Published in final edited form as:

J Periodontol. 2013 May ; 84(5): 567–571. doi:10.1902/jop.2012.120116.

Practice Based Research Networks Impacting Periodontal Care: PEARL Initiative

Frederick A. Curro^{*}, Van P. Thompson[†], Ashley Grill^{‡,§}, Don Vena^{||}, Louis Terracio[¶], and Frederick Naftolin[#]

^{*}Practitioners Engaged in Applied Research & Learning (PEARL) Network, Department of Oral Pathology, Medicine, and Radiology, College of Dentistry, New York University, New York, NY

[‡]Department of Dental Hygiene, New York City College of Technology, City University of New York, Brooklyn, NY

[§]PEARL Network, Department of Dental Hygiene, College of Dentistry, New York University

^{||}PEARL Network, EMMES Corporation, Rockville, MD

[¶]PEARL Network, Department of Basic Science and Craniofacial Biology, College of Dentistry, New York University

[#]PEARL Network, Department of Obstetrics and Gynecology, School of Medicine, New York University

Abstract

In 2005, the National Institute of Dental and Craniofacial Research /National Institutes of Health funded the largest initiative to date to affect change in the delivery of oral care. This commentary provides the background for the first study related to periodontics in a Practice Based Research Network (PBRN). It was conducted in the Practitioners Engaged in Applied Research & Learning (PEARL) Network. The PEARL Network is headquartered at New York University College of Dentistry. The basic tenet of the PBRN initiative is to engage clinicians to participate in clinical studies, where they will be more likely to accept the results and to incorporate the findings into their practices. This process may reduce the translational gap that exists between new findings and the time it takes for them to be incorporated into clinical practice. The cornerstone of the PBRN studies is to conduct comparative effectiveness research studies to disseminate findings to the profession and improve care. This is particularly important because the majority of dentists practice independently. Having practitioners generate clinical data allows them to contribute in the process of knowledge development and incorporate the results in their practice to assist in closing the translational gap. With the advent of electronic health systems on the horizon, dentistry may be brought into the mainstream health care paradigm and the PBRN concept can serve as the skeletal framework for advancing the profession provided there is consensus on the terminology used.

Correspondence: Dr. Frederick A. Curro, New York University College of Dentistry, 380 Second Avenue, Suite 302, New York, NY 10010. Fax: 212/995-4568; fac3@nyu.edu.

[†]Currently, PEARL Network, King's College London Dental Institute, London, UK; previously, PEARL Network, Department of Biomaterials and Biomimetics, College of Dentistry, New York University.

The authors report no conflicts of interest related to this study.

Keywords

Comparative effectiveness research; dentistry; evidence based dentistry; periodontal disease; research subjects

Practice Based Research Networks (PBRNs) offer a venue for dentistry to work in synergy with medicine and other health care providers. The electronic health record may provide the profession with the ability to communicate with other disciplines in health care. As health care becomes more complex and interdisciplinary, the dental paradigm may change from a traditionally solo practice of patient care to being part of the total health care approach to treatment, eventually centered in the medical home model. Some 71% of dentists in the United States are engaged primarily in private practice,¹ and only a small percentage of these participate in the academic environment. The purpose of this commentary is to present a brief overview of the PBRN concept and how it may affect periodontology, patient health, delivery of care, and clinical outcomes from both patient and provider perspectives.

In 2005, the National Institute of Dental and Craniofacial Research (NIDCR) funded a concept that was first proposed in medicine.^{2,3} This concept of a PBRN, known more descriptively as a practice based clinical network, was nurtured by the Agency for Healthcare Research and Quality and funded, until recently, on a per-study basis. The New York University PBRN, termed PEARL, for Practitioners Engaged in Applied Research and Learning, was designed to function as a clinical research unit capable of conducting a variety of studies under the principles of Good Clinical Practice (GCP).⁴ By providing background and perspective related to PBRN studies in periodontics, individuals may better understand the impact of PBRN research. The distinguishing aspects of the NIDCR dental PBRNs were the amount of the funding, the number of practitioners engaged, and the length of time that they were funded. The PBRNs were in a partnership with the NIDCR and committed to conduct a number of studies over a 7-year period.⁵ Each PBRN differs in infrastructure, nature of the clinical studies conducted, and, most importantly, the clinical operations of the studies. Although no consensus on a definition of a PBRN presently exists, PEARL functioned under the following definition: A PBRN is a collaboration between an academic health science center(s) and community practitioners conducting primarily clinical studies of mutual interest to benefit/enhance patient care, delivery, system assessment, quality assurance, and other factors affecting health care policy.⁵

PEARL, an interdisciplinary PBRN network, has both a dental and a medical component and is described as being able to conduct clinical studies that cross multiple health care disciplines. The fundamental tenet of the PBRN concept is that practitioners will accept change more readily if they are participating in and generating data for a study that will be used to support evidence-based clinical practice. The translational gap ranges from 17 to 21 years for research findings to be incorporated by general practitioners.⁶ One reason for this gap is that most research is conducted in highly controlled environments, such as academic settings, and represents only a small percentage of what actually occurs in practice.⁷ Another reason is the lack of knowledge transfer of the safety, efficacy, and effectiveness of an intervention to practitioners. For an intervention to be acceptable to practitioners, it must

meet a list of requirements, including safety, efficacy, reimbursement, and peer acceptability, before it finds its way into clinical practice. The profession of dentistry currently lacks a formal process for the adoption of new technologies. The process is currently dependent on dissemination through dental meetings, continued education programs, and testimonials.

Periodontics represents dentistry in its broadest context, in treating teeth, surrounding tissue, and bone by using regulated products approved for dentistry. For purposes of US Food and Drug Administration (FDA) regulation, approved products for the treatment of periodontal disease include devices, drugs (prescription and over-the-counter), and drug/devices (e.g., doxycycline and delivery systems).

The field of periodontics has been innovative in the development of devices to deliver drugs to targeted sites around the tooth.⁸ Dental drug discovery has been very limited, primarily due to market size, and medications currently used are all prior-approved drugs with additional labeling for use in dentistry.⁹ The studies most likely to be conducted for such drugs/devices to assess incremental change would be large-scale studies of simple design appropriate for a PBRN. Such studies would address issues relating to effectiveness or would be relevant to the later stage of a development program. Large, simple trials (LSTs) can be of interest in dentistry, and especially in the fields of periodontics and cariology, because they are among the most common and costly chronic diseases, and the identification of even moderately effective treatments by LSTs can have a meaningful socioeconomic impact.¹⁰ Data from well-designed PBRN studies might be able to compare the average effectiveness of two types of interventions when applied to a very large population. The large, simple clinical study concept may advance clinical design. Cluster randomized trials are one example and offer a cost-effective approach to comparing the effectiveness of commonly used drugs or procedures in representative groups of individuals. Thus, groups of people rather than individuals are randomized with regard to an intervention.¹¹ LSTs are not primarily concerned with safety; rather, they are concerned mainly with effectiveness, the basis for the PBRN concept, whereas the early phase of a development program is primarily directed toward safety and secondarily with efficacy. Data integrity must be ensured to maintain confidence in the clinical results to initiate change. A potential disadvantage of PBRNs is if the PBRN primary method for acquiring new knowledge is the use of surveys of the network, then results may be reflective of the self-reported practice patterns within the network, and may not be generalized to providers outside the network.

Studies of the magnitude of the National Health and Nutrition Examination Surveys (NHANES) underestimated the prevalence of periodontitis by 50% or more, depending on the periodontitis case definition used, and thus performed below threshold levels for moderate-to-high levels of validity for surveillance.¹² Further, the findings suggest that NHANES protocols produce high levels of misclassification of periodontitis cases and thus have low validity for surveillance and research.¹³ The need for consistency in definitions of terms is further stated in a position paper commissioned by the European Association of Dental Public Health where a systematic review of the literature revealed that only 15 studies of 3,472 gave a definition of periodontitis and indicated how it was measured.^{13,14} Small-scale studies can only add to the uncertainty. Large-scale studies such as those

conducted in a PBRN, although costly up front, may be cost effective from a programmatic perspective. More importantly, such a study could define terms by consensus; the data would, therefore, be more likely to be accepted by the practitioners who conducted the study as well as practitioners at large. The PEARL Network was the first NIDCR funded network to conduct a study directed at periodontics.¹⁵ The PBRN concept provides, for the first time, a venue whereby dentistry can develop strategies to change how practitioners diagnose and treat periodontal disease.

DISCUSSION

PBRNs are groups of practitioners recruited to conduct a study to answer a specific question related to their practice. Practitioners contribute to a study by their findings as they would normally practice medicine or dentistry, undistracted and unbiased as to any predicted or hypothesized clinical outcome. However, for the most part, the practitioners are unfamiliar with the principles of clinical research. This means that the data they contribute, as a network, may demonstrate a level of robustness either of the drug being tested or the procedure being performed. This level of robustness on how effective a treatment is may be demonstrated by point of use in an uncontrolled clinical environment such as a practitioner's office. The lack of control over a clinical study limits the use of a PBRN to study late-stage drug development where safety has been established. PBRN studies require diligent oversight to ensure study compliance and adherence to GCP guidelines to generalize the results. This is a limiting factor for most PBRNs because they collect data from practitioner offices without the assurance of an audit trail for data integrity. Presently, the FDA does not accept clinical data generated by a PBRN because it cannot assure data integrity. The PEARL Network is unique in that it is a GCP Network and with assurance of data integrity. Its mission is to convince the FDA that GCP PBRN studies should be considered for regulatory approval. Any other level of study lacks generalizability for meaningful change to the practice of dentistry. PBRN studies are limited by length of the study and time of follow-up of patients. The selection process for practitioners who participate in a GCP compliant network is critical and time consuming to ensure data integrity. Many networks accept all practitioners who apply without a formal review of practitioner credentials.¹⁶ Without credentialing, a network may have a practitioner participating in a study nullifying the clinical data from that practitioner due to license restrictions. An example of license restrictions would be when a state board of dentistry limits the practitioner from performing endodontics, where that practitioner includes patients and data in an endodontic study. PBRN studies are low risk. Institutional Review Boards (IRBs) most likely would limit practitioners who are inexperienced in research from participating in more complex studies. Use of a placebo is an issue if alternative treatments exist and practitioners are relatively uncomfortable with presenting that arm of a study to a patient. It is the function of a PBRN to monitor patient risk for the IRB and practitioner compliance to the protocol.

The PBRN study concept is the antithesis of the traditional controlled study, requiring practitioner expertise as well as selection of patients and, most importantly, treatment by a specifically controlled protocol. The ability to control a study is critical in the early phases of drug development when the profile of the drug is yet to be determined. An unknown response that could be life threatening requires a controlled environment. But when a drug is

to be approved and released to the market and prescribed by practitioners who are inexperienced in the use of the drug or in conducting the procedure and who had no part in contributing to the database of the drug, is it any wonder that additional unknown drug side effects begin to appear after such widespread use occurs?

Assessing the number of FDA black box warnings raises the question: Are we controlling the clinical studies too much?¹⁷ Controlled studies can limit the robustness of the clinical data, and from a purist point of view, one should not tamper with a PBRN practitioner because you do not want to bias him or her in any form. PBRNs would not be appropriate to conduct early-phase drug development clinical studies but would be limited to those in late-stage development, such as Phase III and IV studies. Most clinical studies conducted in a PBRN would reside in Phase IV, would evaluate treatments that are standard of care, and would assess best clinical outcomes.

PEARL defines the term “clinical trial” to mean those studies that are conducted for a clinical development program or under the drug approval pathway (Phase I to III) so designated by a regulatory agency. The broader term “clinical studies” will be used for studies related to all other purposes, such as additional label claims for a drug and comparative effectiveness studies, as well as cost-effectiveness studies for drugs in the postapproval phase (Phase IV). This is an important but subtle point because for clinical trials, one recruits subjects, and for clinical studies (such as those conducted in PBRNs), one recruits patients. Patients are enrolled in standard of care studies; that is, the practitioner will treat the patient with options that are all considered acceptable, reimbursable, and ethical with no experimental drugs or procedures considered. This minimizes the risk considerably for the IRB to approve practitioners who are part of a practice based clinical research network. Participants recruited to a clinical trial have no options for treatment because their treatment is dictated by the study protocol. The term “clinical trial” is usually used to describe any research involving human subjects,¹⁸ but it can be further defined, accordingly as to the nature of the study.

The responsibility of the data generated by a PBRN to ensure that the outcome is clinically meaningful and generalized to a larger population requires some guidelines to assure data integrity while not compromising the PBRN intent and concept at the practitioner level. Small and often underpowered clinical trials, especially common in oral health research, are very different from large-sample, multicenter clinical trials that have the necessary power and generalizability to support change in practice standards, public health policy, and approval of government regulatory agencies.¹⁹

PBRNs can serve as a “clinical laboratory” to address fundamental clinical periodontal questions. One role of a PBRN is to conduct large simple studies to answer very basic questions to build a foundation of knowledge that allows for more sophisticated therapies and treatment. A potential downside to this approach is that interventions supported by PBRN generated data are based on average outcomes derived from an average population. It ignores the reality of personalized medicine that all people do not respond in an identical manner to the same intervention. On the average, most patients in a PBRN study might benefit from the PBRN supported intervention, whereas other individuals had no health

benefit and still others experienced adverse effects on their overall health. Because the emphasis of PBRN studies is on effectiveness (rather than safety) in the overall population, there is a tendency to ignore the range of possible effects. Large simple trials may answer questions related to optimal time between recall visits by disease classification and stratification at the patient level, treatment practices for periodontal disease management, and surgery versus non-surgical treatment and comparative effectiveness studies.¹⁰ This can be partially attributed to small or incremental treatment effects of the targeted sites, which would require large-scale clinical studies to gain insight and consensus on effectiveness of treatment.²⁰ In general, the size of a study is inversely proportional to the treatment effect.²¹

PBRNs designed to ensure data integrity may be the catalyst for clinical investigators to develop newer models of clinical design that are more cost effective and answer a critical question that can serve as a foundation to build additional knowledge to advance the profession. Without changes in how we conceive, design, conduct, and analyze randomized clinical trials, the nation risks spending large sums of money inefficiently to answer the wrong questions—or the right questions too late.²² For example, predicting a patient's response to routine scaling by the practitioner through point-of-care data may increase the success of therapy and better regulate the interval of treatment.²³ The PBRN approach dilutes individual response effects and mainly focuses on population outcomes. However, it can also signal early trends of side effects because of the large patient population.²⁴ However, the potential downside is if an insurer were to limit treatment options to those effective in the greatest number of people. This would limit the range of treatment options and restrict innovation in dentistry.

CONCLUSIONS

Periodontics represents a confluence of a number of biologic disciplines that can interface with medicine. Periodontics can be viewed as having a basis in microbiology, inflammation, immunology and host defense, genetics, and bone physiology, and is a microcosm and visual laboratory for a number of conditions based on the above disciplines. Many of the clinical studies conducted are of short duration (< 6 months), and basic needed information such as the optimum time for a recall visit and treatment paradigms have yet to be clinically resolved.¹⁰ The PBRN concept offers dentistry an opportunity to become a part of the greater health care model by providing a venue for knowledge transfer within the network and beyond, and acting as a catalyst to initiate change in practice and health care policy. PBRNs provide a venue to engage practitioners in peer learning, as well as contribute clinical outcome results to support evidence based dentistry. PBRNs may provide an additional forum for periodontists to interact with general dentists to increase patient referrals and optimize patient outcomes. The collaboration may also create opportunistic bridges between academia and industry. The PBRN concept provides the dental profession with a platform for change to adapt to future health care needs.

ACKNOWLEDGMENTS

This study was supported by NIH/NIDCR funded U01 DE016755.

REFERENCES

1. American Dental Association, Survey Center. Employment situation of dentists in private practice. ADA News. 2007; 38:1.
2. Lanier D. Primary care practice-based research comes of age in the United States. Ann Fam Med. 2005; 3(Suppl. 1):S2–S4. [PubMed: 16049076]
3. Ship JA, Curro FA, Caufield PW, et al. Practicing dentistry using findings from clinical research: You are closer than you think. J Am Dent Assoc. 2006; 137:1488–1490. 1492, 1494. [PubMed: 17082265]
4. US Food and Drug Administration. [Accessed March 12, 2013] FDA regulations relating to good clinical practice and clinical trials. Available at <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm114928.htm>.
5. Curro F, Vena D, Naftolin F, Terracio L, Thompson V. The PBRN initiative: Transforming new technologies to improve patient care. J Dent Res. 2012; 91:12S–20S. [PubMed: 22699662]
6. Balas, EA.; Boren, SA. Managing clinical knowledge for health care improvement. In: Bommel, J.; McCray, AT., editors. Yearbook of Medical Informatics 2000: Patient-Centered Systems. Stuttgart, Germany: Schattauer Verlagsgesellschaft; 2000. p. 65-70.
7. Green LA, Fryer GE Jr, Yawn BP, Lanier D, Dovey SM. The ecology of medical care revisited. N Engl J Med. 2001; 344:2021–2025. [PubMed: 11430334]
8. Bland PS, Goodson JM, Gunsolley JC, et al. Association of antimicrobial and clinical efficacy: Periodontitis therapy with minocycline microspheres. J Int Acad Periodontol. 2010; 12:11–19. [PubMed: 20593634]
9. Curro FA. The clinical importance of drug evaluation. J Appl Res Clin Dent. 2005; 2:10–17.
10. Hujoel PP, Powell LV, Kiyak HA. The effects of simple interventions on tooth mortality: Findings in one trial and implications for future studies. J Dent Res. 1997; 76:867–874. [PubMed: 9126183]
11. Mazor KM, Sabin JE, Goff SL, et al. Cluster randomized trials to study the comparative effectiveness of therapeutics: Stakeholders' concerns and recommendations. Pharmacoepidemiol Drug Saf. 2009; 18:554–561. [PubMed: 19402030]
12. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA. Accuracy of NHANES periodontal examination protocols. J Dent Res. 2010; 89:1208–1213. [PubMed: 20858782]
13. Leroy R, Eaton KA, Savage A. Methodological issues in epidemiologic studies of periodontitis – How can it be improved? BMC Oral Health. 2010; 10:8. [PubMed: 20409298]
14. Savage A, Eaton KA, Moles DR, Needleman I. A systematic review of definitions of periodontitis and the methods that have been used to identify this disease. J Clin Periodontol. 2009; 36:458–467. [PubMed: 19508246]
15. Rosen A, Martin J, DeStefano T, et al. Periodontal diagnosis and treatment in general practice: PEARL Network findings. J Dent Res. 2011; 90:429.
16. Curro FA, Thompson VP, Naftolin F, et al. Practice-based research network infrastructure design for institutional review board risk assessment and generalizability of clinical results. Therapeutic Innovation & Regulatory Science. 2013; 47:82–89.
17. Cook DM, Gurugubelli RK, Bero LA. Risk management policy and black-box warnings: A qualitative analysis of US FDA proceedings. Drug Saf. 2009; 32:1057–1066. [PubMed: 19810777]
18. Friedman, LM.; Furberg, CD.; DeMets, DL. Fundamentals of Clinical Trials. 3rd ed.. New York: Springer; 1998. p. 2
19. Pihlstrom BL, Barnett ML. Design, operation, and interpretation of clinical trials. J Dent Res. 2010; 89:759–772. [PubMed: 20581353]
20. Yusuf S, Collins R, Peto R. Why do we need some large, simple randomized trials? Stat Med. 1984; 3:409–422. [PubMed: 6528136]
21. Luce BR, Kramer JM, Goodman SN, et al. Rethinking randomized clinical trials for comparative effectiveness research: The need for transformational change. Ann Intern Med. 2009; 151:206–209. [PubMed: 19567619]
22. Spear BB, Heath-Chiozzi M, Huff J. Clinical application of pharmacogenetics. Trends Mol Med. 2001; 7:201–204. [PubMed: 11325631]

23. Beirne P, Worthington HV, Clarkson JE. Routine scale and polish for periodontal health in adults [review]. *Cochrane Database Syst Rev*. 2007; 4:CD004625. [PubMed: 17943824]
24. Rosati K. Using electronic health information for pharmacovigilance: The promise and the pitfalls. *J Health Life Sci Law*. 2009; 2:173–239.