that their score on their most recent administration of the MDAS, the measure of dental anxiety, would be shared with the dental care provider (also the case in the intervention conditions). In addition, control participants will be asked to view a video of nature scenes for a period of time equivalent to the dental anxiety intervention. We cannot foresee any significant risks associated with these procedures.

Recording: Some patients may feel uncomfortable about the treatment sessions being recorded for the assessment of treatment fidelity, but this will be a required procedure. Treatment fidelity ratings as well as informal observations of session video-recordings by the study coordinator will be used for feedback to dental assistants undergoing training. Debriefing interviews, which will be audio-recorded, will provide additional important information about modifications that may need to be made to the dental anxiety intervention in advance of further research on the treatment of dental anxiety.

Risks Associated with Assessment Procedures:

Self Report Measures and Assessor Ratings: No risks are seen associated with these assessment procedures other than discomfort associated with thinking about one's dental anxiety as well as the recording of assessor interviews involving the disclosure of personal information. Recording will be necessary for the measurement of inter-rater agreement on interview measures.

Protection Against Risk:

1. Careful screening to identify patients whose risk for potential adverse outcomes is elevated were they to participate in the proposed research. Such patients will be excluded from the study. As an example, an actively suicidal patient would be excluded from study participation and appropriate clinical treatment provided.

2. Clinical staff will be trained to cope with any anxiety experienced by specific patients during treatment sessions. Here we refer to psychology staff who have experience in the treatment of anxious patients, at least one of whom will be on site (or available by cell phone) at all times to provide support for any patient who is unusually troubled by the experiences of the intervention. As a further safeguard, we have added a section to both the didactic portion of the training for therapy aides (both psychology staff and dental assistants) and the accompanying manual on the identification of and intervention with extreme anxiety reactions that may occur as a result of exposure to the intervention materials. As noted above, we see this risk as quite small, but not impossible.

3. Continuing contact with patients during the follow-up period. Patients will have contact with the same assessors at follow-up assessments as they did at baseline whenever possible. Patients will be encouraged to make contact with project staff between contacts if their dental anxiety or any reaction to the intervention causes undue distress. In that case, a discussion will be engaged about whether or not the patient should be withdrawn from the follow-up phase of the study and given appropriate clinical care. That care may take any of a variety of forms and may be offered through the Psychological Services Center of Temple University or through appropriate referral, depending on resources and the type of treatment desired by the patient.

4. As in any type of treatment or clinical research program, patients' confidentiality must be carefully guarded and respected. All data with identifying information will be stored in locked files or password-protected computer files. Data being analyzed will be identified by subject codes, and identifying information will be removed. All assistants and others working on the project will be educated about the importance of strictly respecting patients' rights to confidentiality and will have completed training concerning proper practice in accordance with HIPAA regulations.

5. In addition to the investigators' responsibility for oversight, study oversight will be under the direction of the NIDCR Medical Monitor. The investigators 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. The IRB and the designated program person at NIDCR will be notified in writing by Dr. Tellez or Dr. Dunne if a serious adverse event occurs. A serious adverse event is defined as follows: death, life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, and medically significant event. Risks of participation will be continuously monitored and appropriate measures implemented in cases of unforeseen adverse events. These events will be reported whether or not they appear to be related to study procedures.

All protocol violations will be discussed in detail; if appropriate, the IRB will be consulted and corrective actions devised. All modifications to the protocol will be submitted for IRB

approval. Summaries of all relevant discussions will be promptly disseminated to study personnel via e-mail and retraining procedures implemented as needed.

10) Potential Benefits to Subjects

An earlier iteration of the dental anxiety intervention demonstrated efficacy in the treatment of dental anxiety in the same population of patients from which the current sample will be drawn. Therefore, it is possible that a portion of the patients in this study will realize a reduction in their own dental anxiety, although this cannot be assured for any specific patient. Patients will receive a thorough assessment of their dental anxiety, and the intervention includes substantial educational material about dental anxiety, which should be to their benefit, regardless of anxiety reduction. Patients will be offered referrals for further treatment of dental anxiety, through the Temple University Psychological Services Center or elsewhere, should they be interested in pursuing this.

11) Costs to Subjects

Dental anxiety intervention is provided without charge. The investigators are not involved in the determination of cost of actual dental procedures, but no additional dental procedures will be conducted in the course of this research.

12) Informed Consent

The protocol will follow INVESTIGATOR GUIDANCE: Informed Consent (HRP-802) to obtain informed consent from participants. The proposed sequence is described as part of the narrative to follow. Although we have been thorough in delineating possible risks to participants, our experience with the prior computer-based version of the dental anxiety intervention suggests that this is truly a minimal risk study. However, we understand that that determination is ultimately one for the IRB rather than the investigators.

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to patients during the screening contact (Time 0) and electronic informed consent will be obtained at the first in-person visit (Time 2). Copies of the signed primary consent form will be emailed to patients for their records at the first Clinic Visit. The rights and welfare of the patients will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. Patients may withdraw consent at any time over the course of the study.

The consent process will be documented in the clinical or research record.

Participants in this study will be patients who have scheduled appointments for non-emergent dental procedures through the Faculty Practice Clinic at TUKSoD (and the Graduate Clinics of TUKSoD, if necessary). All such persons will be contacted by

telephone and asked if they would be willing to be screened for dental anxiety and, if so, if they would be interested in the possibility of participating in a study of the treatment of dental anxiety. If the potential participant gives a positive response, the 5-item dental anxiety screening measure, two additional screening questions (age, impairment as a result of dental anxiety), and a medical screening interview will be administered (see Recruitment Methods section for a more detailed presentation of specific procedures). If the participant meets criteria and continues to express interest in the study, extensive information about the study and the risks and possible benefits of study participation will be provided (the caller will provide a full summary of the primary study consent form over the telephone with the potential participant and verbal consent for full study participation will be obtained). If patients remain interested in participation, they will be scheduled for a second ("baseline") interview and questionnaire administration.

At the Clinic Visit on the day of the dental anxiety intervention (or control session), the primary study consent form will be reviewed with the patient and remaining questions answered. A copy of this signed consent form will be provided to the patient via email, but a physical copy can also be provided upon request. As part of the overall consent procedure, patients will be informed of the nature of the investigation, the types of assessments and treatments involved, the recording of debriefing/assessment interviews and intervention sessions, alternative treatments, and the potential risks involved in participation. In addition, an explanation of how information related to their case will be handled will be presented. The IRB will have approved the protocol and consent form prior to implementation.

13) Vulnerable Populations

Not applicable. Individuals who are vulnerable to coercion or undue influence will not be included in the human subjects activities described herein.

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