

***SAEM Conference
on Emergency Care Research Networks***

***Multicenter Research in the
Pediatric Emergency Care
Applied Research Network***

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for Children Program, Maternal and Child Health Bureau,
Health Resources and Services Administration,
Department of Health and Human Services





No financial or other conflicts
of interest to report



Objectives

A story in three parts:

Part 1

- Define PECARN, brief history and structure

Part 2

- Challenges, pitfalls, benefits of multicenter research

Part 3

- Ongoing PECARN research studies

Pediatric Emergency Care Applied Research Network (PECARN)

- The first ***federally-funded*** PEM research network
 - with a purpose of overcoming inherent barriers to EMSC research
- The ***mission*** is to conduct high-priority, multi-institutional research into the prevention and management of acute illnesses and injuries in children and youth of all ages
 - *Not disease specific*
- Provides the ***leadership and infrastructure*** to conduct multi-center research, to support research collaboration among EMSC investigators, and to encourage translation of research to EMSC practitioners



Barriers to EMSC Research:

Why PECARN is Needed

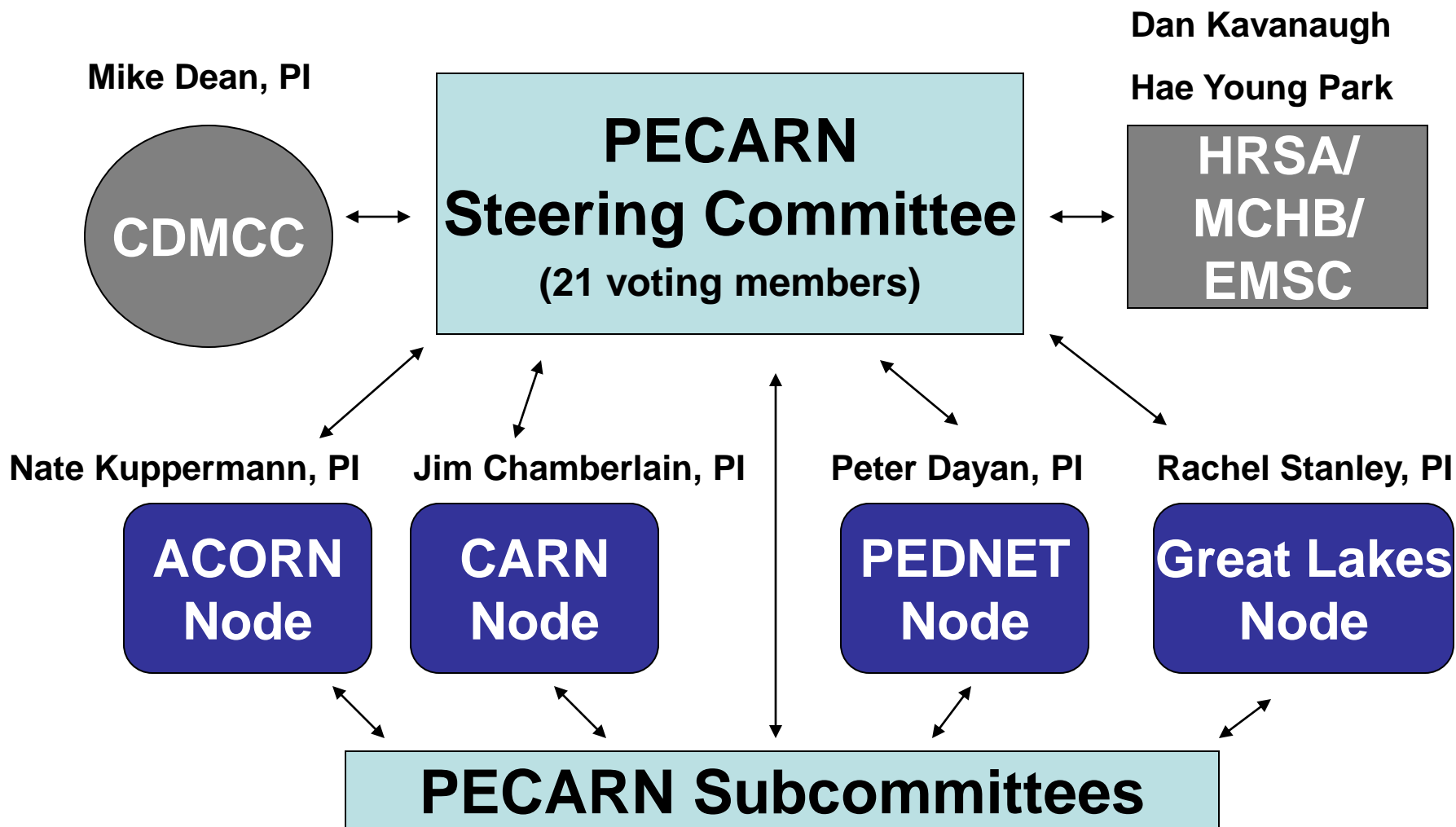
1. Low incidence rates of pediatric emergency events
2. Large numbers of children required to attain diverse and representative study samples
3. Complexity of obtaining informed consent in ED
4. Difficulty in tracking patients from out-of-hospital to hospital care
5. Difficulty in maintaining data quality and integrity in the ED setting
6. Insufficient funding for EMSC research and multicenter networks
7. Need infrastructure to study the process of translating research findings to treatment settings



Conception of PECARN

- AAP PEM CRC network in early 1990's
- APA-EMSC partnership meetings in 1998-99 to address barriers to research in PEM
- Precedents for other collaborative networks
 - Pediatric subspecialty groups (e.g. Vermont neonatal, Oncology)
 - Emergency medicine (e.g. EMNet, ID surveillance)
- HRSA/MCHB's EMSC program announces RFP in June 2001
- PECARN created September 2001

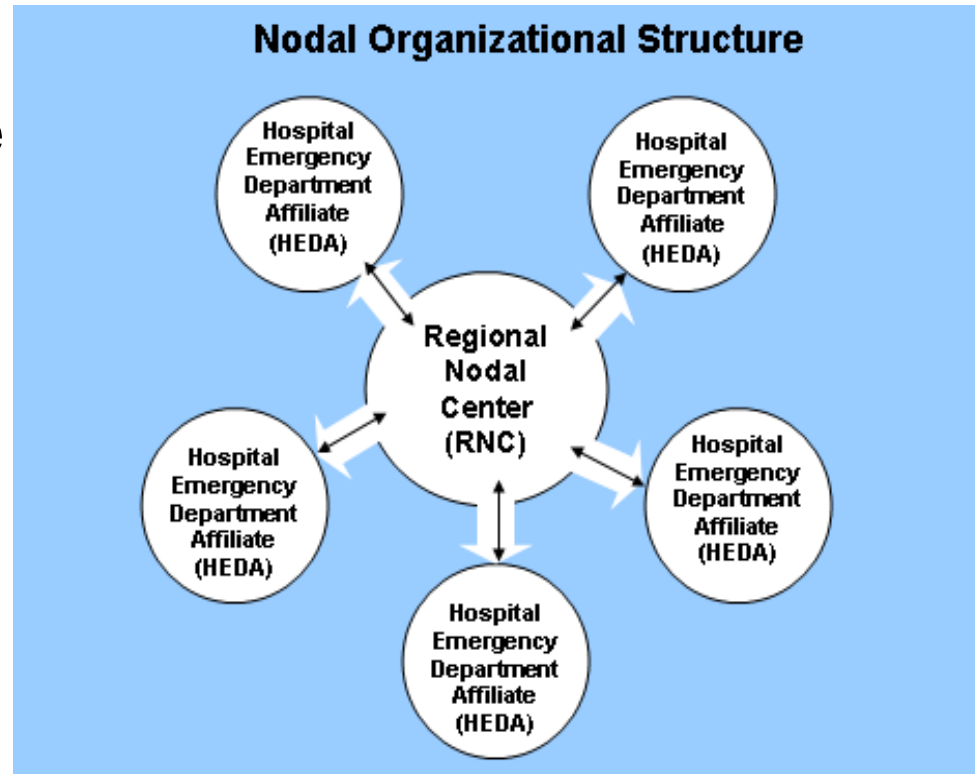
PECARN – Network Structure



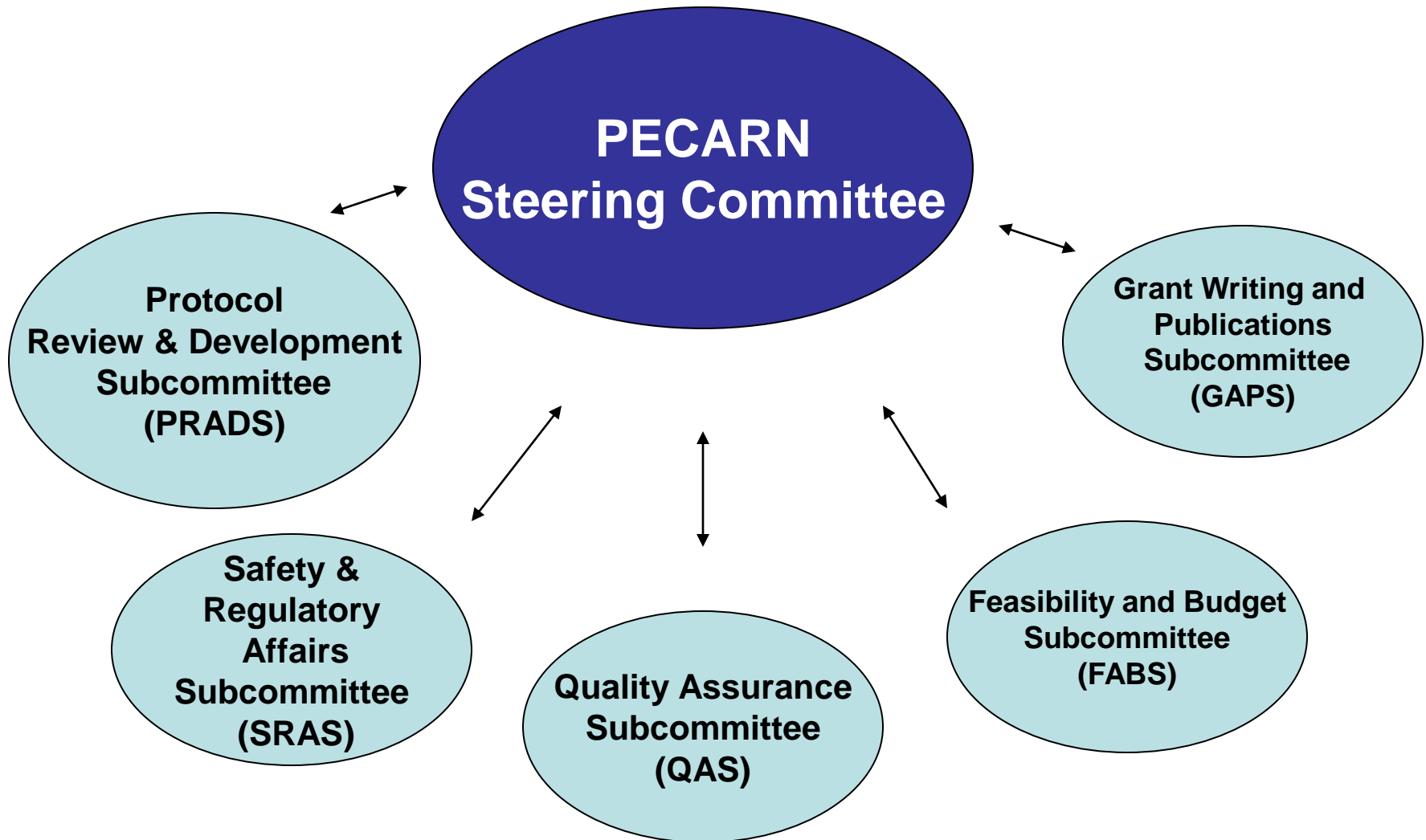


PECARN Hospital and Research Center Structure

- PECARN consists of four research node centers (RNCs) located at diverse sites across the country
- Each RNC hosts a network of hospital emergency department affiliates (HEDAs) for a total of 21 sites across the U.S.



PECARN Subcommittees



Role of the Steering Committee

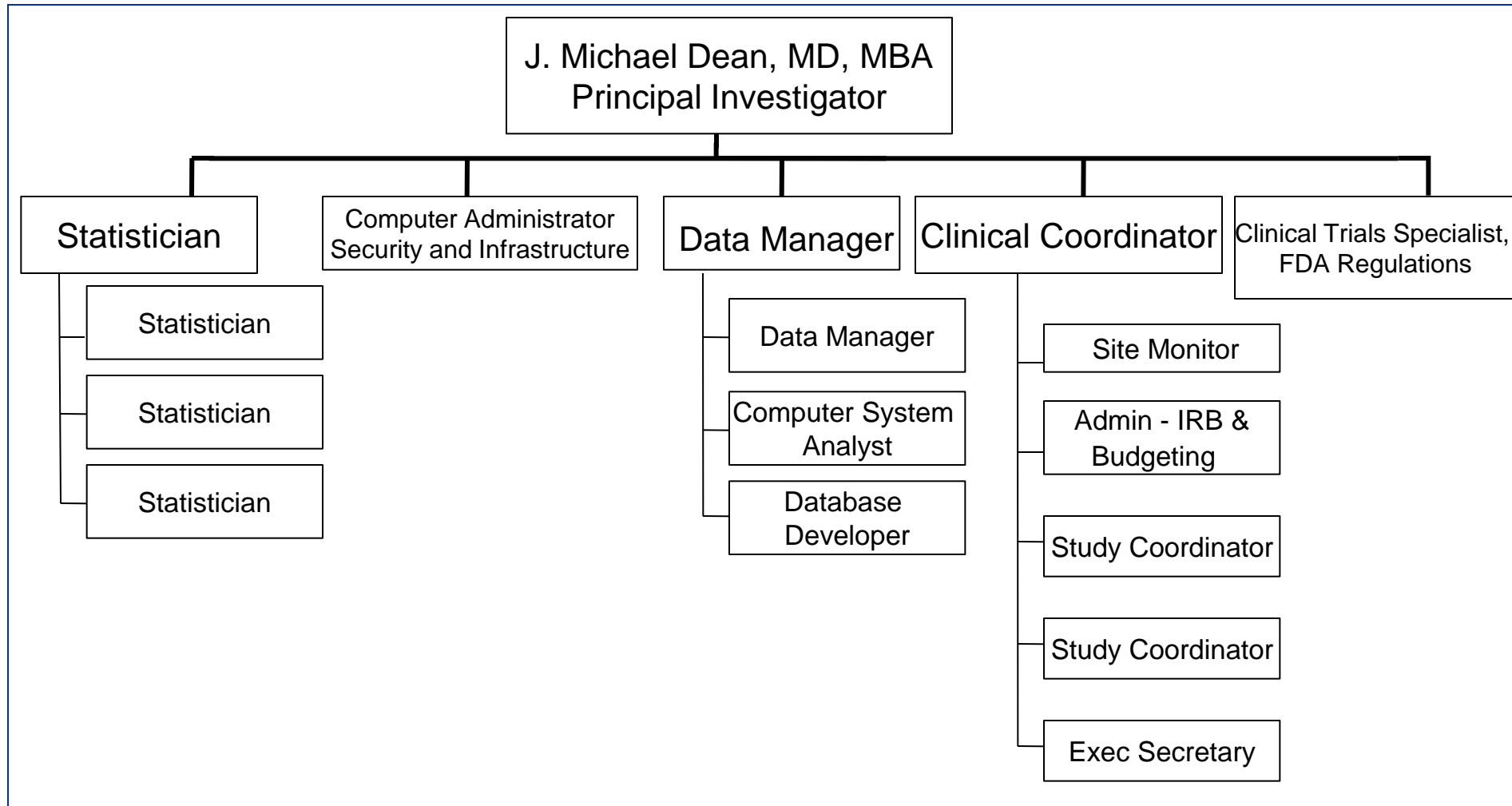
- Primary PECARN governing body
- Equal membership from the 4 nodes / data center
- Review and approve PECARN research proposals, formulate / monitor policies and procedures guiding the network
- Establish scientific and administrative bylaws, policies, and procedures
- Establish **subcommittees** to carry out specific tasks and activities

Role of the CDMCC

(Central Data Management and Coordinating Center)

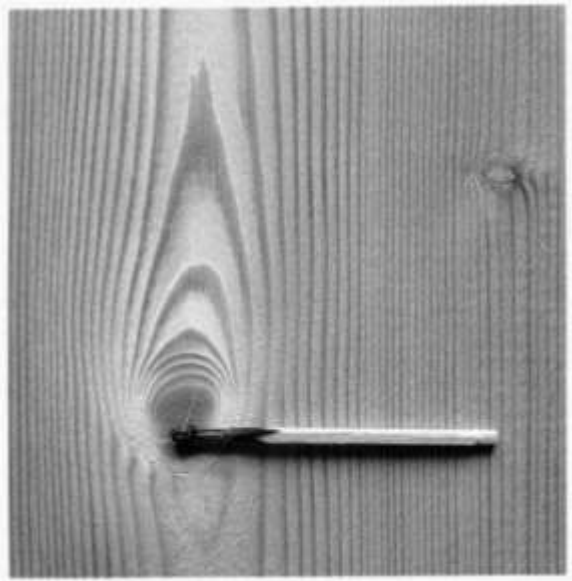
- Protocol development / study design
- Grant development / training
- Training / education
- Manuals, study materials
- Study support, technical expertise
- Overall project management and organization
- Data collection and management
- Data analysis
- Site monitoring

Central Data Management Coordinating Center (CDMCC)

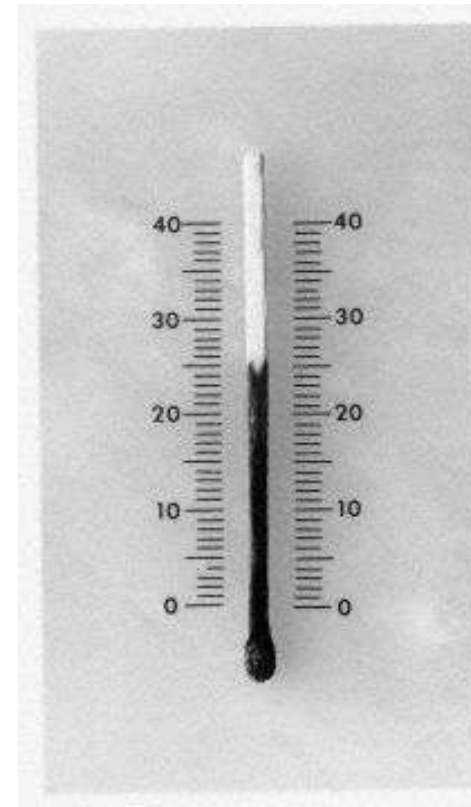


Research Prioritization

- PECARN prioritization process established and published, but success ultimately depends on...

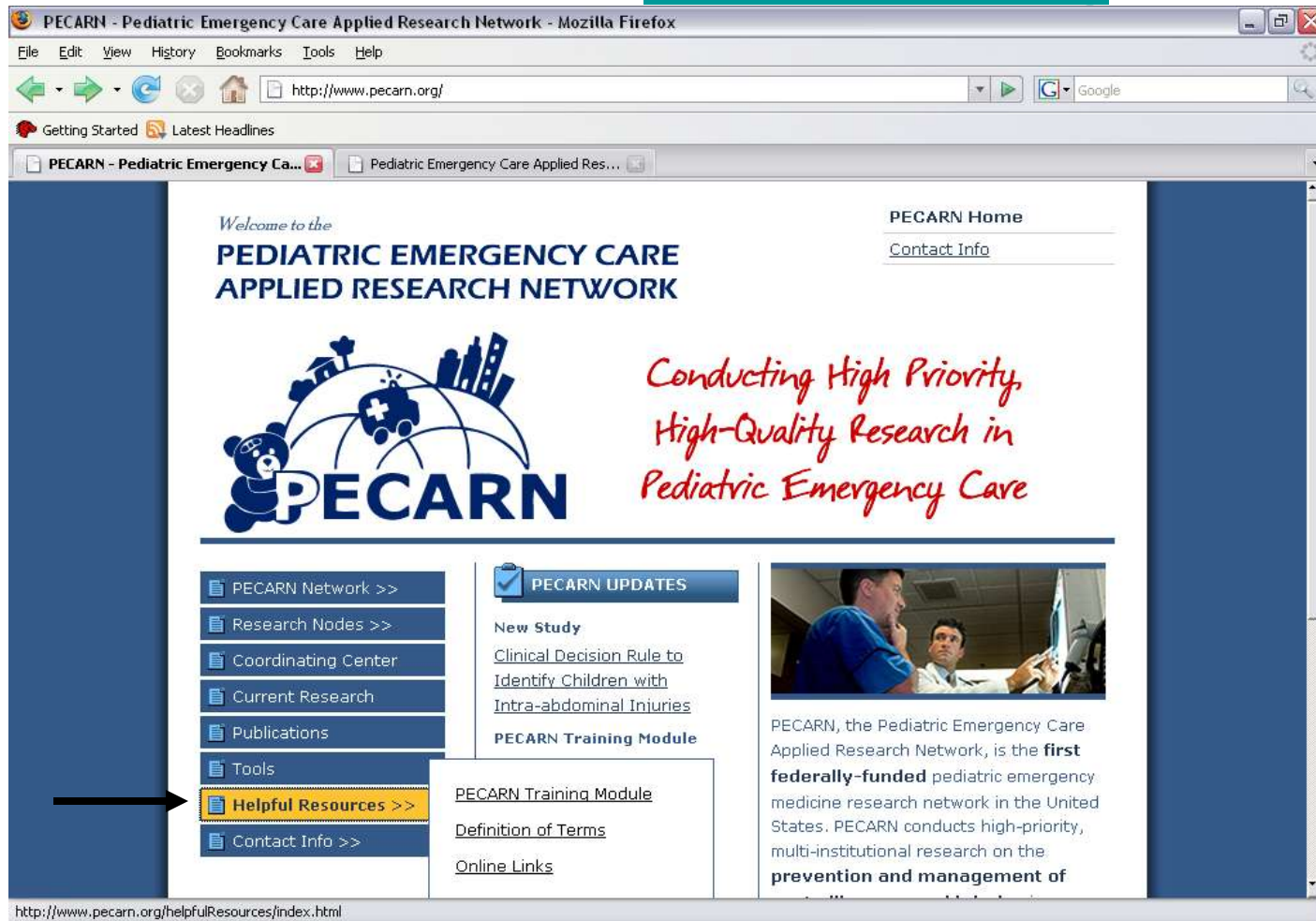


Acad Emerg Med 2008;15:377-383



Research Concept and Protocol Generation Process

PECARN website: www.pecarn.org



PECARN - Pediatric Emergency Care Applied Research Network - Mozilla Firefox

File Edit View History Bookmarks Tools Help


http://www.pecarn.org/

Getting Started Latest Headlines

PECARN - Pediatric Emergency Ca... Pediatric Emergency Care Applied Res...

Welcome to the
**PEDIATRIC EMERGENCY CARE
APPLIED RESEARCH NETWORK**

PECARN Home
[Contact Info](#)

 *Conducting High Priority,
High-Quality Research in
Pediatric Emergency Care*


PECARN Network >>
Research Nodes >>
Coordinating Center
Current Research
Publications
Tools
Helpful Resources >>
Contact Info >>

PECARN UPDATES

New Study
[Clinical Decision Rule to
Identify Children with
Intra-abdominal Injuries](#)

PECARN Training Module

[PECARN Training Module](#)
[Definition of Terms](#)
[Online Links](#)



PECARN, the Pediatric Emergency Care Applied Research Network, is the **first federally-funded** pediatric emergency medicine research network in the United States. PECARN conducts high-priority, multi-institutional research on the **prevention and management of**

<http://www.pecarn.org/helpfulResources/index.html>



The PECARN Training Module

Training Home

What is PECARN?

1. [Research Priorities](#)
2. [Ongoing Research](#)
3. [Funding](#)

PECARN Structure

1. [Organization](#)
2. [Subcommittees](#)
3. [Nodes & HEDAs](#)

Study Submission

1. [Requirements & Guidelines](#)
2. [Interactive Flowchart](#)
3. [Case Study](#)

Assessment

Questions?

PECARN Home

PECARN Training Module Home

The purpose of PECARN is to develop an infrastructure capable of overcoming barriers to pediatric emergency and EMS systems research.

The goal of this training module is:

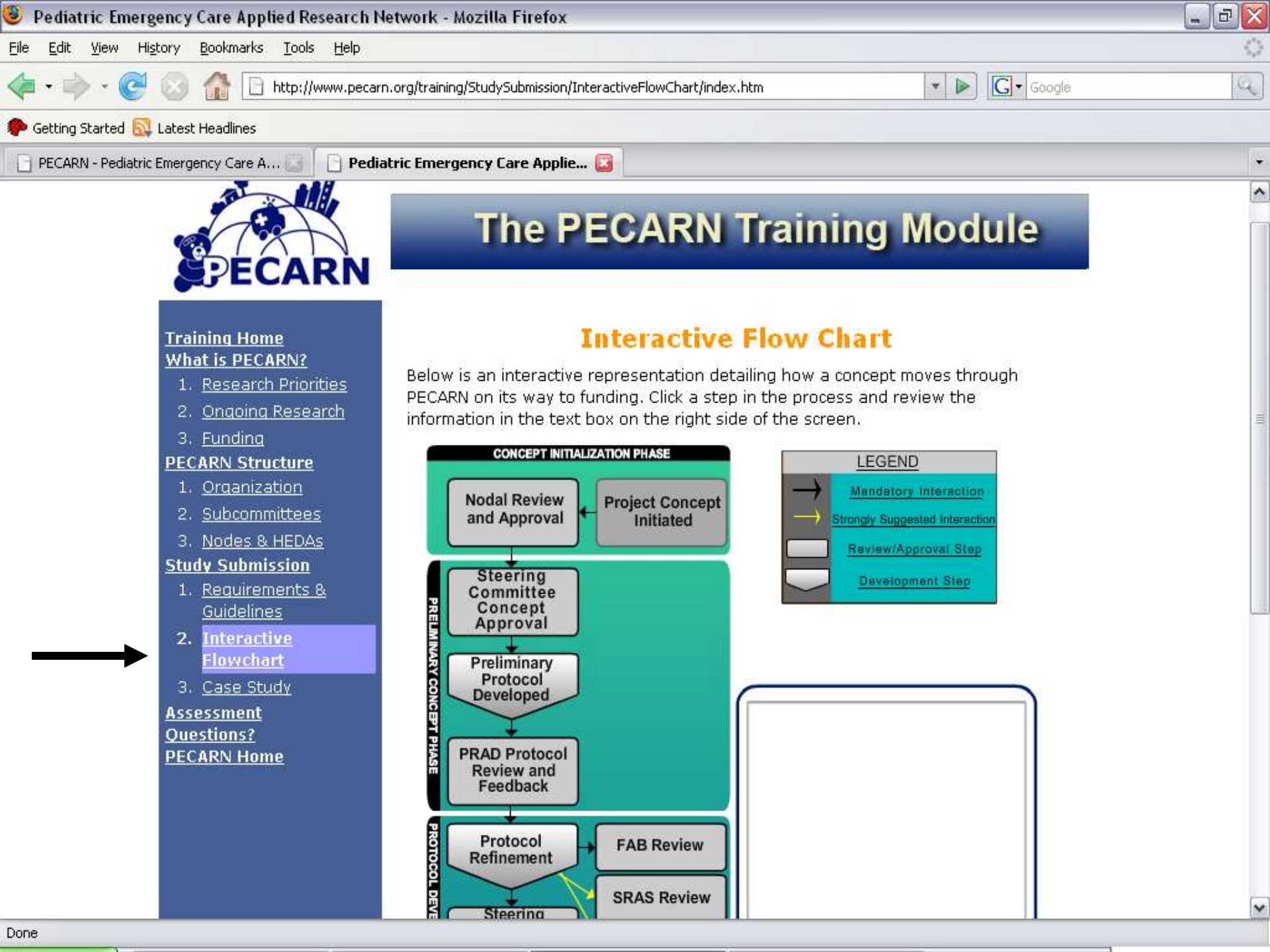
- To inform you about the structure and activities of PECARN
- To facilitate the use of PECARN by non-PECARN investigators



At the end of this training module you will:

- Know the key structural elements and activities of PECARN
- Know the process for non-PECARN investigators to submit research proposals using the PECARN

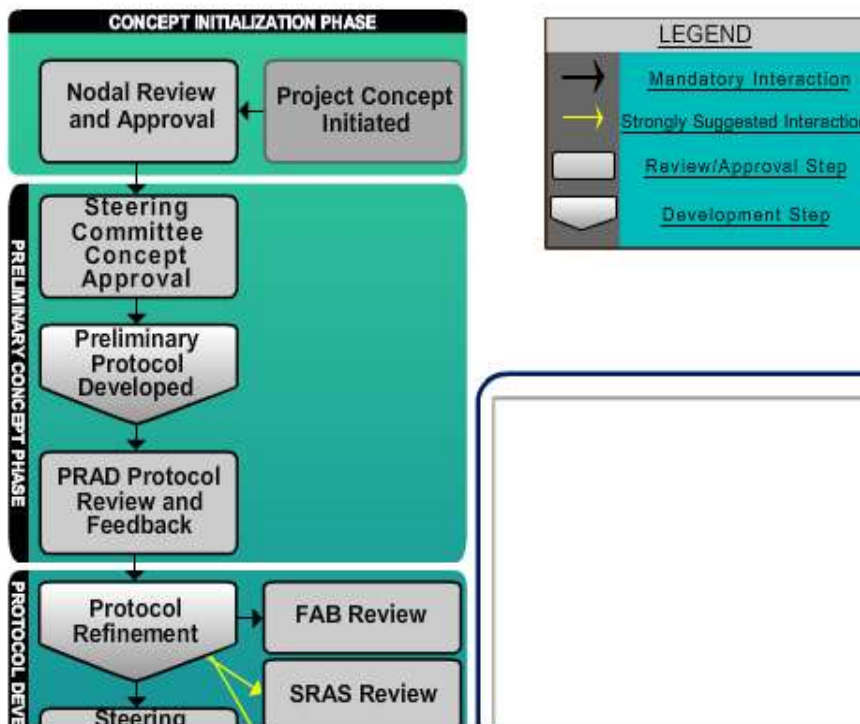
PECARN consists of cooperative agreement between academic medical centers and the Health Resources and Services Administration/Maternal and Child Health Bureau's Emergency Medical Services for Children Program (HRSA/MCHB/EMSC).



The PECARN Training Module

Interactive Flow Chart

Below is an interactive representation detailing how a concept moves through PECARN on its way to funding. Click a step in the process and review the information in the text box on the right side of the screen.



Training Home

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2. [Ongoing Research](#)
3. [Funding](#)

PECARN Structure

1. [Organization](#)
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Study Submission

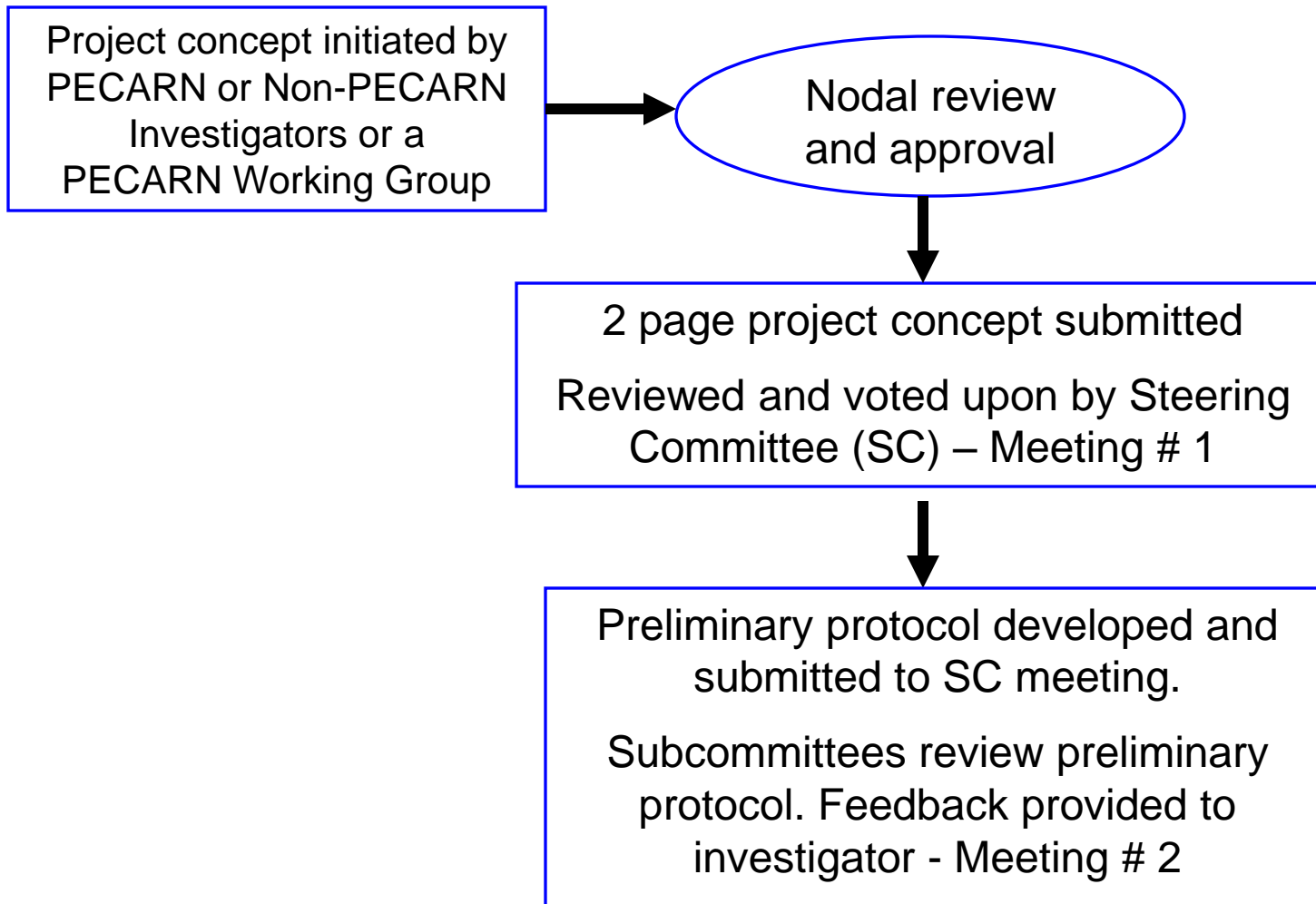
1. [Requirements & Guidelines](#)
2. [Interactive Flowchart](#)
3. [Case Study](#)

Assessment

Questions?

PECARN Home

Research Concept Review and Development Process



Research Concept Review and Development Process



Protocol revised and submitted

Protocol review/vote for approval by SC
(Meeting #3)



If approved, protocol developed into grant
application

(Substantial input from Feasibility and
Budget Subcommittee, and other
Subcommittees)

Grant submitted to agency



PECARN Strengths

- Seven years experience as a network
- 21 Hospital Emergency Department Affiliates
- Serving ~800,000 acutely ill and injured children
- Wide geographic and hospital representation
- Senior-level EMSC researchers and clinicians
- Outside investigators invited to participate
- Have leveraged our strengths to successfully obtain extramural funding and accomplish important research

PECARN Research Successes

Selected sample...

- 5 completed, ~ 7 ongoing projects, many sub-studies
- 10 federal grants
- 10 published manuscripts and many under preparation
- 40 abstracts presented (*9 at this meeting*)
- Pre-hospital research infrastructure established





Part 2:

Challenges, Pitfalls and Benefits of Multicenter Research

Network Research Volume

- Investigator and research coordinator burnout – no project, and no investigator is completely funded
 - Not too many, but not too few
- Any role for unfunded studies?
 - In first stages of network development, network data registry
 - Routine annual data download to track network, data for grants/projects
- 1-3 larger projects vs. several smaller projects
- (Unfunded) nodal pilot studies allow for development of larger studies and support grant applications
- Need to carefully track network resources
 - Network becomes more poor with each funded grant!
 - Research coordinator time is most valuable resource
- Want to get a lot accomplished, but not get overcommitted...



Workload and Commitment Challenges in Networks

- Senior investigators are (too) busy
- Senior investigators need to subordinate individual goals into the network
- In PECARN, the 4 node and data center PI's are committed that the network will play a substantial role for remainder of their careers
- Junior investigators need to weigh benefits / drawbacks of involvement with a network



Leadership and Human Resources

- **Who's in charge?**
 - PI
 - Funding agency
 - DSMB
 - Steering Committee
 - Data Coordinating Center
- **Are there enough personnel?**
 - Experienced and junior investigators
 - Statistical/epidemiological expertise
 - Research coordinators
 - Independent data center



Leadership, Communications and Meetings

- Strong leadership of a study/network essential
- Participants dispersed, varied experience: frequent electronic / telephonic communication
- However, nothing replaces the face-to-face
 - meet 3-4 times annually plus a retreat
- Build travel and meetings into study budget
- Use all available work time at meetings (avoid superfluous guest speakers)
- Play/social time absolutely necessary
 - ***development of teamwork is critical***



The IRB Challenge

- IRBs around the U.S. overburdened, frequently under-experienced membership, facing increasing regulatory hurdles
 - ~ 500 IRBs, > 105,000 annual initial reviews, ~ 120,000 annual reviews, ~ 65,000 amendments
- Little time to discuss individual projects
- Institutional IRBs value their independence
- Increasing complexity of research projects
- **Tip:** get to know your IRB Chair well!

The IRB Challenge

- **Potential solution: Central IRB** for multicenter studies (model developed by the NCI)
- CIRB reviews only a few protocols per month
- “Facilitated” (i.e. brief) review at the local level
- Local IRB decides whether relevant local issues
- Local IRB can exert local restrictions but can not make substantive changes to protocol
- Local IRB oversees performance locally
- PECARN has considered moving to a CIRB

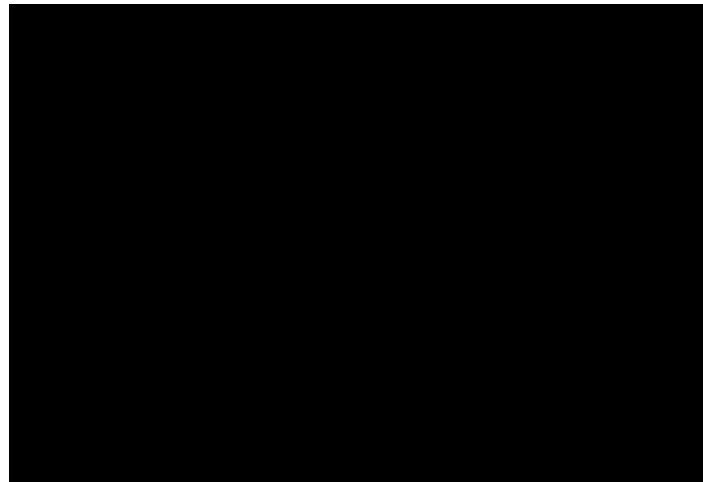
The IRB Challenge

- Nevertheless, PECARN has been very successful with our IRBs:
 - 16 projects of all types approved by 20+ IRBs from around the country (no rejections!)
 - No alterations of protocols, but minor adjustments at different sites (careful negotiations)
 - Many successful amendments
 - Good tips from some IRBs
- Time consuming
 - However, our IRBs supportive, non-obstructionist
- **Tip:** take your network road show to your IRB



Coordinating the Network and Individual Studies

Physicians and scientists are individuals thinkers and can be quirky and headstrong; steering the ship can be difficult:





Challenges in Network Research

- Multicenter research is much more complex than single institution research
 - Training of investigators and staff
 - Explicit protocol development – the “MOO”
 - Uniform standards for clinical research (GCP)
 - Site monitoring requirements
 - Data transmission and security
 - IRBs have different standards

Research Quality and Site Monitoring

- Maintaining high standards of quality more difficult than in single-center studies
- Strong emphasis on training / standardization
- Include “Good Clinical Practice” training

Then...

- Site monitoring regardless of study type
- Subject recruitment, data completion and quality
- Frequency of visits depends on study type, cost
- **Carrot and stick**
 - reward good sites
 - be prepared to terminate site involvement





Data Management and Transmission

- Epidemiologists, statisticians involved early
- Independent data center / data manager
- Paper data collection forms should be simple
- Electronic, web-based data entry of de-identified data (HIPAA), with logic and range checks
- Original data forms/source documents at site
- Double data entry as quality check
 - triple data entry controversial
- Queries for missing or inconsistent data
 - start early in study



(Financial) Costs of Network Research

- Multicenter research is expensive
- Federal agency funding caps are limited
- After distribution to > 20 sites, not much money left per site
 - much volunteerism and good will necessary
- Budgets typically under-fund training, site monitoring, etc. – miscalculations are costly!
 - have a feasibility and budget subcommittee
- **Keep study simple, focused, on budget**

Other Tips

- Be nimble, prepared to change processes
- Be prepared to rapidly respond to RFAs
- Study run-in periods very useful
 - adjust studies as necessary early on
- **OUTSTANDING** and regular communications
- Engage many funding agencies
- Have a road show
- Nurture future leaders – have terms of office

Benefits to Network Involvement

- Definitive results that have the potential to change practice
 - *“what do you want to have accomplished at the end of your career?”*
- Authorship
- Funding
- Relationship development

Benefits:

definitive results and authorship



The NEW ENGLAND
JOURNAL of MEDICINE

A Multicenter, Randomized, Controlled Trial of Dexamethasone for Bronchiolitis

Howard M. Corneli, M.D., Joseph J. Zorc, M.D., Prashant Mahajan, M.D., M.P.H., Kathy N. Shaw, M.D., M.S.C.E., Richard Holubkov, Ph.D., Scott D. Reeves, M.D., Richard M. Ruddy, M.D., Baqir Malik, M.D., Kyle A. Nelson, M.D., M.P.H., Joan S. Bregstein, M.D., Kathleen M. Brown, M.D., Matthew N. Denenberg, M.D., Kathleen A. Lillis, M.D., Lynn Babcock Cimpello, M.D., James W. Tsung, M.D., Dominic A. Borgjalli, D.O., M.P.H., Marc N. Baskin, M.D., Getachew Teshome, M.D., M.P.H., Mitchell A. Goldstein, M.D., David Monroe, M.D., J. Michael Dean, M.D., Nathan Kuppermann, M.D., M.P.H., for the Bronchiolitis Study Group of the Pediatric Emergency Care Applied Research Network (PECARN)

Volume 357(4), 26 July 2007, pp 331-339



Investigator Credit and Authorship

- One of the most complex issues to navigate
- Universities and journals getting used to this:
 - 22% of publications in JAMA in 2001 from multisite networks (up from 6% in 1991)
- All authors/investigators receive credit in the acknowledgement section
- Large trials often known better by their study names than by individual authors
- PECARN studies big enough that many a priori subanalyses – *first authorships distributed*
- Advanced authorship agreements necessary



Investigator Credit and Authorship

- Credit/accountability for all authors/investigators regardless of who is on the authorship line
- Research group name **always** on the byline
- Types of individual authorship on the byline:
 - All authors on the line, depending on journal
 - “Corporate authorship” with “writing committee” listed in acknowledgements
 - Lead authors listed, followed by the network name (i.e. “Smith, Jones and Heller, for the ... Network”)
- The NLM is working to improve its ability to capture author names in writing committees

Friendships and the Network

- Intense work and social play – ***strong bonds***
- Socialization helps promote communal spirit
- However, it is essential that critique of projects and monitoring of work remain uninhibited
- Frank discussions of quality issues become difficult as friendships / mentorships form....
- Nevertheless, ***you must do the right thing...***





Benefits, Drawbacks for Junior Investigators

Benefits:

- Tremendous ability to accomplish large-scale important work
- Excellent opportunities for mentoring
- Excellent opportunities for networking
- Excellent opportunities for publishing

Drawbacks:

- Junior investigators cannot risk burying all their projects and efforts into a network
- Long, complicated, high-risk studies



Part 3:

Ongoing PECARN Research Studies

Ongoing/Completed PECARN Research

- Patient safety and error reduction
- Evaluation of blunt head trauma
- Evaluation of blunt abd. trauma
- C-Spine immobilization
- Steroids in acute bronchiolitis
- The burden of mental illness and psychiatric emergencies in PED
- Therapeutic hypothermia in pediatric cardiopulmonary arrest
- Diagnostic categorization of illnesses and injuries in the PED
- Management of status epilepticus
- Quality of pediatric emergency care
- RNA transcription biosignatures to diagnose febrile infants

Future Goals of PECARN

1. To follow the identified PECARN research priorities
 - more interventional RCTs
2. To design and implement a plan to study/encourage the transfer of network findings to EMSC practitioners (*“Knowledge Translation”*)
3. To increase collaboration between PECARN researchers and those outside the network, including other networks
4. To increase out-of-hospital research
5. To enhance bi-directional exchange of information and ideas between the EMSC research and treatment communities
6. Further nurture/develop young investigators

PECARN-PERC Collaboration



QUESTIONS?



- **PECARN website and module:**
www.pecarn.org
- **EMSC Program Director,**
Dan Kavanaugh, MSW, LCSW-C:
301-443-1321 or dkavanaugh@hrsa.gov
- **Chair, PECARN Steering Committee,**
Nathan Kuppermann, MD, MPH:
916-734-1535 or nkuppermann@ucdavis.edu

