

Department of Health and Human Services Public Health Services Grant Application <i>Do not exceed character length restrictions indicated.</i>	LEAVE BLANK—FOR PHS USE ONLY.		
	Type	Activity	Number
	Review Group		Formerly
	Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT (Do not exceed 81 characters, including spaces and punctuation.)
Blood Sugar Testing in Dental Practice

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION NO YES
 (If "Yes," state number and title)
 Number: _____ Title: _____

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR New Investigator No Yes

3a. NAME (Last, first, middle) DPBRN c/o Barasch, Andrei	3b. DEGREE(S) DMD MDS	3h. eRA Commons User Name abarasach
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3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT Diagnostic Sciences	
3f. MAJOR SUBDIVISION School of Dentistry	

3g. TELEPHONE AND FAX (Area code, number and extension) TEL: 205-996-4418 FAX: 205-975-0603	E-MAIL ADDRESS: abarasch@uab.edu
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4. HUMAN SUBJECTS RESEARCH <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes	4b. Human Subjects Assurance No.	5. VERTEBRATE ANIMALS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
4a. Research Exempt <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	4c. Clinical Trial <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	5a. If "Yes," IACUC approval Date
If "Yes," Exemption No. _____		5b. Animal welfare assurance no.

6. DATES OF PROPOSED PERIOD OF SUPPORT (month, day, year—MM/DD/YY) From _____ Through _____	7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD 7a. Direct Costs (\$)	8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT 7b. Total Costs (\$) 7c. Direct Costs (\$) 7d. Total Costs (\$)
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9. APPLICANT ORGANIZATION Name _____ Address _____	10. TYPE OF ORGANIZATION Public: → <input type="checkbox"/> Federal <input checked="" type="checkbox"/> State <input type="checkbox"/> Local Private: → <input type="checkbox"/> Private Nonprofit For-profit: → <input type="checkbox"/> General <input type="checkbox"/> Small Business <input type="checkbox"/> Woman-owned <input type="checkbox"/> Socially and Economically Disadvantaged
11. ENTITY IDENTIFICATION NUMBER DUNS NO. _____ Cong. District _____	

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE Name _____ Title _____ Address _____ Tel: _____ FAX: _____ E-Mail: _____	13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION Name _____ Title _____ Address _____ Tel: _____ FAX: _____ E-Mail: _____
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14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF PI/PD NAMED IN 3a. <i>(In ink. "Per" signature not acceptable.)</i>	DATE
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15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.	SIGNATURE OF OFFICIAL NAMED IN 13. <i>(In ink. "Per" signature not acceptable.)</i>	DATE
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DESCRIPTION: See instructions. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the mission of the agency). Describe concisely the research design and methods for achieving these goals. Describe the rationale and techniques you will use to pursue these goals.

In addition, in two or three sentences, describe in plain, lay language the relevance of this research to public health. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

The incidence of diabetes mellitus has been increasing at epidemic proportions, making this chronic disease the most common medical condition in dental patients. Hyperglycemia has been identified as a potential risk factor for periodontal disease, dental infection and poor response to treatment. Additionally, an estimated 4% of Americans are undiagnosed diabetics, and more than 80% of the diagnosed patients are not well controlled. Early diagnosis and intervention have been shown to improve outcomes and reduce morbid medical complications in diabetes patients. Thus, identifying hyperglycemia in dental practice could lead to a significant improvement in both dental and medical outcomes.

We propose to study the prevalence of hyperglycemia in dental patients in the private practices of DPBRN dentist-investigators. The global aim of this study is to determine the feasibility of glucose testing and diabetes screening in private dental practice. The specific aims of this study are: 1) To quantify the percentage of DPBRN patients who meet the American Diabetes Association screening criteria and to describe the characteristics of these patients. 2) To quantify the acceptability of conducting glucose testing in the dental office and barriers to regular screening, as reported by DPBRN patients and practices.

These aims will be met by enrolling 25-35 DPBRN practitioner-investigators, each of whom will during a 3 month period test and record random glycemic indices in new and recall patients in their practices. This will be done using a glucometer that DPBRN will provide each practice. Patients with glucose >200mg/dL post-prandial or >120 pre-prandial will be referred to their physician for further testing and possible treatment. (200mg/ml has been widely accepted as indication of metabolic pathology, regardless of meals). We will analyze and describe patients at risk for diabetes and those with elevated glucose. Questionnaires filled by both tested patients and dental practitioners will be analyzed to identify barriers to glucose testing in private dental practice.

Public health impact: Position papers from American Diabetes Association and American Heart Association have stressed the importance of screening and early detection of diabetes. We will determine the feasibility of screening in private dental practice and will quantify the prevalence of hyperglycemia in private practice dental patients, which will provide indication of either undiagnosed or uncontrolled disease. This may result in improved glycemic control and medical and dental outcomes of this important chronic disease among dental patients. Results of this study will inform the design of a randomized, controlled clinical trial of medical outcomes in hyperglycemic dental patients.

PERFORMANCE SITE(S) (organization, city, state)

RESEARCH PLAN:

A. Specific Aims

The number of cases of diabetes mellitus (DM) has been increasing at an epidemic pace, becoming one of the most common medical conditions encountered in dental practice.¹ According to the American Diabetes Association, 7.0% of the US population has this disease. The prevalence of diabetes (diagnosed plus undiagnosed) in people over the age of 40 increased from 8.9% in 1980 to 12.3% in 1994, making diabetes one of the most common and costly chronic conditions in the United States.² DM is the third leading cause of death and the chief cause of blindness, end-stage renal disease and non-traumatic limb amputation.¹⁻³ Interventions to control blood sugar have been demonstrated to decrease these and other outcomes in DM.³ Detecting DM and treating it adequately are therefore major public health objectives.

An estimated 4% of Americans, or approximately 30% of those with prevalent disease, suffer from DM but have not been diagnosed, and about 65% of diagnosed patients are not optimally controlled.⁴ DM typically develops after many years of metabolic derangements characterized by impaired fasting glucose and impaired glucose tolerance. Pre-DM affects 54 million Americans, or 18% of the population; that means that fully one-quarter of Americans have either DM or pre-DM (4). Both conditions have been associated with increased physical morbidity including significant risk for cardiovascular, renal, periodontal, neuropathic and ocular disease.^{5,6} Intensive glucose control significantly reduces vascular complications in both type 1 and type 2 DM, and lifestyle interventions can prevent or delay the progression of pre-DM to frank DM.⁷ Thus, detection of pre-DM, unrecognized DM, and uncontrolled DM in the community may provide significant benefits to affected patients as well as to the society at large. The American Heart Association and American Diabetes Association have both called for new strategies to improve screening and detection of DM and pre-DM. The dental office is a unique setting for screening, and our group has demonstrated that it can be a site for preventive health intervention, such as smoking cessation.^{8,9} **We propose to study the feasibility of screening for pre-DM, DM and uncontrolled DM in community dental practices.**

Context within which the study will be conducted

The Dental-Practice Based Research Network, DPBRN, is a group of dental practices that have joined together to investigate research questions and to share experiences and expertise. A comprehensive description of DPBRN can be found in the "parent" U01 grant application, which has already been provided to the DPBRN Protocol Review Committee. An additional resource is DPBRN's web site at <http://www.DentalPBRN.org>. Because DPBRN is committed to being guided by the needs and desires of practitioners, the intent for its studies is to address topics that are of direct relevance to general dentists in clinical practice, to conduct studies that are simple in design and which require minimal training, and to conduct studies that do not unduly interrupt the busy flow of daily clinical practice.

The main decision-making body of DPBRN is its Executive Committee. The Executive Committee would like for DPBRN ultimately to conduct randomized controlled clinical trials (RCT) on topics such as the medical outcomes of DM screening in dental practice and/or the risks of wound infection after oral surgical procedures in diabetic dental patients. However, to justify such RCTs, we first need to determine the feasibility of glucose testing within the private dental practice.

We are aware of an ongoing study of glucose testing in dental offices being conducted in Minnesota under the auspices of the Delta Dental Insurance Company. It is our understanding that the Delta Dental study is limited to diabetes screening of high-risk individuals only. Alternatively, the current study seeks to quantify the effectiveness of glucose testing in private dental practices for a broader population, with the explicit purpose of establishing the basis for a national screening process and to provide clinical information for treatment decision-making for dental practitioners. In addition to its epidemiologic goal of quantifying the prevalence of hyperglycemic patients presenting to dental practices, we will determine barriers to glucose testing in the dental office, paving the way for effective dissemination.

The **Specific Aims** of this project are:

1. To quantify the percentage of DPBRN patients who meet the American Diabetes Association screening criteria and to describe the characteristics of these patients.

Rationale: The percentage of DPBRN patients who have at least one risk factor for diabetes will provide the basis for all studies of DM in dental practice. This patient population and its demographic characteristics have not been described. Determining which sub-groups of DPBRN patients most commonly meet the American Diabetes Association screening criteria will provide invaluable data to inform large-scale testing in the dental care system and to inform the design of DM-related RCTs in dental practice.

2. To quantify the acceptability of conducting glucose testing in the dental office and barriers to regular screening, as reported by DPBRN patients and practices.

Rationale: Screening will be accomplished by asking patients to self-report whether they meet specific American Diabetes Association risk criteria, and if so, to conduct a simple and commonly-used glucose test (hand-held glucometer sold in retail stores and used regularly by DM patients). Glucose testing is a simple and inexpensive procedure that can be easily performed by a dental auxiliary worker. This new responsibility may be a welcome addition that will increase the worker's self esteem and increase job satisfaction. DM screening and glucose testing would expand the scope of the dental profession and may provide an important segue into fostering further involvement of the dental profession in the links between systemic and oral health. Glucose testing may also provide the dental practitioner with important information regarding the patient's ability to tolerate invasive procedures and his/her risk for periodontal disease, thereby improving daily clinical practice independent of screening's contribution to broadening the profession's scope of practice. However, addition of a new, unfamiliar procedure to a routine may be viewed with apprehension by dental staff, particularly since there currently is no reimbursement for glucose testing under dental plans. If found feasible, glucose testing may become a routine part of dental visits (much like blood pressure screening), opening the door to a new screening strategy that could lead to earlier diagnosis and improved control of DM, as well as broaden the scope of the dental profession. The prevalence of diagnosed and undiagnosed hyperglycemia is an important factor in determining the need for and possible effect of forthcoming RCTs.

B. Background and Significance

B.1. Diabetes and Pre-Diabetes.

The Third National Health and Nutritional Examination Survey (NHANES III) estimated the prevalence of diagnosed DM to be 7%.³ Pre-DM affects another 18% of the population. Even more worrisome, the prevalence of DM (diagnosed plus undiagnosed) in people over the age of 40 increased from 8.9% in 1980 to 12.3% in 1994.¹⁰ Analyses of NHANES 1999-2000 have shown that optimal glycemic control rates were present in only 35% of DM patients.² Indeed, DM is one of the most common and costly chronic diseases, with estimated expenditures approaching \$132 billion in 2002.^{2, 11} DM is the third leading cause of death in the US, and the chief cause of blindness, end-stage renal disease and non-traumatic limb amputation.¹²

At the cellular level, abnormalities have been demonstrated,¹³⁻¹⁹ including impaired hepatic glucose uptake, alterations in immune function, early senescence and premature apoptosis in a variety of cells, including keratinocytes,¹⁴ osteoblasts¹⁷ and macrophages.¹⁹ It is thus certain that DM also affects the oral cavity. Nevertheless, with the notable exception of periodontal disease, oral effects of DM remain unclear. Impaired wound healing is a common consequence of DM and contributes to the high rate of infection and amputation.^{13, 14} The underlying pathophysiology of this process is not fully understood. Increased cellular apoptosis,²⁰ poor oxygenation,²¹ decreased amounts of growth factors²² and increased inflammation²³ may play a role in the deficient healing process. Furthermore, bone healing may be impaired by glycation end products through over-expression of their cellular receptor.¹⁸ Specific defects in immune function have been described in cellular studies. However, the relevance of these findings *in vivo* has not been elucidated.²⁴

DM leads to a host of deleterious health outcomes falling into microvascular and macrovascular categories. Microvascular complications include damage to small caliber blood vessels, affecting the nerves, the kidneys and the retinas. The clinical manifestations of microvascular disease include blindness, painful neuropathy, sensory neuropathy leading to Charcot joints, gastroparesis, neurogenic bladder, and impotence. The macrovascular complications result from accelerated atherosclerosis in medium size vessels, leading to

excess risk for myocardial infarction, stroke, heart failure and peripheral vascular disease. Amputations are a dreaded outcome of DM, usually resulting from a combination of both impaired circulation and insensate feet.

Clinical hyperglycemia, regardless of diagnosed DM, is associated with adverse medical and surgical outcomes, including acute vascular syndromes and infections. Wahab et al reported that patients with acute coronary syndrome and a blood glucose >198mg/dL had significantly worse outcomes independent of a history of DM.²⁵ Similarly, Norhammar et al found that elevated glycemia in acute myocardial infarction patients was a risk factor for re-infarction, congestive heart failure and future cardiovascular events, regardless of a history of DM.²⁶ A study of DM and normal patients in the Intensive Care Unit demonstrated that hyperglycemic patients in both groups had higher mortality.²⁷ Similarly, pre-diabetic patients have risks for all diabetic complications, albeit at lower levels than those for patients with frank DM. Therefore, whether in pre-DM, or in DM, hyperglycemia appears to confer deleterious effects.

Glycemic control remains the major therapeutic objective for prevention of organ damage and other morbid complications of DM. Robust experimental evidence has proven that glycemic control can improve the microvascular outcomes for both type 1 and type 2 DM.^{7, 28} Macrovascular outcomes have not been shown to be decreased by glycemic control, but diabetic patients do benefit from blood pressure and lipid control.²⁹⁻³¹ More aggressive blood pressure and lipid targets are therefore recommended in individuals with DM. Multiple therapies exist to control DM, ranging from lifestyle modifications to oral medications, and, ultimately, insulin. Evidence-based guidelines point the way to glycemic control in DM.

Pre-DM is a recently described phenomenon, fueled by the exciting findings of the Diabetes Prevention Trial, which demonstrated that progression to DM can be decreased by more than half through lifestyle modification, or by use of metformin.³² Detecting both DM and pre-DM are therefore important public health objectives.

B.2 Detection of DM.

Despite the well-known morbidity of DM, detection remains suboptimal. Fully 30% of individuals who meet criteria for this disease remain unaware of their condition, and optimal screening strategies remain a matter of scientific inquiry. Because of cost and the lack of evidence of the benefits of earlier treatment, neither the US Preventive Services Task Force nor the American Diabetes Association (ADA) support community screening; rather, the ADA recommends opportunistic screening in the health care setting.³³ The dental practice is a health care setting, and therefore the feasibility of glucose measurement in the dental office is worthy of scrutiny.

B.3 Glucose testing methods.

Glucose can be tested at the point of care using widely available, easily applied methods. Glucose monitors have been developed and are routinely used by both patients and health care professionals for both screening and disease monitoring in office-based and hospital-based settings. Glucose monitors are routinely accurate to within 10% of serum glucose values obtained by venous blood sampling. Methods are user-friendly and standardized so that children can be taught to perform self-testing quickly and accurately.

B.4 Glucose testing in the dental office.

The proposal to test glucose in the dental office is not new. In 2002, a German group reported that DM screening of periodontitis patients can be accomplished using blood from gingival tissues during routine periodontal examination.³⁴ The correlation between the oozing blood and a capillary finger stick was very high ($r=.98$). Others have proposed screening for DM,³⁵⁻³⁷ or have recommended that glucose testing equipment be available for emergency medical management in the dental office.³⁸⁻⁴⁰ However, in 2007, among the 852 DPBRN general practices and 268 specialty practices, fewer than 10 routinely screen for DM even in high risk patients, and the vast majority (>98%) did not have on-site glucose monitors (unpublished preliminary data acquired for this study). Therefore, glucose testing is not a widespread practice in dental offices.

B.5 Significance.

Our study will evaluate the feasibility of glucose testing in the dental office. Since past propositions for glucose testing appear to have gained little traction with practicing dentists, an analysis of the barriers to implementing

such testing can point the way to strategies for implementation. In addition to opening the door to opportunistic screening among appropriate candidates in the dental office, if found feasible, glucose testing in the dental office will enable practice-based research on such important topics as post-operative infectious complications and pre-operative hyperglycemia. It is not clear whether the evidence for post-operative infectious risk incurred by hyperglycemia reported in the surgical literature carries over to the dental surgical setting. Such studies can only be carried out if glucose can be assessed at the point of service, in the dental office.

C. Research Design and Methods

C.1. Study Setting: Dental Practices of the DPBRN.

This study will be open to all dental practices enrolled in DPBRN, be they general dentists or specialists. More than 250 of these private practitioners have fulfilled UAB IRB requirements and have been trained to be investigators in DPBRN-sponsored clinical studies. The other DPBRN dentists who wish to participate in the study will complete training prior to study initiation at their practice.

The DPBRN comprises a group of dental practitioners in practices from Alabama, Mississippi, Florida, Georgia, Minnesota, Oregon, Washington, and Scandinavia. General dental practices represent 76% of the total with the remaining 24% relatively evenly divided between Oral and Maxillofacial Surgery, Periodontics, Prosthodontics, Endodontics, Pedodontics and Orthodontics. At least one orientation session was attended by 306 of the enrolled dentists of whom 253 have completed training for human research.

C.2. Enrollment. We will enroll 25 practices (five practices selected at random from a group of willing participants in each DPBRN region) to implement glucose testing among 375 of their patients (15 for each practice). Since 50% of adult Americans are overweight or obese, we anticipate that most practices will be able to complete this number within approximately 3 months. It is important to implement this study over a sufficient time period to permit unanticipated problems to emerge, and also to obtain stable estimates of eligibility and uptake among patients, and work load for staff. We will solicit interest by sending all practices an informational flyer about the opportunity to participate, with the toll-free number to call if interested.

C.3. Methods used to accomplish Specific Aim 1 (To quantify the percentage of DPBRN patients who meet the

American Diabetes Association screening criteria and to describe the characteristics of these patients). All eligible patients scheduled for a routine dental examination will have a screening form filled out. The percentage of patients with at least one risk factor will be obtained from among all scheduled eligible patients, providing an estimate of the volume of adults who are potential screening candidates who present to DPBRN offices. Because DM is a separate criterion, we can provide estimates of the volume of recognized DM patients, as well as those who have no recognized DM but at least one other screening criterion.

Each enrolled practice will participate in a training session. The study protocol will be reviewed and discussed, and questions will be answered by the investigators. Practitioners and/or their delegated staff will be trained in the use of a commercially available glucose meter, which will be provided free of charge to all participating offices, along with test strips, lancets and calibration equipment.

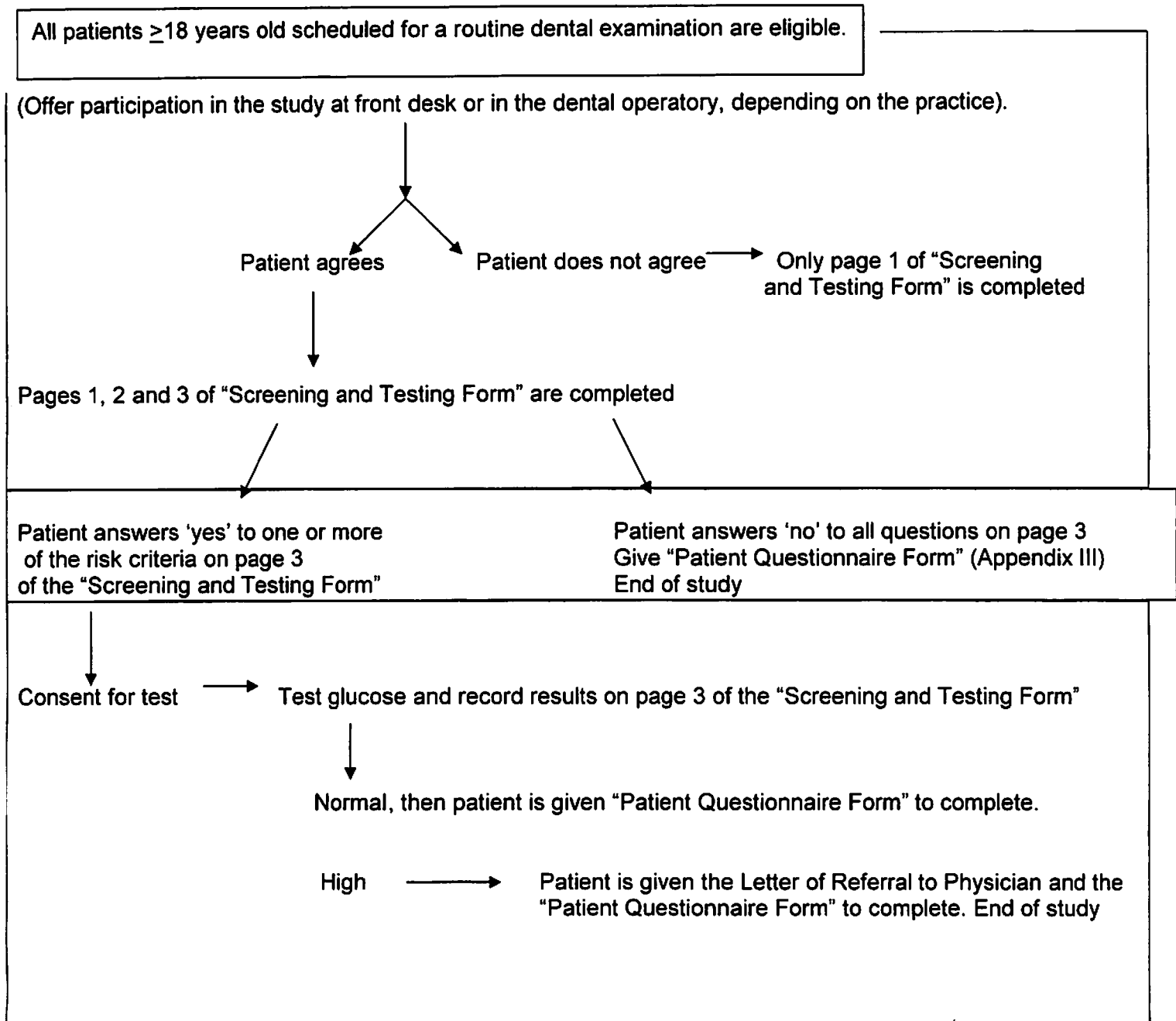
We will use the American Diabetes Association and the US Preventive Services Task Force recommendations for patients who should have glucose screening in health care settings.³³ **All patients with body mass index (BMI) ≥ 25 kg/m², or with a history of hypertension or hypercholesterolemia, or with a diagnosis of DM or pre-diabetes, will be offered glucose testing.** The protocol will include a BMI chart so that practices can quickly determine this value using patient-reported height and weight (Screening and Testing Form, Appendix I). Hypertension, hypercholesterolemia and DM will also be patient-reported.

Although the American Diabetes Association recommends fasting plasma glucose for screening, we will implement a protocol to test random glucose for several reasons. First, in the feasibility phase, maximizing patient acceptability and user-friendliness for dental staff is important. Second, random blood sugar is informative; if in the normal range, the likelihood of DM is low. Even modest elevations could indicate a pre-DM state worth evaluating further, including risk stratification. Third, among diabetic patients, random glucose levels can be informative, especially if the patient can provide additional information about when they last ate.

If glucose testing is found feasible in the dental office, we will examine the possibility of fasting glucose testing in future, through such strategies as early morning appointments or returning the following morning for the test.

We will initially restrict the study to adults over the age of 18. While diabetes is increasing in children, rates in this population are still far below those for adults. Children require special consideration for IRB issues, adding complexity to the protocol. At this early stage of evaluating the feasibility of glucose testing in the dental office, we will therefore focus on adults.

Flow Diagram



C.1.1. Patient eligibility for testing. Once practices are enrolled, each will implement the protocol and begin offering glucose testing to consecutive patients over the age of 19 who are scheduled for a visit with an exam, for a period of four weeks. The protocol will proceed in stages as follows.

Front desk protocol. Patients presenting to a participating dental office for initial or recall examinations who are over age 18, regardless of their dental history, dentate status, chief complaint, gender, race or ethnicity will be eligible to enroll if they present for a visit that includes a routine dental examination. Patients undergoing continuing treatment where an exam is not part of the visit will not be eligible. The front desk staff will inform the eligible patients of the possibility to enroll and, if the patient is interested, will provide the "Patient Information for Consent" form (Appendix II). If the patient gives verbal consent for participation, the front desk staff will place a study form packet on the chart. The presence of the study form packet will signal to the dentist or other designated staff to screen the patient and offer glucose testing if they screen positive.

We expect this "front desk protocol" to be the typical procedure. However, on our experience with DPBRN practices to date, some practices will prefer that this part of the protocol take place in the dental operatory(s) since all eligible patients will obtain their dental examination there.

Exam room protocol:

1. Screening. Eligible patients will be screened by the participating dentists or other staff in each office. Screening will take place in the privacy of the exam room. The dentist/staff person will inform the patient that the practice is offering a special blood sugar screening program, and that the patient may be eligible to have their blood tested. They will then proceed with the screening questions:

1. Has a doctor ever told you that you have high blood pressure or high cholesterol?
2. Has a doctor ever told you that you have diabetes or pre-diabetes?
3. What is your height?
4. What is your weight?

The dentist or staff will determine the BMI from the chart on page 3 of the "Screening and Testing Form" (see Appendix 1). S/he will fill out a screening form on each eligible patient, including in addition to the answers to the 4 screening questions the patient's sex and age. Because the rate of acceptance of testing among patients is informative, the dental office will provide the data on these forms to the Coordinating Center for individuals who are approached but decline to participate. This will provide an estimate of the participation rate as well as of differences between the participating and non-participating patients that might bias the results of a study. The dental staff will be trained to politely inquire if the patient is willing to share any reasons they have for not participating, and these will be recorded on the screening form.

2. Consent for testing. Patients who meet at least one of the screening criteria will be offered the opportunity to participate in the remainder of the study. All patients will be given study ID numbers and the study forms will be attached to their dental record. All aspects of the study will be explained verbally by the local investigator who will also answer all patients' questions and concerns. In addition, the Principal Investigator's telephone number at the UAB will be available to address any issues that arise, with which the local staff is unfamiliar. If the patient consents, all his/her data, including glucose level, will be kept in strict confidentiality with the rest of his/her dental record at the participating private practice. The glucose reading together with the patient's demographic information (age, gender, race and ethnic group), and the pertinent medical history will be provided to the study investigators at the DPBRN Coordinating Center in de-identified tabular form only, using standardized data collection forms developed for this study, and including only the patient's random study ID, and no personal health information.

C1.2. Glucose testing. We acknowledge that variation in practice structure will likely result in variation in how the protocol is implemented. Based on most practices' organization, we anticipate that in a majority of cases, the dentist or hygienist will be the professionals performing the glucose testing. On calling the patient to the room, the dentist or their assigned trained staff member will note eligibility based on the forms appended to the chart by the front desk clerk. Eligibility and screening are described above. If the patient screens positive, the dentist or trained dental staff person will inform the patient about the details of the test, and answer all questions. Enrolled patients will have his/her random plasma glucose assessed with the study glucose meter at the beginning of the dental visit. The office staff trained in the use of the glucose meter will first explain the procedure to the patients. S/he will then perform the following procedure: One of the patient's finger tips will be

wiped with alcohol gauze and allowed to dry. A lancet device designed for glucose testing will be used to prick the lateral aspect of the patient's finger tip. A drop of blood will be expressed from the finger and placed on a test strip designed for use with the glucose meter, and direct pressure will be immediately applied to the wound. The strip will then be inserted into the glucose meter, which will provide an electronic reading of capillary blood glucose within minutes. The patient's finger tip will then be covered by a sterile adhesive dressing, as necessary. The glucose reading will be recorded on the patient's study form. Note will be made of whether the patient is in a fasting state (has not eaten in 12 hours) (Appendix 1).

Patients will receive a card with their glucose reading and information about how to interpret the reading, as well as literature designed for patients from the American Diabetes Association about diabetes and pre-diabetes. If the glucose value is abnormal, the dentist will advise patients that they may benefit from more formal evaluation, and to discuss the result with their physicians. The card will include a paragraph that briefly describes the study and what was done in the dental office. The card will serve as a referral to the physician. The phone number and email address of the PI will be provided for additional questions (see "Physician Referral Note" in Appendix V).

According to American Diabetes Association guidelines, the appropriate follow-up for a hyperglycemic patient is a fasting glucose measurement or a glucose tolerance test. Both procedures are relatively routine, minimally invasive and inexpensive. However, we acknowledge that some expense and inconvenience may be encountered as a possible result of our study and we will inform the patient of such. We will recommend that the patient reads carefully the provided literature before visiting their physician to give them an opportunity to formulate questions, and that they follow the physician's advice.

Following the glucose testing and the provision of results, the patient will then undergo usual dental care.

C.2 .Methods used to accomplish Specific Aim 2 (To quantify the acceptability of conducting glucose testing in the dental office and barriers to regular screening, as reported by DPBRN patients and practices).

C2.1. Overview.

We will conduct a barriers analysis from the practitioner perspective. We have conducted limited informal interviews with DPBRN Executive Committee members and randomly selected DPBRN office staff and dentists to identify barriers and benefits they perceive to glucose testing in the dental office. Based on this formative work, we have designed a feasibility study that addresses the identified barriers, and builds on the identified perceived benefits. The study will demonstrate the feasibility of glucose testing in the dental office as a routine part of care, and set the stage for future studies of outcomes of DM screening and post-operative infectious risk. The American Dental Association sees dentistry as a potential entry point to the overall health care system⁴¹), and DPBRN Study 10 is a result of DPBRN's agreement with that vision.

C.2.2 Assessment of barriers and benefits and design of the pilot feasibility study.

We have conducted semi-structured interviews with members of the DPBRN Executive Committee to solicit assessment of barriers and benefits to glucose testing in the dental office. We have generated a draft list of potential barriers and benefits of glucose testing in dental practice. Responders were asked to rate possible barriers and benefits as *very important*, *important*, *neutral* or *not important*. They were also given the opportunity to add possible barriers and/or benefits that were not on the list. New items were similarly ranked by other responders. Barriers and benefits that received at least two *important* or *very important* rankings were listed in the Dentist Questionnaire form (Appendix IV).

As in previous DPBRN studies, we will field-test all instruments for this study.

C.2.3. Pilot feasibility study. For the feasibility study, we will aim to enroll 25 practices (five practices selected at random from a group of willing participants in each DPBRN region) to implement glucose testing among 375 of their patients (15 for each practice). Since 50% of adult Americans are overweight or obese, we anticipate that most practices will be able to complete this number within approximately 3 months. It is important to implement the pilot study over a sufficient time period to permit unanticipated problems to emerge, and also to

obtain stable estimates of eligibility and uptake among patients, and work load for staff. We will solicit interest by sending all practices an informational flyer about the opportunity to participate, with the toll-free number to call if interested.

C.2.4. The Dentist/Staff Questionnaire. This questionnaire will be used to ask all the dentists and/or staff to rate the most important barriers and benefits of glucose testing, from the perspective of having completed this protocol (Dentist/Staff Questionnaire, Appendix IV). At the conclusion of the study, each participating dentist and any staff who performed the glucose testing will be provided the questionnaire by the Regional Coordinator, who will know how many dentists/staff conducted glucose testing at each practice, and therefore the anticipated number expected to complete the questionnaire. The questionnaire will be completed anonymously, and will be included in the sealed box in each practice that will also contain the anonymous patient surveys. This box will be picked up in each practice by the Regional Coordinator for forwarding to the Coordinating Center (see below). A bar code on the form will link these questionnaires to the enrolment forms from the same practice, such that the specific answers can be connected to the practice characteristics.

C2.4. Patient satisfaction survey.

After completing the dental treatment the patient will be asked to complete a short questionnaire regarding his/her personal impressions of glucose testing in the dental office (Patient Questionnaire, Appendix III), regardless of whether the patient has a blood sugar test done. The questionnaire will include a question about how satisfied the patient was with receiving glucose testing that day, answered using a Likert scale (with 5 response options ranging from Very Dissatisfied to Very Satisfied). S/he will also be asked if the glucose testing will change their likelihood of returning to the dental practice, or the likelihood of referring family and friends. This form will be given to the patient by the practitioner and completed in the exam room after the practitioner has left, providing privacy to maximize disclosure. The questionnaire will include only the patient's study ID and no other identifying information. The patient will be asked to place the questionnaire inside a sealed box at the front desk on their way out of the practice. At the end of the study, the DPBRN Regional Coordinator will collect the de-identified patient information forms and the sealed boxes with completed questionnaires and mail them to the Coordinating Center for data entry and analysis.

C.3. Process evaluation.

This study is being implemented in potentially widely dispersed community practices with considerable variation in office structure and staff mix. It is likely that barriers to implementation will vary across offices to some degree, and the team dynamics across practices are also likely to differ. Therefore, we anticipate a variety of challenges to arise as the study is being implemented. We plan to track progress during implementation and to evaluate staff and dentist impressions as the study progresses and after the study is completed.

C.3.1. Process evaluation during implementation.

The Regional Coordinator will play an important role in the process evaluation. The Coordinator will identify a practice champion who is particularly interested in the topic area, and who will serve as the contact person with the Regional Coordinator, and possibly the Coordinating Center investigative team. This person may in some practices be a hygienist, one of the dentists, or a dental assistant. The Regional Coordinator will help the practice to plan the implementation through a series of weekly conference calls. The Coordinator will document the differences in implementation across the 25 participating practices (i.e. person responsible for study implementation and glucose testing, patients' attitude, study progress) in writing and provide a weekly report to the investigators. Once the study is implemented, the Coordinator will check in with the practice contact weekly until the conclusion of the study (375 patients have been tested). Ad hoc e-mail and telephone communication will also be encouraged. Problems that cannot be solved by the practice will be brought to the study team for collaborative input.

C.3.2. Data quality.

Data will be collected on standardized forms. Regional Coordinators will have been fully trained in this protocol and are experienced in good clinical research practice. On receipt at the Coordinating Center, data forms are also reviewed there for completeness and missing data. If any questions arise about the data, the

Coordinating Center will contact the Regional Coordinators directly, who will then contact the practices for clarification, or if necessary, visit the practice to obtain relevant documentation. All data are double-entered on receipt by the Coordinating Center.

D. Data Analysis

D.1 Specific Aim 1 To quantify the percentage of DPBRN patients who meet the American Diabetes Association screening criteria and to describe the characteristics of these patients.

D.1.1. Patient enrollment data.

Front office staff will identify all adult patients presenting for examinations, representing the denominator of possible eligible patients for screening. As detailed above, approximately 50% of adults are likely to screen positively, and we will formally evaluate the proportion of positive screens of all eligible patients both overall and its variation across practices. Furthermore, we will track agreement to participate among eligible candidates, recording the age, sex, race, obesity status and medical conditions screened for. Using this information, we will determine the response rate for glucose testing of all patients offered testing as a simple proportion, and examine the overall response rate as well as variation across the participating practices. We can also examine whether age, sex, race, obesity status or the presence of medical conditions predict agreement to be tested. This will be useful information for a larger study, since extra efforts may need to be made for some types of patients to encourage testing.

The percentage of study participants who meet the American Diabetes Association screening criteria will be calculated, along with a 95% confidence interval, based on the normal approximation to the binomial distribution. Logistic regression will be used to evaluate the association between age, sex, race and obesity status with agreement to participate in the study. Practice type will be included in the model in order to ascertain whether this is independently associated with uptake; that is, whether patients in specialty practices are more or less amenable to glucose testing. The proposed sample size of 375 participants will provide sufficient precision to estimate the percentage meeting the screening criteria within $\pm 5.1\%$. Given the expected proportion of 50%, this would result in an expected 95% confidence interval of (44.9%, 55.1%). Based on this same expected proportion of participation, the proposed sample size would provide 80% power to detect an odds ratio of approximately 1.8 for the association of the hypothesized predictors with participation.

D.1.2. Glucose test results. Glucose test results will be examined for distribution across all enrolled participants, with note made of the proportion in the abnormal range. The proportion of tests done on DM patients will also be available. Because we will collect information on patient age, sex, race, obesity status and medical conditions, we will be able to examine predictors of abnormal random glucose, and of random glucose level in these dental practice patients. Glucose level will be categorized as "normal" or "abnormal". Abnormal glucose may be defined as above 110 mg/dl (fasting), or above 200 mg/dl (post-prandial) (the range at which random glucose correlates highly with presence of DM). Multiple logistic regression will be used to evaluate the patient characteristic and medical condition variables as predictors of abnormal glucose levels. A stepwise variable selection approach will be used to develop a predictive model. Performance of the predictive models will be evaluated based on the area under the receiver operating characteristic curves, as well as by calculating sensitivity and specificity of the models for prediction of the observed glucose categories using the best-performing probability cutpoint for each model. The proposed sample size will provide approximately 80% power to detect an odds ratio of 1.8 for the association between a predictor variable and glucose category, assuming equal-sized groups.

D.2. Specific Aim 2: To quantify the acceptability of conducting glucose testing in the dental office and barriers to regular screening, as reported by DPBRN patients and practices.

D.2.1. Pilot feasibility study data.

The data from this study will be of 5 types: (1) patient enrollment data, (2) glucose test results, (3) patient satisfaction data, (4) staff survey data, and (5) process evaluation data. Data on practice characteristics have already been collected from the DPBRN enrollment questionnaire.

D.2.2.a Patient satisfaction data.

Patients will be asked satisfaction questions at the time of exit from the practice. Responses to these questions will be on a 5-point Likert scale. We will examine the distribution of the responses, and will examine the associations of satisfaction or dissatisfaction, with the age, sex, race, obesity or medical conditions of the patients, using multiple regression analysis. For the evaluation of association with the potential predictor variables, the Likert scores will be summed to calculate an overall measure of satisfaction. Scores on individual questions may be dichotomized as "satisfied" (scores of 4 or 5, the most satisfied), or "dissatisfied" (scores of 1 or 2) for the purpose of evaluating association with potential predictors. Univariate associations will be evaluated using the odds ratio as the measure of association. Multivariable associations will be modeled using multiple logistic regression analysis.

D.2.2.b Process evaluation data.

The ongoing process evaluation during the implementation phase of the pilot study will result in qualitative reports that the study coordinator will bring to the study team. While a list of unexpected barriers will be kept, no formal analysis of these data is anticipated. The types of problems encountered during implementation will be important for planning of the future studies.

D.2.2.c. Dental practitioner survey.

On study completion, staff who conducted the glucose testing and the dentist will complete a survey assessing barriers and benefits to glucose testing again, from the perspective of having just completed the study. Between 25-50 individuals are expected to complete this survey. We will calculate descriptive statistics on each item, evaluating the distribution across the Likert scale, and identifying the items with the most extreme responses as being either important or not important. This information will be vital in planning future studies.

E. Human Subjects

E.1 This is cross-sectional study that tests the feasibility of glucose monitoring in dental practice. For this purpose, human subjects are required.

E.2 This is an observational study and it does not involve any therapeutic methods.

E.3 Protection of human subjects from research risks:

E.3.1 No exemptions apply.

E.3.2 Patients who are scheduled for dental examination in a DPBRN practice will be eligible to enroll in this study.

E.3.3 We will collect demographic information and medical data from the patient's dental record and record their plasma glucose reading at the time of the dental appointment.

E.3.4 All dental patients 19 years old or older at the participating practices will be invited to enroll in this study if they are presenting for a routine dental examination.

E.3.5 Potential risks: Personal data of patients may be divulged during data gathering and analyses;

- There are minimal physical risks to the patients in this study, which consist of mild discomfort from the glucose test needle prick.

E.3.6 Protection against risks: We will not use patient names or social security numbers in our analyses or data collections. All study documentation will be kept in a locked room with restricted access. All datasets will be password protected. Thus, patients' identity will be protected.

The finger prick will be performed per manufacturer's instructions after thorough cleansing of the skin; hemostasis will be achieved prior to the patient's departure

E.3.7 Benefits from participation:

Patients participating in this study may be alerted to possible presence of DM or pre-DM or to inadequate glycemic control. In such case, they will be advised to follow up with their physician for definitive diagnosis and treatment. Early diagnosis and improved glycemic control may be of significant benefit to the patients' health.

E.4 Data safety and monitoring plan:

We will regularly monitor the raw data to insure that all entries are correct and complete.

Additionally, a monitoring committee will be formed, which will comprise the DPBRN Steering Committee. This committee includes the Network Chair, PI of the DPBRN Coordinating Center, and PIs of each of DPBRN's five regions. This committee will supervise the safety and effectiveness of the study and will recommend conclusion of the protocol if significant risks have become apparent. A report on safety will be presented to the monitoring committee monthly semiannually by the principal investigator. The committee will review the report and make recommendations. The principal investigator must respond and/or implement the committee's recommendations within one month. A copy of these reports and recommendations will be provided to the IRB.

E.5 Inclusion of women:

Female dental practitioners enrolled in DPBRN as well as female dental patients will be eligible to participate in this study. DM affects both men and women. We anticipate that females will comprise about 55% of the patients enrolled in this study. Both genders will be eligible to enroll. Current data do not suggest significant differences in early diagnosis outcomes between males and females. Nevertheless, we will study the possible modifying effects of gender on outcomes of interest.

E.6 Inclusion of minorities:

DPBRN dentists and their patients of all races and ethnicities will be eligible to enroll in this study. Of the 155 dentists who participated in DPBRN Study 2, approximately 4% were African-American and 10% were Asians. We anticipate that the practice enrollment percentages in DPBRN Study 10 will be similar.

Patient race is also expected to be similar to Study 2 and is shown in the table below:

PARTICIPANT RACE DPBRN Study 2					
BRACE	Frequency	Percent	Cumulative Frequency	Cumulative Percent	
WHITE	3050	82.21	3050	82.21	
BLACK	445	11.99	3495	94.20	
AMERICAN INDIAN/ALASKA NATIVE	10	0.27	3505	94.47	
ASIAN	107	2.88	3612	97.36	
NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER	9	0.24	3621	97.60	
OTHER	89	2.40	3710	100.00	

Current data suggest that DM outcomes are worse for ethnic minorities. We plan to closely examine race and ethnicity as possible effect modifiers by adding race/ethnicity-by-outcome assessment interaction terms.

E.7 Inclusion of children:

Pediatric populations do not have the same disease characteristics as their adult counterparts. Additionally, testing of children with a needle prick may pose extraneous difficulties in a dental practice. For this study we propose to test only adults 19 years of age or older. Because NIH defines adult as 21 years old or older, this study will include children. We anticipate that about 5% of DPBRN Study 10 patients will be 19 – 21 years old, and therefore will be classified as children.

F. Animals: Not applicable

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