The Promise of Practice-based Research
Are networks the paradigm for pediatric clinical research?

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UTHSC San Antonio
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DISCLOSURE
Relevant Financial Relationship(s)
- Advisory Boards
  - Pfizer
  - sanofi pasteur

Off Label Usage
None

Learning Objectives
- Describe the characteristics of practice-based research
- List the patient and disease characteristics that make networks attractive in pediatrics
- Identify pediatric networks that would be appropriate for your participation.

The Need for Evidence Based Medicine
“Americans should be able to count on receiving care that meets their needs and is based on the best scientific knowledge. Yet there is strong evidence that this frequently is not the case. Between the health care we have and the care we could have lies not just a gap, but a chasm”
CROSSING THE QUALITY CHASM
Institute of Medicine Report, 2001

“The Cow Pock – or – the Wonderful Effects of the New Inoculation!”
J. Gillray, 1802

“To assess it at its lowest value, this has proved to me a most interesting hobby, something to turn the face from the clod and to add interest to the daily round, which, instead of being monotonous, becomes full of delightfully exciting incidents. I have written this and a previous paper in the hope that other country doctors will realize what is peculiarly their opportunity and, I feel strongly, their bounden duty.”
William N. Pickles,
Epidemiology in country practice, 1935

January 29, 2009
The progress of medicine will be hampered and delayed till the general practitioner becomes an investigator.

Sir James MacKenzie
Principles of Diagnosis & Treatment of Heart Affections, 1916

February 18, 2008

Overview
- Introduction
- Practice-based research networks
  - History
  - Rationale
- Examples of PBRN

May 2011

Acknowledgements
- Mort Wasserman – PROS/Univ of Vermont
- Jim Taylor – PSPRN/Univ of Washington
- Larry Nazarian – Rochester, NY*


March 24, 2008

Practice-Based Research

Why do clinical research in networks?
- Diseases rare
- Adverse outcomes
  - Infrequent
  - Distant from the exposure
- Sample size

January 29, 2009

Credentials
- AAP – Pediatric Research in Office Settings (PROS)
- National Medical Association - NMAPedsNet
- APA – CORNET, the Continuity Clinic Research Network
- PRIS – Pediatric Research in Inpatient Settings
- MUSC – South Carolina Pediatric Practice Research Network (SCPPRN)
- Oklahoma – in process

March 24, 2008
Clinical Research Networks

- O’Neil
  - “Without these networks, clinical trials in rare diseases could not be done. Most studies are under-funded for the time they require, though.”
- Jarvis
  - “They are vital, especially for rare diseases, e.g., juvenile dermatomyositis.”

Why Do Research in Practices? – General Pediatrics

- Sutton’s Law: that’s where the majority of patients and problems are!
- Practices are the best place to study the prevention of health problems
- Practices are a good place to study problems over time
- Patients in practices are more representative of any clinical problem than those seen in hospitals
- Practices are a good place to study the problems that cause substantial morbidity, but don’t result in hospitalization (e.g., psychosocial problems)

Once upon a time...

All medical research was practice-based research!!

Practitioner Researchers

- Edward Jenner -- smallpox vaccine
- James MacKenzie -- cardiac physiology
- Burtis Breese -- streptococcal infections
- T. Berry Brazelton -- child development
- William Carey -- temperament and behavior
- O.J. Roddey, Herb Clegg -- infectious diseases
- Bruce Taubman -- toilet training
Decline in Practice-Based Research
- Rise in biomedical laboratory research
- Decreased medical school emphasis on primary care (until the very end of the 20th century)
- Increased requirements for sophistication in clinical research -- beyond clinical description, using epidemiology, biostatistics, & social sciences

Models of Practice-based Research
- Single study "networks"
- Industry directed networks
- Regional clinical research networks
- National/International clinical research networks
  - Specialty specific
  - Disease specific

Infrastructure Support*
- What do you need?
  - Director, coordinator, roster, meetings, communication, human subjects protection
- Costs
  - $69,700 to $287,600 for simple to moderately complex network

Pitfalls
- Infrastructure
- IRB
- Analytic
- "Interest"

IRB in Multisite Studies
- 88 PROS practices, 75 IRB

The IRB
- How many would you like?
- Purpose: a committee that has been formally designated to approve, monitor, and review research involving humans with the aim to protect the rights and welfare of the research subjects.
- How much do they "like" pediatric research?

*Green, 2005, Annals of Family Medicine
Sampling by cluster

- About clusters
  - Examples of clusters; community, school, neighborhood, clinic
  - Those within the cluster are more similar to each other than those in other clusters
- Why sample by cluster?
  - Availability, accessibility, cost, efficiency
- We always cluster sample

Cluster Sampling Complicates Statistics

- Observations no longer
  - Independent
  - Identically distributed
- Problems for variance estimation
- Non-sophisticated methods estimates of variance are too broad

Grade inflation or sample size deflation

<table>
<thead>
<tr>
<th>Design effect</th>
<th>ICC</th>
<th>Sample in cluster</th>
<th>&quot;true&quot; sample size</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.01</td>
<td>.001</td>
<td>100</td>
<td>91</td>
<td>Calories, middle school lunch</td>
</tr>
<tr>
<td>7.45</td>
<td>.050</td>
<td>100</td>
<td>17</td>
<td>Daily drug dose, geriatrics</td>
</tr>
<tr>
<td>13.9</td>
<td>.100</td>
<td>100</td>
<td>9</td>
<td>Immunization UTD, practice</td>
</tr>
<tr>
<td>72.0</td>
<td>.55</td>
<td>100</td>
<td>2</td>
<td>Suture type in episiotomy, hospital</td>
</tr>
</tbody>
</table>

Maintaining Interest

- Keeping practices involved but not overwhelmed.
- Multiple little projects v. one big project
  - Funding rules
- Funding can undermine interest

Regional PBRN's

- Frequently oriented around academic medical center
- Types of practices
  - Primary care practices (private, other)
  - Continuity clinics
  - Underserved populations
    - Inner city
    - Rural

Pediatric PBRN's

- National PBRN’s – 4
  - PROS, SCOR, NMAPedsNet, CORNET
- Regional PBRN’s – ~12
  - Including – Dartmouth (CECH), CHOP (PeRC), SCPPRN, PPRG, Cincinnati, PSPRN, Dayton, Utah, St Louis, Cleveland, and Pittsburgh
Pediatric Clinical Research Networks

<table>
<thead>
<tr>
<th>N = 52</th>
<th>N = 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty specific - 35 (50)</td>
<td>Specialty specific - 35 (50)</td>
</tr>
<tr>
<td>Primary Care – 20 (29)</td>
<td>Primary Care – 20 (29)</td>
</tr>
<tr>
<td>Disease specific – 15 (21)</td>
<td>Disease specific – 15 (21)</td>
</tr>
</tbody>
</table>

Geographic coverage, n (%)  
Regional 15 (25)  
National 17 (25)  
International 21 (41)  
Network age, median (mean ± SD)*  
6 (1.14 ± 1.45)  
No. of data collection efforts completed, median  
6 (1.14 ± 1.45)  
No. of peer-reviewed articles published, median (mean ± SD)*  
10 (2.31 ± 3.81)  

*Analysis were conducted by excluding the Children's Oncology Group.

January 29, 2009

Pediatric Oncology Group (POG)

- Founded – 1955
- Data collection efforts – > 1,000
- Articles – > 5,000

January 29, 2009

CORNET Research Goals

1) To study health and health care issues of minority and underserved children

CORNET Research Goals

3) To study resident education within the continuity setting
Demographics of CORNET Sites
- 100 pediatric training programs (52%)
- 117 clinical practice sites
- Mean of 52 residents/program (16-150)
- >4,500 categorical pediatric residents
- Care for > 750,000 pediatric patients

CORNET Program Locations
- Representation in 40 states

The Bright Futures Study
- RCT of preventive health strategies on oral health (intervention) and iron deficiency (active control)
- Children 12-36 months
- 27 institutions participated
- 143 pediatric residents participated through study
- Hank Bernstein/Janet Servint Co PIs
- Funding by the Maternal and Child Health Bureau

CORNET
- Ongoing studies
  - Bright Futures – group randomized trial of oral health education
  - Secondary Sexual Characteristics in Boys (SSIB) – with PROS
  - Adolescent Immunization in the Medical Home – with Greater Rochester PBRN
  - How is Continuity Measured in Continuity Clinics?
  - Health Care of Pediatric Residents and Their Families

Pediatric Research in Office Settings Network (PROS)
- Practice-based research organization within the American Academy of Pediatrics
- 1,800 practitioners, 720 practices
- Members in 50 states, Puerto Rico and Canada (2008)

http://www.aap.org/pros/
PROS Organization

- Director, Full-time staff
- Steering committee of practitioners, staff, independent researchers
  - Carefully review study proposals
  - Make recommendations
- One coordinator/chapter
  - Coordinators meet twice yearly
  - Researchers propose studies
  - Coordinators approve/disapprove study, modify design and study forms

PROS Studies

- Management of febrile infants < 3 months
  - 2,755 infants enrolled, 501 practitioners
  - Rate of bacteremia/meningitis 1.9%
  - Variable care
  - Current clinical guidelines
    - Would not have improved care
    - Would have resulted in more hospitalizations and laboratory testing

- Immunization status of children vaccinated by practicing pediatricians
  - Data collected on 13,520 children from 42 states
  - 79.4% of children fully immunized at 8 months of age
  - Evaluated association of patient demographic characteristics, practitioner policies and beliefs, and parental health beliefs on immunization status
  - IPV not associated with lower rates
  - Large variation in practice rates (21-100%)

Is PROS Representative?

- PROS – Stratified random sample of 57 practices and 1,706 visits
- NAMCS – 33 practices and 948 visits
- Similarities
  - Gender, ethnicity, payment
  - Acute visits, diagnoses, proportion referred
- Differences
  - Race, age

How PROS Works

- Ideas from practitioners
- PROS studies
- New knowledge
- Recommendations, health care
- Improved child health outcomes
SCPPRN
South Carolina Pediatric Practice Research Network
www.musckids.com/scpprn

SCPPRN – description

<table>
<thead>
<tr>
<th>Description of 8 SCPPRN practices from 2007 survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practitioners</td>
</tr>
<tr>
<td>Date:</td>
</tr>
<tr>
<td>Site of office</td>
</tr>
<tr>
<td>Visits/year</td>
</tr>
<tr>
<td>Patient Race</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Patient Insurance</td>
</tr>
<tr>
<td>Private</td>
</tr>
<tr>
<td>Medicaid</td>
</tr>
<tr>
<td>Unfunded</td>
</tr>
<tr>
<td>Number with EMR</td>
</tr>
</tbody>
</table>

SCPPRN
Founded in 2005 based on a HRSA grant.
Part-time director, half time coordinator, steering committee with practice representation.
SCPPRN is a practice-based research network established by concerned primary care physicians who see a need for outcomes-based research that is “relevant” to their practice.

Immunization Project
- Results 349 patients
  - Race/ethnicity - 21% Hispanic, 38% white, 38% black and 3% other
  - Immunization rates – mean 76%, range by practice 70% to 92%
  - Practice immunization routines

Rates of Being Too Heavy for Age Appropriate Child Passenger Restraint Among SC Children

<table>
<thead>
<tr>
<th>Entire Sample</th>
<th>520 lbs. N, (%)</th>
<th>20-40 lbs. N, (%)</th>
<th>&gt;40 lbs. N, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>159 (33.6%)</td>
<td>36 (16.4)</td>
<td>383 (80.0)</td>
<td>96 (20.0)</td>
</tr>
<tr>
<td>By Race/Ethnicity*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>87 (33)</td>
<td>16 (17)</td>
<td>156 (60)</td>
</tr>
<tr>
<td>Black</td>
<td>78 (29.9)</td>
<td>15 (16)</td>
<td>170 (61)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>32 (19.4)</td>
<td>6 (15.8)</td>
<td>52 (79)</td>
</tr>
<tr>
<td>By Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>99 (37)</td>
<td>27 (21)†</td>
<td>216 (79)</td>
</tr>
<tr>
<td>Female</td>
<td>100 (36)</td>
<td>12 (11)</td>
<td>167 (81)</td>
</tr>
</tbody>
</table>

Immunization Project
- Results 349 patients
  - Race/ethnicity - 21% Hispanic, 38% white, 38% black and 3% other
  - Immunization rates – mean 76%, range by practice 70% to 92%
  - Practice immunization routines

Office practices – with variation: Immunization rates

<table>
<thead>
<tr>
<th>Office Practices</th>
<th>7 participating</th>
<th>UTD-yes</th>
<th>UTD-no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment (2/2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunization rates in the practice are assessed at least annually</td>
<td>79.3</td>
<td>84.9</td>
<td></td>
</tr>
<tr>
<td>Providers get feedback about their immunization rates compared to other providers/practices*</td>
<td>79.5</td>
<td>84.7</td>
<td></td>
</tr>
<tr>
<td>Records (2/6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunization records from previous providers are routinely available at the time of the first visit for patients transferred into the practice</td>
<td>79.6</td>
<td>83.6</td>
<td></td>
</tr>
<tr>
<td>Providers are prompted about immunizations due at sick or acute visits</td>
<td>82.5</td>
<td>80.2</td>
<td></td>
</tr>
</tbody>
</table>

P<.05
Number of procedures and UTD

<table>
<thead>
<tr>
<th># office practices</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTD</td>
<td>89</td>
<td>84</td>
<td>81</td>
<td>...</td>
<td>76</td>
</tr>
</tbody>
</table>

Trend P=.08

Conclusions

- The practice a child attends is the strongest predictor of being up to date at 8 months of age
- In this group of practices Hispanic ethnicity was associated with being up to date
- Office practices, as measured, do not predict being up to date beyond practice
- Where there was variation, recommended office practices were usually associated with a lower immunization rate

Question

- What are the characteristics of an office that are associated with more complete immunization of children?
- How should those characteristics be measured?

Selected SCPPRN Publications/Presentations


Sept 26, 2006

Lessons Learned:

1. Network participants generate ideas
   1. Paul Hieko – car seat proposal, dental varnish
   2. Abe Moskow – developmental screening
   3. Francis Rushton – psychosocial screening
2. Subspecialists generate ideas
   1. Bernie Maria – Headache/Migraine
   2. Carol Wagner and Bruce Hollis – Vitamin D and infection
3. Trainees are invaluable
   1. Fellows – Shannon Kennedy, Susan Hocevar, Jimmy McElligott, Sarah Mennito
   2. Residents –7

May 2011
APA and Research Networks

- **APA** – Academic Pediatric Association
  - **CORNET** – COntinuity Research NETwork (CORNET)
    - Janet Serwint
    - [http://www.ambpeds.org/research/research_cornet.cfm](http://www.ambpeds.org/research/research_cornet.cfm)
  - **PRIS** – Pediatric Research in Inpatient Settings (PRIS) Network
    - Rajendu Srivastava
    - [http://www.ambpeds.org/research/research_pris.cfm](http://www.ambpeds.org/research/research_pris.cfm)

Adolescent Vaccine Decision Making Study

- Examine the communication between parents, adolescents and providers in vaccine decisions
- Design an intervention to improve physician communications with adolescents and parents around vaccination
- Collaboration between two regional pediatric networks

Practice-based Research Challenges and Opportunities

- Support
- Human subjects
- Interest

- Examine health and health care where most patients and providers live

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**Table:**

<table>
<thead>
<tr>
<th>Network</th>
<th>Founded</th>
<th>Mission</th>
<th>Sites</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Research in Office Settings (PROS)</td>
<td>1986</td>
<td>Office practice</td>
<td>750</td>
<td>2.7 mil</td>
</tr>
<tr>
<td>Pediatric Emergency Care Applied Research Network (PECARN)</td>
<td>2001</td>
<td>Pediatric ED</td>
<td>22</td>
<td>950,000 visits</td>
</tr>
<tr>
<td>Continuity Research Network (CORNET)</td>
<td>2001</td>
<td>Continuity clinics</td>
<td>100/129</td>
<td>750,000</td>
</tr>
<tr>
<td>Pediatric Research in Inpatient Settings (PRIS)</td>
<td>2001, 2009</td>
<td>Hospitalized patients</td>
<td>168 hosp</td>
<td>&gt;0.5 mil discharges</td>
</tr>
</tbody>
</table>

The progress of medicine will be hampered and delayed till the general practitioner becomes an investigator.

Sir James MacKenzie
Principles of Diagnosis & Treatment of Heart Affections, 1916

February 15, 2008

Opinion: The intersection of practice-based research and quality of care

- The appropriate clinical question answered in a scientifically rigorous manner will lead to change in care by itself
- Clinical guidelines largely based on the opinions of subspecialists may both fail to change care and tend to undermine the legitimacy of the organizations that promulgate them

Sept 26, 2006

Poverty and Race

- What is poverty?
- What proportion of children affected?

Sept 26, 2006

Medicaid in South Carolina

Sept 26, 2006