ORIENTATION HANDBOOK FOR

THE NATIONAL DENTAL PRACTICE-BASED RESEARCH NETWORK

(NATIONAL DENTAL PBRN)

A network about, with, and for practitioner-investigators and their patients

the nation's network

Practical science done about, in, and for the benefit of "real world" clinical practice.

Disclaimer: This document has a version number and applicable date because specific content is subject to change.

A BRIEF HISTORY OF THE NATIONAL DENTAL PBRN

The National Dental Practice-Based Research Network (National Dental PBRN) began in April 2012 with a grant funded by the National Institute of Dental and Craniofacial Research (NIDCR), one of the Institutes of the National Institutes of Health (NIH). The NIDCR press release for this grant is publicly available at http://www.nih.gov/news/health/apr2012/nidcr-12.htm. The award period is April 6, 2012 to March 31, 2019. The grant number is U19-DE-22516.

In 2005, NIDCR funded three regional networks for the period 2005-2012. These three networks were "The Dental PBRN" (DPBRN), Northwest PRECEDENT, and the PEARL network. The DPBRN was administratively based at the University of Alabama at Birmingham (UAB) and comprised four U.S. regions and one Scandinavian region. The PRECEDENT network was administratively based at the University of Washington and Oregon Health & Science University, and comprised practitioners from several states in the western and northwestern U.S. The PEARL network was administratively based at New York University and predominantly comprised practitioners from the Northeast U.S. Many lessons were learned during this seven-year period, most of which are described in more detail in the article: *Lessons learned during the conduct of clinical studies in The Dental PBRN. Journal of Dental Education 2011; 75(4): 453-465.*

With its release of a funding opportunity announcement in 2011, NIDCR declared that it would fund the next phase of evolution of its PBRN initiative in 2012 as a single, nationwide network, and would no longer support regional networks.

NETWORK ADMINISTRATIVE STRUCTURE

The mission of the nation's network is "To improve oral health by conducting dental practice-based research and by serving dental professionals through education and collegiality". It is committed to maximizing the practicality of conducting research in daily clinical practice across geographically dispersed regions, so its structure is designed to focus some activities at the regional level (e.g., close interactions with practitioners), and other activities that can be done on behalf of the entire network centrally (e.g., study development).

The network comprises six regions of the United States. Practitioners in all of the U.S. states and territories are eligible for enrollment. Training for some studies may be provided via webinar or telephone conference call and therefore may be open to broad geographic areas. Other studies will require in-office training, and enrolled practices may be clustered within driving distance near the regional administrative bases. The locations of the regional administrative bases for these regions are shown below. The network's central administrative base is at UAB. The network's Coordinating Center is at Westat in Rockville, MD. Contact information for each of these sites is provided in a different document. Each region and the Coordinating Center has its own budget contracted with the National Network Director.

Western Region (region #1)
Administratively based at the Center for Health Research, Portland, OR.
This region comprises Alaska, American Samoa, California, Colorado, Guam, Hawaii, Idaho, Montana, Nevada, Northern Mariana Islands, Oregon, Utah, Washington, Wyoming.

Midwest Region (region #2)
Administratively based at the HealthPartners Institute for Education and Research in Minneapolis, MN.
This region comprises Illinois, Indiana, Iowa, Michigan, Minnesota, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin.

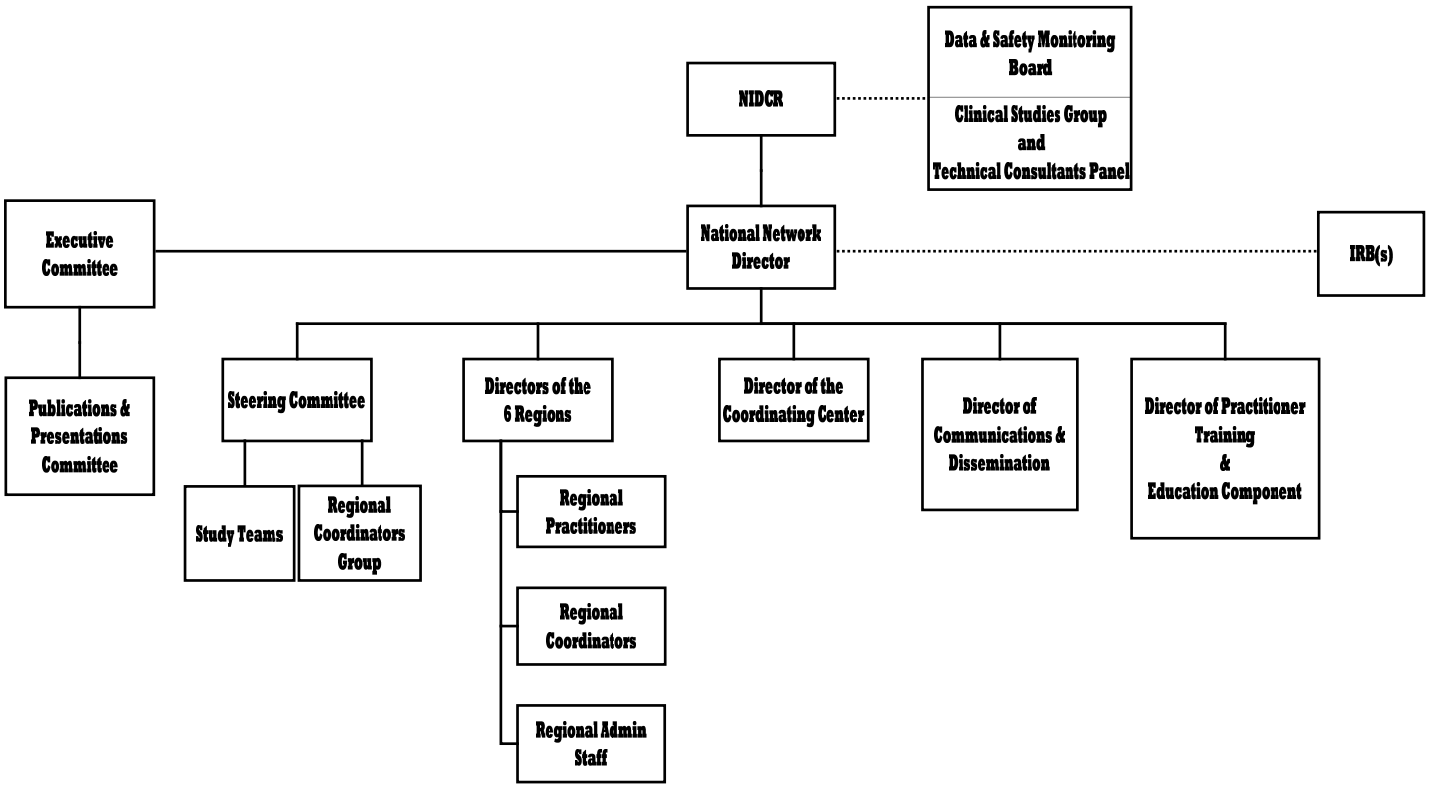
Southwest Region (region #3)
Administratively based at the University of Texas Health Science Center at San Antonio in San Antonio, TX.
This region comprises Arizona, Kansas, New Mexico, Oklahoma, Texas.

South Central Region (region #4)
Administratively based at the University of Alabama at Birmingham in Birmingham, AL.
This region comprises Alabama, Arkansas, Kentucky, Louisiana, Mississippi, Missouri, Tennessee, West Virginia.

South Atlantic Region (region #5)
Administratively based at the University of Florida in Gainesville, FL.
This region comprises Florida, Georgia, North Carolina, South Carolina, Virginia.

Northeast Region (region #6)
Administratively based at the University of Rochester in Rochester, NY.
This region comprises Connecticut, Delaware, District of Columbia, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Puerto Rico, Rhode Island, US Virgin Islands, Vermont.

The Coordinating Center for the national network is administratively based at Westat in Rockville, MD.



The network's organizational chart is shown above.

NIDCR (www.NIDCR.NIH.gov) is the main funder of the network. It is the federal government's lead agency for scientific research on oral, dental, and craniofacial health and disease. NIDCR is one of the National Institutes of Health in the U.S. Department of Health & Human Services, and is the main funder of oral health research in the nation. The Institute has been the NIH leader in its commitment to PBRN research, thus providing an unprecedented opportunity for the dental profession to improve the nation's oral health. Dr. Donald DeNucci is the NIDCR Program Official for the national PBRN initiative.

National Network Director (NND). The NND is responsible for overall scientific and administrative leadership, operations and fiscal management, and chairing the Executive Committee, among other duties. The NND is Dr. Gregg Gilbert at UAB.

Coordinating Center (CC). The Coordinating Center provides expertise in study design and statistical support, develops and maintains databases and information systems, conducts data analyses, participates in publications, among other duties. It is composed of faculty biostatisticians and staff with expertise in data management and analysis, study design, informatics, and communications technology. The Director of the CC is Dr. James Korelitz at Westat. The CC coordinates more than just data, so a DCC appellation would not be the preferred term so as to maintain continuity with terminology used in the 2005-2012 cycle.

National Director of Communications & Dissemination. This director oversees the network's communication and dissemination policies and activities, and directs the network's web site, its quarterly newsletter, a monthly e-update, and a member-only electronic mail list server. The Director of Communications & Dissemination is Dr. Sonia Makhija at UAB.

National Director of Practitioner Training & Education Component (PTEC). This director oversees the network's practitioner training and education activities. The Director of PTEC is Dr. Valeria Gordan at the University of Florida.

Executive Committee (EC). The EC is the key decision-making body of the network. It is composed of six practitioners representing each of the six Nodes, the National Network Director, and the Coordinating Center Director. NIDCR Program Official(s) serve in an ex officio non-voting advisory capacity. The main role of this committee is to prioritize research topics for protocol development and to review protocols prior to submission. The NND serves as the Chair of the EC. The EC meets on a monthly to quarterly basis, depending on the volume of anticipated work. The EC evaluates study ideas, study design, practitioner remuneration, network operations, among other duties.

Steering Committee (SC). The SC decides how best to implement the decisions of the EC; assists investigator groups with developing study applications into a more-final form before they are sent to the Executive Committee; and seeks to maximize coordination of tasks across regions, in conjunction with the Regional Coordination Group. Its voting members are the NND, Director of the CC, the Director of each of the six Regions. The Deputy Directors of each Region and a representative from the Regional Coordination Group also attend. The committee meets monthly by telephone conference and annually face-to-face. The NND serves as the Chair of the SC.

Regional Coordination (RC). The RC group comprises the Regional Coordinators from each region, a representative from the NND office, and a representative from the CC. It meets monthly by telephone conference and annually face-to-face to discuss regional coordination and implementation issues and makes recommendations to the SC regarding improving network operations. The Chair position of this committee rotates among the network's regions on an annual basis effective January 1st of each calendar year.

Study Teams. Once a protocol concept has been approved, a Study Team is formed. This team administers the study from protocol development, to feasibility and pilot testing, to data collection, to data analysis, to study closure. The team includes subject experts and is protocol-specific. The team is constituted by the NND in concert with the proposed Study Principal Investigator (SPI) and the NIDCR CSG. While forming the Study Team, the network may solicit expertise nationally/internationally if advisable, or only use expertise already available in the network, depending on what the study topic and study design may require. The composition of the team varies with the stage of the study. The study is typically administered via monthly conference calls of the team, whose only agenda items have to do with that study. During the protocol development phase, the minimum composition is the SPI, the subject expert(s), the NND, a Regional Coordinator, and a practitioner. At a later stage of protocol development, representatives from each region join the monthly Study Team conference calls during the data forms development, feasibility testing, pilot testing, and data collection phases. After data collection for the study has ended and its data set(s) are locked, the Study Team typically dissolves and at that point the SPI takes responsibility for leading data analyses and manuscript preparations, a process which itself may involve conference calls of personnel involved in manuscript preparation from the study.

NIDCR Clinical Studies Group (CSG). The CSG formalizes the process for Institute evaluation and approval of network projects. It is composed of NIDCR Program Officials, OCTOM (Office of Clinical Trials Operations & Management), and others from the Institute. Once a study concept has been approved by the Executive Committee, it is sent for review by the CSG. The CSG comprises experts in study methodology, scientific content, patient safety, and program knowledge. The CSG can approve with or without recommendations, or disapprove the concept. If disapproved by the CSG, no further study development occurs. If the concept is approved by the CSG and a Complete Protocol is developed and approved by the EC, the CSG evaluates the Complete Protocol and provides feedback as needed during an iterative process with an eye toward eventual approval of the final Complete Protocol.

NIDCR Technical Consultants Panel. This is a panel of study-specific subject experts recommended by NIDCR and chosen by the NND to guide specific aspects of protocol development.

NIDCR Data & Safety Monitoring Board (DSMB). The DSMB is an independent group of experts that advises NIDCR and study investigators on clinical studies, especially those that involve an intervention. The responsibilities of the DSMB include: (1) monitoring human subject safety by reviewing and evaluating the accumulated study data, and, when appropriate, efficacy or effectiveness; (2) review study conduct and progress; and (3) make recommendations to NIDCR concerning the continuation, modification, or termination of the study. Study-specific data as well as relevant background information about the disease, patient population, procedures and progress of the study are considered.

Publications & Presentations Committee (P&P). The network has a Publications and Presentations Policy, which is available at the network's public web site. One component of this policy is the P&P Committee. The purpose of this committee is to implement the publications and presentations policy and to review and approve all of the network's manuscripts, publications, abstracts, and study-

related presentations. The committee comprises a practitioner, representatives from two network regions, and representatives from the Office of the NND and CC. This committee encourages network publications and presentations, manages the publications process, and ensures compliance with the policy. The Chair of the P&P is Dr. Brad Rindal at the HealthPartners Research Foundation.

Practitioner Compensation System (PCS): The PCS provides timely and accurate compensation to practitioners and patients engaged in network projects. It is an efficient system that is linked to predetermined deliverables. The system includes an adjudication functionality to address disputes associated with compensation claims.

The National Dental PBRN EXECUTIVE COMMITTEE

The Executive Committee (EC) is a key decision-making body for the nation's network. Its members comprise one practitioner from each of the six regions of the network, the National Network Director, the Director of the network's Coordinating Center, and the NIDCR program official (in an *ex officio*, non-voting role). Practitioner members serve for three-year terms. Practitioners constitute the majority voting authority on the Executive Committee.

The duties of the EC are to make certain decisions and policy regarding studies done in the network and matters that directly affect the network's practitioners. It makes decisions about changes in study procedures as necessary; reviews and implements recommendations from the Institutional Review Board and/or Data and Safety Monitoring Board; reviews progress of studies in achieving their goals; and reviews data collection procedures. The EC also prioritizes research topics for study development, and reviews studies prior to further development at successive stages. The EC usually meets every month. The typical meeting is held by videoconference or teleconference, but once each year it meets face-to-face.

The EC agenda and supporting documents are sent as an Adobe "pdf" (portable document format) file by email in advance of the EC meetings. This usually occurs one week before the meeting. This packet also has the call-in number.

In addition to formal meetings, it is not uncommon for EC members to have "virtual" discussions of topics by email in between EC meetings. For some topics that do not require much discussion, formal votes are also handled by email.

These are the eligibility criteria for nomination as a practitioner representative on the EC:

1) must be a licensed practitioner engaged in the regular practice of dentistry or dental hygiene;
2) must be a general dentist or a dental hygienist who sees patients in a general practice setting;
3) must have participated in at least one network clinical study (i.e., the network Enrollment Questionnaire is not sufficient);
4) must have access to e-mail, be able to receive attachments via e-mail, and be willing to communicate via e-mail on a regular basis;
5) must be able to participate in the regularly-scheduled DPBRN Executive Committee meetings that are held by videoconference or teleconference and during face-to-face meetings at locations throughout the U.S.

The current members of the EC are listed at the network's public web site.

The EC makes decisions by majority vote. For an EC meeting in which any votes are taken, a simple majority of the EC membership must be in attendance, although at least three of practitioners must be present. This does not preclude the EC from having a discussion during a meeting that does not have such a quorum, but no vote can be taken.

THE STUDY DEVELOPMENT PROCESS

A key operating principle for the nation's network is that all studies answer questions that can improve the daily clinical practice of dentistry. Furthermore, the research itself is done within the practices of the network members. This situation creates a healthy tension between the needs of a sound research project and the need to minimize disruption of daily clinical practice. In this sense, the process cannot require the researchers to become practitioners nor the practitioners to become full-time researchers. The overall process of study development is shown on the next page (National Dental PBRN Protocol Development Process Timeline). Importantly, practitioners provide input at each step of the process. This is especially true of the practitioners on the Executive Committee. It is imperative to the success of the nation's network that it conducts studies that practitioners find useful, interesting, feasible, and that have the potential to provide results to improve daily clinical practice. Ideas for studies are obtained from responses provided on the enrollment questionnaire, in face-to-face meetings (e.g., at orientation sessions delivered in continuing education format, at annual meetings of practitioners, or in visits to the practice), from the academic community, or at the network's public web site. Ideas for studies are discussed and prioritized by the Executive Committee. Some study ideas are rejected by the Executive Committee, typically because they are judged not to be of broad interest to practitioners, judged not to be sufficiently impactful on routine clinical practice, or because they are not feasible to conduct in daily clinical practice.

The first step is for the proposed Study Principal Investigator (SPI) is to complete the Study Concept Template, which is shown on page 9. The completed Study Concept Template becomes an agenda item for a meeting of the Executive Committee. It is helpful if the proposed SPI can attend this meeting (via telephone) to discuss the study concept and to answer any questions that the committee has. If the Executive Committee approves the study concept, the NND will forward it to the NIDCR Clinical Studies Group (CSG) for additional consideration. The NIDCR CSG will provide its decision using a Study Concept Evaluation Card, oftentimes providing additional feedback during an interactive, iterative process that may involve conference call(s) between NIDCR, the SPI, and the NND. If the NIDCR CSG approves the concept, then a Study Team is proposed.

The Study Team is proposed to the NIDCR CSG by the SPI and the NND. Biographical sketches (using the PHS Biographical Sketch Format page at http://grants.nih.gov/grants/funding/phs398/phs398.html) of primary study team members, and short biographical narratives of other team members, are submitted by the NND to the NIDCR CSG for approval. At its initial phase during the development of the full protocol, a Study Team comprises the SPI and other scientific content expert(s) that the SPI, NND, and NIDCR CSG judge to be appropriate. Typically the Study Team would also include at least one practitioner and a Coordinating Center biostatistician. While forming the Study Team, the network feels free to call on expertise nationally/internationally if warranted, or only use expertise already available in the network, depending on what the study topic and study design may require.

Once the Study Team is approved by the NIDCR CSG, the Study Team develops the study concept into a Complete Protocol using the applicable NIDCR protocol template. For minimal- risk studies, the template is located at http://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/MinimalRiskProtocolTemplate.htm. For intervention protocols, the template is located at http://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/InterventionProtocolTemplate.htm. After the Complete Protocol has been approved, budget documents (PHS 398 Form Pages 4 and 5) and the PHS 398 Targeted/Planned Enrollment Table (all available at http://grants.nih.gov/grants/funding/phs398/phs398.html) should be submitted for review and approval.

Typically, preliminary versions of the protocol are reviewed by the Executive Committee to maximize the study's applicability to and impact on daily clinical practice, feasibility, and scientific merit. After the Complete Protocol is approved by the Executive Committee, the NND forwards it to the NIDCR CSG for its review and approval, oftentimes during an interactive, iterative process that may involve conference call(s) between NIDCR, the SPI, and the NND. A DSMB may be advisable for certain studies, and if so, the Complete Protocol may be reviewed by the DSMB. If approved by the DSMB, the Complete Protocol is then submitted to the Institutional Review Board from each of its regions for review of human subjects considerations. Approved versions of data collection forms for each study are pilot tested with practitioners on the Executive Committee and selected practitioners across the network. Pilot testing may lead to changes in these forms to optimize use in a diverse range of practice settings. Version control of these forms is important, so investigators are directed to follow the guidelines at http://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/VersionControlGuidelines.htm. Once final versions of all forms have been completed, a study is implemented across the network.

National Dental PBRN Protocol Development Process Timeline

Study Concept (Study Concept Template form) reviewed by The National Dental PBRN Executive Committee (EC)

EC-approved study concept undergoes consideration at NIDCR Clinical Studies Group (CSG) meeting

2 weeks

Modification of study concept and reconsideration at NIDCR CSG meeting, if warranted

2 weeks

2 weeks

After CSG acceptance of study concept, NIDCR Medical Monitor determines whether or not DSMB is required

After the Study Concept is approved, a Study Team and Technical Consultants Panel are proposed and approved

2 weeks

Development of Complete Clinical Protocol using NIDCR Template

8 weeks

EC reviews and certifies that Complete Clinical Protocol is ready for submission to NIDCR

12 weeks

14 weeks

NIDCR CSG evaluates Complete Clinical Protocol

2 weeks

Modification of Complete Clinical Protocol and reconsideration at NIDCR CSG meeting, if warranted

2 weeks

4 weeks

NIDCR DSMB evaluates Complete Clinical Protocol

3 weeks

Final Protocol, Version 1.0 for submission to IRBs

5 weeks

9 weeks

After IRB approval, CTOA documents approved and uploaded

Study implementation

National Dental PBRN Study Concept Template

(use Calibri 11-point font and do not exceed seven pages)

Protocol Title	<Insert protocol title>
Principal Investigator/Study Team **Network Node/Institution**	<Insert name of Principal Investigator. Insert names of Study Team members/investigators to date.> <Insert PI's National Dental PBRN node and institution/affiliation.>
Background and Scientific Rationale	<Describe the research problem and provide compelling scientific rationale for the research.> <Summarize prior studies that may provide background to this research. Summarize experience and/or history relevant to the research.> <Briefly discuss any literature that may provide background and rationale for this study.>
Specific Aims	<List specific aims of the study>
Expected Risks/Benefits	< Include expected risks and benefits to subjects and/or society.>
Eligibility	<Identify the subject/donor population being evaluated by the protocol.> <List inclusion and exclusion criteria.> <Indicate the source of subjects/donors.> <Describe specifically and state the justification for any vulnerable population or any excluded populations, for example: minors.>
Subject Enrollment	<Describe participant identification and screening.> <Describe the primary strategy for participant recruitment and enrollment.>
Study Design and Procedures • **Study Model**	<Describe the study design and study groups or cohorts.>
• **Intervention**	<Describe intervention if there is an intervention>
• **Biospecimens Collected**	<List any biospecimen types to be collected and purpose for each sample type. Will biospecimens be retained for future research? If so, is DNA extraction and analysis possible from retained specimens?>

• **Other Data Collected**	<Specify other types of data that will be collected, e.g., photographic or radiographic images, periodontal measurements, questionnaire responses, etc. For survey studies, describe the development or selection of the questionnaire>
• **Outcome Measures**	<Specify primary and/or secondary outcome measurement(s) or observation(s) used to assess the effect of an intervention or to describe the patterns of disease, traits or associations with exposures or risk factors which are the focus of the study. If appropriate to study design, you may wish to include independent and dependent study variables.>
• **Time Perspective**	<What is the temporal relationship between the observation period and time of participant enrollment? Is the study prospective, retrospective, cross-sectional or other (explain)?>
• **Enrollment**	<What is the participant target enrollment - per site and study total?>
• **Retention**	<Describe the primary strategy for participant retention, if applicable.>
Study Sites	<List which National Dental PBRN region(s) would be involved>
Planned Accrual Period	<Insert time (months, years, etc.)>
Planned Study Duration	<Insert time from first participant-first visit to last participant-last visit (months, years, etc.)>
Duration of Subject Participation	<How many study visits are required for each participant? What is the expected duration of subject participation?>
Justification for why the National Dental PBRN is the best setting for the study as compared to an academic health center or similar setting	
Feasibility to conduct high quality study and recruitment potential	
Potential to change clinical practice	
Impact on the oral health of the public	