Title of Project: National Center for Pediatric Practice Based Research & Learning

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Structured Abstract:

**Purpose:** To improve the delivery of and learning from pediatric primary care at the local, regional, and national levels.

**Scope:** To build infrastructures, formalize relationships, and integrate electronic health record (EHR) data from two pediatric practice-based research networks (PBRNs) – the American Academy of Pediatrics’ (AAP) national Pediatric Research in Office Settings (PROS) and the Children’s Hospital of Philadelphia’s (CHOP) Pediatric Research Consortium (PeRC) – into the Center for Pediatric Practice-Based Research and Learning (C-PRL).

**Methods:** Coordinated activities of center administrative and research cores allowed for responses to rapid-cycle funding opportunity announcements as well as the development of investigator-conduct initiated primary care research.

**Results:** C-PRL yielded a collaborative and innovative research program that leveraged the strengths of PROS, PeRC, and their parent organizations to advance pediatric health care and research, especially research that leverages the EHR. Many impactful relationships, publications, products, and federally funded grants emerged and continue to be developed from the C-PRL collaboration.

**Conclusion:** C-PRL played a transformative role in launching a new wave of collaborative, EHR enabled research of national scope that has continued beyond the funding period.

**Key Words:** pediatric, practice-based research network (PBRN), primary care, electronic health records (EHR).

Purpose (Objectives of Study):

The Specific Aims of this project were:

1. Link two pediatric practice-based research networks (PBRNs) in a National Center for Pediatric Practice-Based Research and Learning (C-PRL):
   - The American Academy of Pediatrics’ (AAP) national network, Pediatric Research in Office Settings (PROS):
     - PROS is the nation’s largest and second oldest pediatric PBRN
     - PROS is enhanced by its subnetwork for electronic health record (EHR) data collection, and its affiliation with the AAP’s Quality Improvement Innovation Network (QuillN)
   - The Children’s Hospital of Philadelphia’s (CHOP) Pediatric Research Consortium (PeRC)
     - PeRC is arguably the nation’s most innovative pediatric PBRN

2. Enhance established, and create new, working relationships between PROS/AAP and PeRC/CHOP via the C-PRL.

3. Through the C-PRL, leverage the dissemination and implementation capacities of PROS, PeRC, and their parent organizations to improve delivery of pediatric primary care at local, regional, and national levels.

These aims were achieved through coordinated activities of Administrative and Research cores, allowing responses to rapid-cycle Agency for Healthcare Research and Quality (AHRQ) funding opportunity announcements (FOAs), as well as the development of investigator-initiated primary care research grants. In addition, the C-PRL infrastructure allowed for wide dissemination of new knowledge and broad implementation of selected findings in its member practices.

Scope:

**Background:** The best child health care outcomes are achieved through evidence-based practice. Evidence-based practice, however, requires practice-based evidence, and the coalitions of primary care practices and clinics known as practice-based research networks (PBRNs) have provided some of the highest quality and most generalizable practice-based evidence. PBRNs face numerous problems, however, in conducting important and timely research in primary care settings. Principal challenges include (1) maintaining an infrastructure to address the complex work of primary care research; (2) amassing a large enough cohort of member practices to address the sample size issues presented by data clustering; and (3) aggregating a knowledgeable and sophisticated cohort of researchers with the expertise needed to conduct practice-based research on a broad range of issues. Individual pediatric PBRNs have dealt with and partially solved some of these challenges, but none have been able to address them fully.

**Significance:** In the United States, children’s primary care services, including preventive services, acute illness care, and care for chronic problems, are delivered in community-based settings. Although children’s primary care visits are made to pediatricians, family physicians, and internists, the proportion of visits made to pediatricians in all age groups has been increasing steadily since 1980 (Freed GL et al., 2004). In 2006, for the first time, the majority of primary care visits made by children in all age groups, including adolescents, were to pediatricians (Freed GL et al., 2010). As such, infrastructures to monitor, study, and understand the care delivered in pediatric practices and clinics have never been more important.
Innovation: A major innovation of the C-PRL was the affiliation of the national PROS research network, which is based at the AAP – the largest membership organization of pediatricians in North America - with the broad and diverse core of researchers, resources, and expertise from PeRC /CHOP. C-PRL brought together a group of investigators that was available to respond nimbly and quickly to research opportunities. Another major innovation was C-PRL’s emphasis on research using clinical informatics. Existing EHR-based information systems in PROS and PeRC were used for planning research projects, delivering research interventions and collecting research data.

Methods:

PROS, the national practice-based research network of the AAP, partnered with CHOP and its PeRC practice-based research network, to form an innovative national center with unparalleled resources for pediatric primary care child health research, dissemination, and implementation. PROS served as the Administrative Core, and PeRC/CHOP as the Research Core for the C-PRL.

PROS Directors, initially Richard C. “Mort” Wasserman, MD, MPH and later Alexander Fiks, MD, MSCE, served as Director of the C-PRL.

Although PROS and PeRC retained their individual network identities and governance structures, a C-PRL Steering Committee was created to oversee all joint activities of the C-PRL. The Steering Committee set priorities for the center and ruled on matters of policy as it related to the center. As such, it was responsible for the equitable distribution of infrastructure resources.

Results:

Accomplishments, by grant year, are presented below.

Year 1:

- A PROS Rapid Response Listserv was created and used numerous times. The Listserv included 16 leaders and staff members from PROS, PeRC, and QuIlN, as well as 25 PROS practitioners. It was utilized to obtain practitioner input on AHRQ rapid response opportunities.
- PeRC leaders attended the PROS Steering Committee meeting, and an official QuIlN liaison to the PROS Steering Committee was approved.
- PROS was awarded the “Comparative Effectiveness Research through Collaborative Electronic Reporting” (CER²) grant from the Health Resources and Services Administration (HRSA grant # R40MC24943).
  - PROS, CHOP, and research groups at MetroHealth/Case Western Reserve, Boston University, and the American Academy of Family Physicians (AAFP) were involved.
  - Over the course of 5 years, this grant created a fully elaborated system to employ clinical data in EHRs for conducting comparative effectiveness research on pediatric drug therapeutics.
- Dr. Fiks was appointed as one of two new PROS Associate Directors.
- In collaboration with their parent organizations, PROS (and the AAP Child Health Informatics Center) and PeRC (and the CHOP PolicyLab group) jointly provided policy recommendations on Meaningful Use Stage 3 to the Office of the National Coordinator for Health Information Technology.
- Dr. John Lantos – a nationally recognized bioethicist – delivered a presentation entitled “Research Ethics and Electronic Health Records” at the spring PROS Chapter Coordinators meeting.
- Dr. Wasserman served as Chair of the Academic Pediatric Association’s (APA) Pediatric Clinical Research Network Special Interest Group (PCRN SIG). The PCRN SIG group of network leaders meets annually at the Pediatric Academic Societies’ (PAS) meeting. At the 2013 PCRN SIG meeting, information was disseminated about 1) incorporating American Board of Pediatrics (ABP) Maintenance of Certification (MOC Part IV) into network research and 2) consultation to a new network focused on health care transitions for special needs/chronically ill youth.

Year 2:

- C-PRL investigators (with Dr. Fiks as PI) were awarded the “Pediatric Patient Engagement as a Criteria for Meaningful Use Stage 3” grant by AHRQ (1R18 HS022689).
  - This was the first prospective study to include both PeRC and PROS practices.
  - This grant informed policy regarding the implementation of Meaningful Use Stage 3 for EHRs. The research assessed the feasibility and impact on pediatric asthma care of implementing, in a national sample of practices, a patient portal designed to provide education, collect patient-reported outcomes, and enable parents to report their treatment preferences and goals.
  - This study provided a framework for working with the CHOP and AAP IRBs to approve joint research projects.
• EHR data from PROS and PeRC were merged to conduct focused analyses on a number of topics related to pharmacoepidemiology, including the use of medications to address problems with children’s sleep, variations in mental health diagnoses and prescribing, the impact of stimulants and atypical antipsychotics on children’s growth, and trends in the use of alpha agonists.
  o These analyses resulted in multiple abstracts presented at the 2014 Pediatric Academic Societies and AcademyHealth Child Health Services Research Interest Group meetings. These abstracts included new methods, developed by C-PRL and its collaborators, that 1) advanced strategies for assessing normal and abnormal growth and 2) enhanced the capture of race and ethnicity in pediatric EHRs.
• At the 2014 PCRN SIG meeting, information was disseminated about 1) family engagement in network research (co-presented by Dr. Fiks) and 2) consultation was provided to two new networks focusing on child abuse pediatrics and patient safety.

Year 3:
• PROS leaders participated in regular QuIIN Practice Improvement Network (PIN) conference calls; Dr Kairys - Medical Director of QuIIN - attended the PROS Chapter Coordinator and Steering Committee meetings; and Dr Craig - Chair of QuIIN’s outpatient network - served on the PROS Steering Committee.
• PROS regularly advertised opportunities to participate in QuIIN projects through its listserv.
• Products (website links, keychains, etc...) from the completed PROS Teen Driving Study on establishing parent-teen driving contracts were disseminated throughout PROS.
• A collaborative R01 grant between PROS, CHOP, and Seattle Children’s Research Institute was awarded by NICHD: Dialogue Around Respiratory Illness Treatment (DART)
  o This study developed and tested a distance learning quality improvement intervention focused on improving providers’ communication practices, as well as their treatment decisions, during pediatric acute respiratory tract infection (ARTI) visits. This grant leverages the EHR-infrastructure created through the partnership between PROS and PeRC.
• At the 2015 PCRN SIG meeting, consultation was provided to two new networks focusing on 1) pediatric obesity and 2) young adult health.

Year 4:
• Dr. Fiks was appointed Director of PROS. This transition further cemented the partnership between AAP PROS and CHOP PeRC.
• Ms. Stacy Williamson, MSE, NREMT, was appointed PROS Family/Parent Partner and became a voting member of the Steering Committee.
• CHOP’s PeRC network also developed a Parent Advisory Board that guides its research today.
• A collaborative R01 grant between PROS, CHOP, and the University of Michigan was awarded by NHLBI: Population Effects of Motivational Interviewing on Pediatric Obesity in Primary Care (BMI2+)
  o BMI2+ is a cluster-randomized trial testing the effectiveness of a motivational interviewing counseling intervention delivered by clinicians and dieticians to the parents of overweight / obese youth. The impact of the intervention on BMI percentile change in the entire population of overweight and obese youth ages 3-11 years in 18 PROS practices will be examined. This grant leverages the EHR-infrastructure created through the partnership between PROS and PeRC.
• New funding was received for a collaborative, 1-year project between PROS, CHOP, and the NICHD-funded Duke Pediatric Trials Network: Task Order #38 - Protocol Development IV.
  o This study utilized the EHR data in the CER² dataset to provide information on the frequency of use of five specific drugs in children, and to identify signals of side effects or adverse drug events through examination of visit patterns, diagnosis and procedure codes, and laboratory values. Summaries of findings were submitted to the Pediatric Trials Network and NICHD to focus future research to best address critical questions of pediatric medication safety and effectiveness.
• C-PRL was 1 of 8 sponsors of the Certificate Program in Practice-Based Research Methods (PBRM-Cert)
  o Dr. Fiks was a member of the program’s Steering Committee
  o Dr. Fiks delivered multiple lectures about using EHRs in research to program participants
  o Dr. Fiks mentored a CHOP fellow that participated in the program – Dr. Deepak Palakshappa. Drs. Fiks and Palakshappa co-authored 2 publications as a result of this effort (see “publications” section).
• At the 2016 PCRN SIG meeting, the group discussed the issue of network leadership transitions. In addition, consultations were provided to two new networks focusing on 1) urgent care and 2) the Reach Out & Read program.
Year 5:

- Melissa Stockwell, MD, MPH was appointed the new PROS Associate Director
- A collaborative R01 grant between PROS, CHOP, and Columbia University was awarded by NICHD: Text Message Reminders for 2nd Dose of Influenza Vaccine (Flu2Text)
  - This project is comparing the effectiveness and timeliness of personalized text message reminders with embedded influenza vaccine health literacy-promoting information versus usual care on receipt of the second dose of influenza vaccine in a diverse pediatric population.
- New funding was received for a second 1-year project between PROS, CHOP, and the Duke Pediatric Trials Network: PTN Task Order #36 - Pediatric Trials Network Database.
  - This study utilized the EHR data in the CER2 dataset to characterize the safety profile of the antipsychotics risperidone and aripiprazone, as well as prescription patterns of these medications in ambulatory primary care over time. Summaries of findings were submitted to the Pediatric Trials Network and NICHD to focus future research to best address critical questions of pediatric medication safety and effectiveness.
- Dr. Fiks became co-chair of the PCRN SIG group and led its annual meeting. Topics discussed included best practices for inter-network collaborations, a topic that directly builds on learnings from C-PRL, and the new Single IRB rule for multi-site trials. Consultations were provided to two nascent research networks focusing on:
  1) telehealth
  2) increasing access to clinical trials for those in rural und underserved areas.

Year 6 (no-cost extension year):

- A collaborative R01 grant between PROS, CHOP, and the University of California Los Angeles (UCLA) was awarded by NCI: Improving HPV Vaccination Delivery in Pediatric Primary Care: The STOP-HPV Trial
  - This is a randomized controlled trial of a bundled, multiple component intervention to increase the HPV vaccination rates of adolescents ages 11-17 years. This grant leverages the EHR-infrastructure created through the partnership between PROS and PeRC.
- A collaborative grant between PROS and CHOP was awarded by CDC: A Novel Metric for Benchmarking Antibiotic Use to Inform Outpatient Stewardship
  - The study uses the CER2 dataset to develop an evidence-based benchmark rate of antibiotic prescribing for children with acute respiratory tract infections. This would be a tool to guide national efforts to measure outpatient antibiotic stewardship.
- At the 2018 PCRN SIG meeting, the network leaders (led by co-chair Dr. Fiks) heard from a representative of NICHD about the funder’s perspective on PBRN research, discussed opportunities and challenges in network research, and provided consultations to two new networks focused on 1) primary care (regional) and 2) children with special healthcare needs.

Discussion

The Center for Pediatric Practice-Based Research and Learning (C-PRL), led by Dr. Alexander Fiks (Director of AAP PROS and Medical Director of CHOP’s PeRC Network), yielded a large, collaborative, and innovative program that continues to leverage the strengths of pediatric PBRNs to advance primary care child health research, dissemination, and implementation in practice. Over the course of the 6-year project, C-PRL accomplished the following:

1) Established and maintained infrastructure and a governance structure

In its first year, C-PRL established formal infrastructure and a governance structure. Throughout the project, PROS served as the Administrative Core and PeRC/CHOP as the Research Core. The Steering Committee oversaw all joint activities, and assisted with setting priorities and equitably distributing infrastructure resources. This approach accelerated research as CHOP became a robust data coordinating center for PROS research with the AAP often providing the IRB of record and overseeing the implementation of studies (and dissemination of results) in practices from around the United States.

2) Generated collaborative grant applications and obtained funding for studies, including rapid responses to AHRQ limited-competition funding opportunities

C-PRL implemented large rigorous trials across the country, many of which leveraged the unique EHR infrastructure created through the partnership between PROS and PeRC. These R01-funded projects addressed a wide array of timely topics, including antibiotic prescribing, overweight and obesity treatment, and influenza and HPV vaccination. Several studies utilized EHR data from the Comparative Effectiveness Research through Collaborative Electronic Reporting (CER2) super-network for secondary data analyses, which links clinical data for >1.5 million children across approximately 222 sites to determine the use,
effectiveness and side effects of medications prescribed in childhood. These results inform the ongoing work of the Pediatric Trials Network.

During the award period, C-PRL investigators - led by Dr. Fiks - responded to an AHRQ limited-competition funding opportunity. The investigators were awarded funds to conduct a prospective study that assessed the feasibility of an EHR-linked portal and impact on asthma management. Results from the study ultimately informed policy regarding the implementation of Meaningful Use Stage 3 for EHRs. Both C-PRL’s administrative and research cores were highly engaged in this process.

3) Leveraged the dissemination and implementation capacities of PROS, PeRC, and their parent organizations

The PROS and PeRC teams jointly published 13 manuscripts on topics that included health information technology (HIT); EHR research methods; pediatric hypertension, asthma, and ADHD; and pediatric medication prescribing and use. As mentioned above, results also were provided to federal officials in charge of implementing and refining the federal program for the meaningful use of EHRs. Findings were additionally disseminated through presentations at national conferences, webinars, lectures, and AAP News research articles. The C-PRL structure continues to facilitate dissemination of research through the AAP’s publications, Committees, Sections and creation of clinical practice guidelines. Links to CHOP’s PolicyLab and Center for Pediatric Clinical Effectiveness also continue to support dissemination.

4) Provided mentoring and career development opportunities for junior investigators

This was accomplished in 3 ways. First, Dr. Fiks participated as a Steering Committee member and as a mentor in the Certificate Program in Practice-Based Research Methods (PBRM-Cert). Second, PROS leaders and staff mentored several investigators conducting their first national study with PROS, some of which used CER2 data for their research. In addition, PROS leaders and staff provided guidance to several junior members of study teams as they prepared abstract submissions for presentation at national conferences. Finally, as Chair (Dr. Wasserman) and later Co-Chair (Dr. Fiks) of the Academic Pediatric Association’s (APA) Pediatric Clinical Research Network Special Interest Group (PCRN SIG), C-PRL leaders helped to foster the development and enhance the operations of collaborative inter-institutional research networks intended to improve child health. They provided consultation for nascent clinical research networks on topics such as goal setting, creating a research agenda, sustainability / funding, and governance. They also participated in discussions regarding IRBs for multi-site trials, internetwork collaborations, outreach to young investigators, strategies for family engagement, and leadership transitions. Ultimately, through their work with the PCRN SIG, C-PRL leaders offered research network leaders opportunities to learn about the work of others, discuss their challenges, and share best practices.

Conclusion

The funding of C-PRL supported the creation of a highly effective collaborative infrastructure that supported the development, implementation, evaluation and dissemination of pediatric research on a national scale.

Significance

C-PRL collaborations continue to advance pediatrics by supporting impactful scholarship in a broad range of fields. Multiple publications, presentations, and training activities disseminated new approaches for pediatric research that have influenced practice-based research and help to better existing and inform the creation of new networks.

Implications

National pediatric practice-based research is thriving, providing foundational knowledge to continue to advance primary care delivery in order to improve child health outcomes.
List of Publications and Products:

Publications:


Presentations/Webinars:


Wasserman R, "Psychotropic meds in pediatric primary care: exploring use and safety with national EHR data". University of Vermont College of Medicine Pediatric Grand Rounds, given to pediatric faculty, residents, medical students, local pediatric and family medicine practitioners. Burlington, VT, February 2015.


Grundmeier R, “Proliferation of Psychotropic Polypharmacy in Pediatric Primary Care: Results From 800,000+ Children in the Cer2 EHR Dataset”. Platform presentation at Pediatric Academic Societies Annual Meeting. San Diego, CA, May 2015.


Fiks A, "What Recent Immunization Research Teaches Us About Effective Patient Care". Margaret Jenkins Memorial Grand Rounds Lecture, Medical University of South Carolina. Charleston, SC, May 2016.


Fiks A, "What Health Information Technology Can (and Can't) Do for Pediatric Care". Pediatric Grand Rounds, University of Vermont. Burlington, VT, July 2016.


