



Multicenter Collaborative Research in Pediatric Emergency Care

*(and the Pediatric Emergency Care Applied
Research Network - PECARN)*

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Today's Objectives

A Story in two parts:

Part 1

- Define PECARN
- Brief history of PECARN
- Ongoing research studies

Part 2

- Challenges, pitfalls and strengths of multicenter research

What Is PECARN?

- PECARN is the first federally funded national EMSC research network
- PECARN is funded through HRSA/MCHB/EMSC with the purpose of developing an infrastructure capable of overcoming inherent barriers to pediatric EMSC research
- PECARN provides the leadership and infrastructure to conduct multi-center research studies, to support research collaboration among EMSC investigators, and to encourage informational EMSC exchanges

What Is PECARN?

- PECARN is comprised of 4 multi-institutional nodes and a data coordinating center (CDMCC)
- PECARN provides the leadership and infrastructure to conduct multi-center research studies, to support research collaboration among EMSC investigators, and to encourage translation of results to practitioners

PECARN's mission is to conduct high priority research into the prevention and management of acute illnesses and injuries in children of all ages

Barriers to Research: Why PECARN is Needed

1. Low incidence rates of pediatric emergency events require pooling of centers to conduct research.
2. Large numbers of children are required to attain diverse and representative study samples.
3. An infrastructure is needed to test the efficacy of treatments, as well as the transport and care that precede the arrival of children to hospital EDs.
4. A mechanism is needed to study the process of transferring research results to treatment settings.

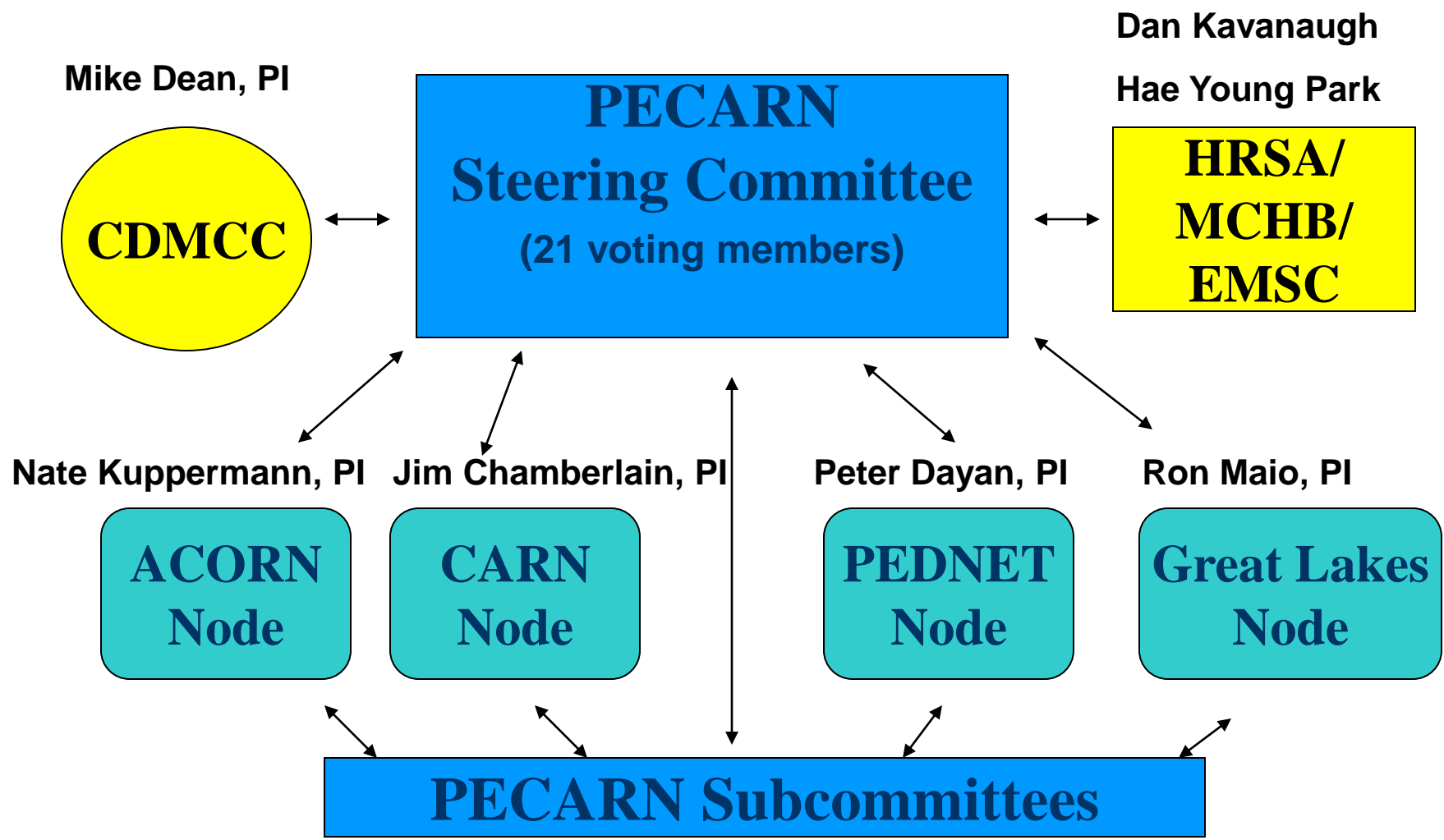
Conception of PECARN

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

Structure of PECARN

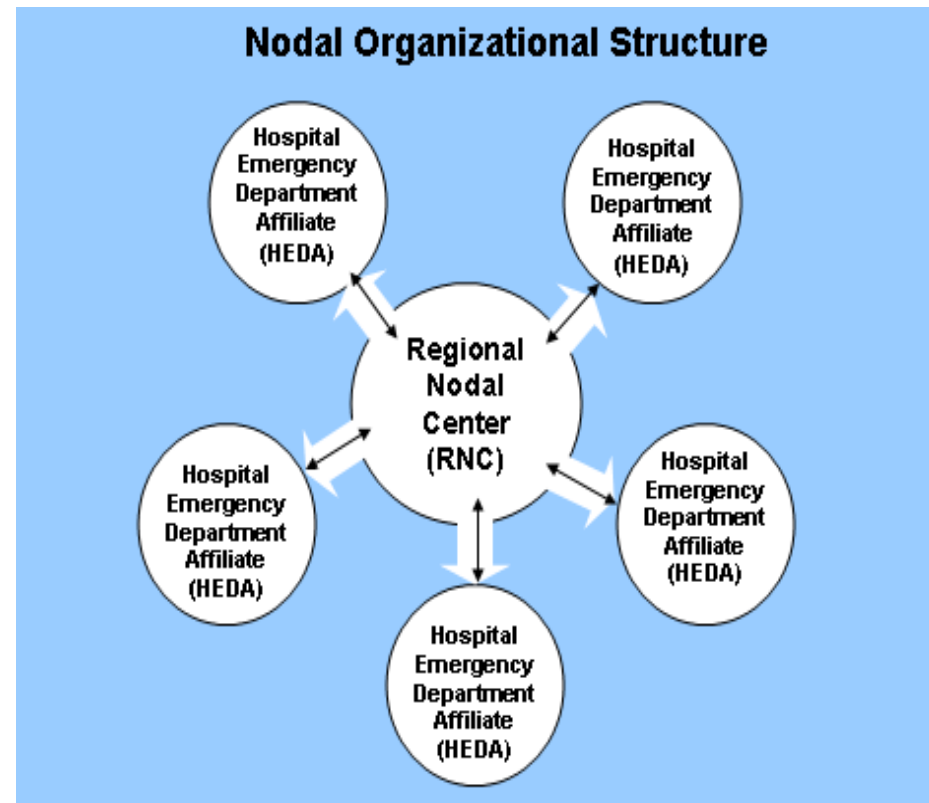


PECARN – Network Structure



Nodal Structure

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





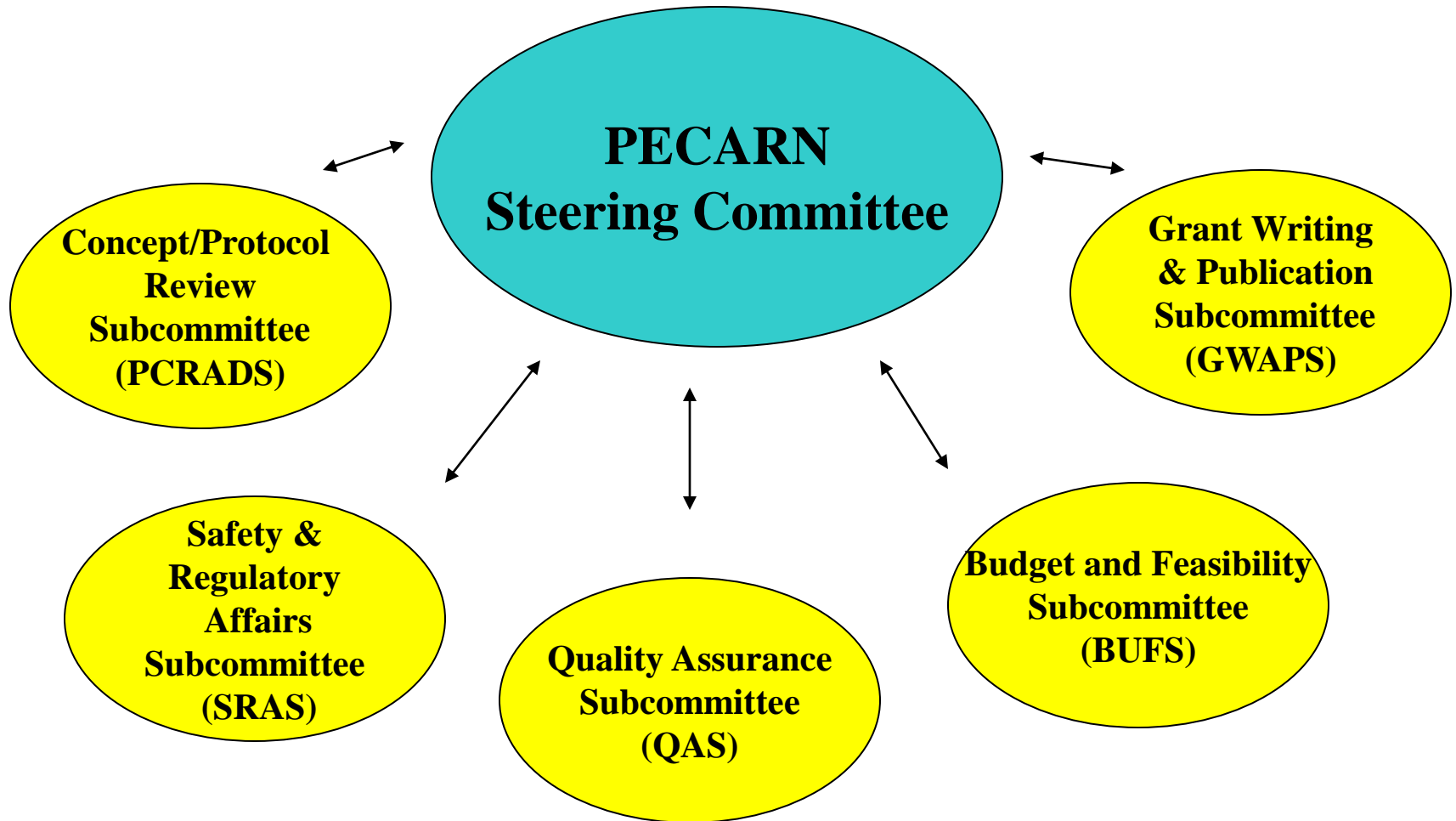
PECARN Data Center (“CDMCC”)

- Organization of network/sites
- Network leadership
- Protocol development/Study design
- Grant writing
- Subcommittee leadership
- Training/Education
- Manuals, study materials
- Study support, technical expertise
- Data collection
- Data Analysis
- Maintains the website (www.pecarn.org)

PECARN Steering Committee

- The primary PECARN governing body
- Equal membership from each node and the CDMCC
- Responsible for reviewing and approving specific PECARN research proposals
- Formulates and monitors policies and procedures guiding the research activities of the network
- Establishes scientific and administrative bylaws, policies and procedures
- Establishes subcommittees to carry out specific tasks and activities

PECARN Subcommittees



PECARN Strengths and Accomplishments

- 21 Hospital Emergency Department Affiliates
- Serving ~ 800,000 ill and injured children
- Wide geographic and hospital representation
- Senior-level EMSC researchers and clinicians with expertise in epidemiology, statistics, health services research
- 4 manuscripts published, several under development, more than a dozen abstracts

PECARN Research Projects *(others in development)*



1. PECARN Core Data Project

Funded Through Core
PECARN Network
Funding

Objectives and Status

1. Describe the PECARN patient population
2. Determine availability, completeness, and agreement of core data from electronic and chart review
3. Test ability to collect, transfer, manage data from all sites
4. Establish benchmarking among sites
5. Examine practice pattern variation in management of
 - *asthma*
 - *long bone fractures*

- The 25 participating hospitals (at origin) of PECARN serve urban, suburban and rural patients.
- Annual ED pediatric censuses ranging from 4,000 to more than 86,000.
- All 25 hospitals are non-profit, and include academic, community, general and free-standing children's hospitals.
- Seventeen of the 25 are Level One Trauma Centers, and all 25 centers care for children with blunt head trauma.
- Racial and ethnic diversity of this population is substantial:
 - 47.5% of PECARN pediatric patients are African-American
 - 35.6% are non-Hispanic Caucasian
 - 11.1% are Hispanic
 - 1.4% are Asian or Pacific Islander
 - 0.2% are American Indian or Alaskan Native
 - 4.2% are of unknown race

2. The Effectiveness of Oral Dexamethasone for Acute Bronchiolitis: A multi-center randomized controlled trial

Co-funded by EMSC
Program and and
HRSA/MCHB
Research Program

Objectives and Status

- To assess the effectiveness of oral dexamethasone for acute moderate-to-severe outpatient bronchiolitis in a multi-center randomized control trials with respect to
- Have enrolled ~ 600 patients to date
- Data enrollment completed April 2006

3. Hypothermia for Pediatric Cardiac Arrest Planning Grant

Funded through the
NIH/NICHD

Objectives and Status

I. Describe cohort of pediatric patients after cardiac arrest from either outpatient or inpatient setting.

One year pilot data collection

- Patient characteristics
- Event characteristics
- Time intervals to outcomes
- Patient outcomes [survival, neurologic]

II. Delineate factors associated with outcomes

III. Characterize cohort eligible, and prepare for future RCT of hypothermia (or other) intervention

IV. ~ 500 patients enrolled; data being analyzed

4. Childhood Head Trauma: A Neuroimaging Decision Rule

Co-funded by EMSC
Program and and
HRSA/MCHB
Research Program

Objectives and Status

- To develop and validate a clinical decision rule for the use of neuroimaging that identifies children at high risk and those at zero risk of TBI needing acute intervention after blunt head trauma
- Long term goal is to identify the evidence on which to base appropriate ED evaluation of head-injured children
- Prospective data collection on ~ 40,000 patients with minor head injury (GCS 14 or 15), started June 2004
- Have enrolled ~ 33,000 children to date
- Data collection complete in August 2006

5. Referral Patterns and Resource Utilization for Pediatric Emergency Department Patients Presenting With a Psychiatric or Mental Health Problem

Funded Through
Core PECARN
Network Funding

Objectives

- To ascertain the sources of referral into the institution for children with mental health issues
- To ascertain the organization and utilization of resources used in the care of pediatric patients with psychiatric complaints and possible variation in these by PECARN site

6. Creating a Diagnosis Grouping System for Childhood ED Visits

Funded through an EMSC
Targeted Issues Grant

Objectives and Status

- To develop a diagnosis grouping system (DGS) using ICD-9 codes to describe child ED diagnoses for research and reporting.
- To develop a severity classification system based on resource use.
- Methods involved Delphi and Nominal Group Consensus processes using the PCDP data
- The DGS has 22 major groups and 73 subgroups; 48 ICD-9 codes account for ~ 50% of all ED diagnoses.
- Nearly 50% of ICD-9 codes are rated “3” in severity, on a 1-5 scale.
- Data has been validated with NHAMCS and state ED data sets.
- Next steps include correlating the severity scale with actual measures of ED resource use.

7. Bioterrorism Surveillance

Funded Through AHRQ
Grant of Participating
Hospital (Harvard
Medical School)

Objectives and Status

- To develop and evaluate an information infrastructure for PECARN that creates an automated data stream of real-time clinical information from the EDs of PECARN hospitals to a data analysis center located at Children's Hospital of Boston
- Data will be used for
 - Bioterrorism surveillance
 - General-purpose public health surveillance
 - Clinical research
- Centers currently being organized

8. Predicting Cervical Spine Injury (CSI) in Children

Funded through an EMSC
Targeted Issues Grant

Objectives and Status

- To identify a set of variables that separate injured children at negligible risk for CSI from those at non-negligible risk
- To test the criteria that identify these children in EMS systems
- Will use case-control methods, as well as formal focus groups of EMS personnel
- **Ultimate goal** is to refine spinal immobilization policies in the out-of-hospital and ED settings for injured children
- Data collection ongoing

9. Lorezepam for Pediatric Status Epilepticus

Funded through the
NIH/NICHD

Objectives and Status

- Funded by the NIH in response to the FDA's Best Pharmaceuticals for Children's Act
- Ultimate objective is to obtaining FDA approval for pediatric lorazepam dosing
- Study has two components:
 - Pharmacokinetic study of lorazepam in children with SE
 - RCT of lorazepam versus diazepam for SE in children
- Pharmacokinetic study complete in May 2006
- RCT with exception from informed consent being planned

Future Goals of Network

1. To finalize and implement a formal research agenda to guide future research proposal development
2. To design and implement a plan to study/encourage the transfer of network findings to EMSC practices
3. To collaborate more closely with EMSC practitioners and researchers in order to enhance bi-directional education and exchange of ideas and information between the treatment and research communities

Part 2: Challenges, Pitfalls and Strengths of Multicenter Research

Social Challenges in Networks

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

Strengths, Pitfalls for Junior Investigators

Strengths:

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

Pitfalls:

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

Leadership, Communications & Meetings

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

Herding Cats

Physicians and scientists are individuals
thinkers and can be quirky:

Study Challenges in Networks

- Multi-institutional research is much more complex than single institution research
 - Training for investigators and staff
 - Protocol development much more explicit – the “MOO”
 - Uniform standards for clinical research (GCP)
 - Site monitoring requirements
 - Data transmission and security
 - IRBs have different standards
- Costs are high, and budgets tend to under-fund training, site monitoring, etc.
- **Keep study simple, focused, and well budgeted**

Study Challenges in Networks

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

Facing the IRBs in a Network

- IRBs overburdened, frequently under-experienced membership, facing increasing regulatory hurdles
 - 491 IRBs, ~ 105,000 annual initial reviews, ~ 116,000 annual reviews, ~ 63,000 amendments
- Little time to discuss individual projects
- Institutional IRBs value their independence
- Increasing complexity of multicenter research projects

Facing the IRBs in a Network

- **One potential solution:** A 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 is considering ways to “centralize” its IRB process

Research Quality and Site Monitoring

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

Then...

- Site monitoring of all centers regardless of whether observational or interventional study
- Subject recruitment, data completion and quality
- Frequency of visits depends on study type, cost
- Carrot and stick

Data Management and Transmission

- Epidemiologists, statisticians involved early
- Independent data center / data manager
- Paper data 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 local site
- Double (triple?) data entry should be considered as a quality check – controversial
- Queries for missing or inconsistent data

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
- Advanced authorship agreements necessary
- ***But what about the authorship byline?***

Investigator Credit and Authorship

- Research group name **always** on the byline
- Types of individual authorship on the byline:
 - All authors on the line, depending on journal
 - “Corporate authorship” (i.e. network name alone) with “writing committee” listed in acknowledgements
 - Lead authors listed, followed by the network name (i.e. “Jaffe, Knapp and Heller, for the ... Network”)
- Ancillary studies spread authorship opportunities
- 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 bonding***
- Socialization helps promote communal spirit
- However, it is essential that critique of projects and monitoring of work remain uninhibited
- Frank discussions of quality issues may become difficult as friendships and mentorships form
- Nevertheless, ***you must do the right thing...***

Summary

- EMSC/PEM research needs networks because important PEM adverse events are rare
- Networks need both seasoned and junior investigators, and strong willed leadership and federal partners
- Networks need a strong, independent data center
- With research conducted in this setting, the evidence-based practice of EMSC/PEM will greatly improve