Howard Corneli, MD, from PCMC in Salt Lake City, won this year’s EMSC National Hero’s Award for Outstanding EMSC Research Project “Oral Dexamethasone for Bronchiolitis: A multi-center randomized controlled trial.” Dr. Nate Kuppermann, chairman of the PECARN Steering Committee, accepted the award on behalf of Dr. Corneli.

This award highlights an individual who has completed a significant EMSC-related research study that confirms current practice or has the potential to impact the provision of pediatric emergency care at a national or international level.

Connecting Data Elements with Study Research Questions
By Bonnie LaFleur, Ph.D., MPH, CDMCC Statistician

Ensuring that the data elements collected for a study are compatible with the study objectives is a critical piece of a clinical research enterprise. As with many aspects of clinical research, there are tradeoffs to be considered when deciding which variables should be collected. As tempting as it may be to collect variables that may not be needed in support of part of the primary research question(s), there are disadvantages that may outweigh any possible benefits from collecting potentially extraneous data. In this article, we will clarify why this is important, from grantsmanship and theoretic perspectives. There are many motivations for the idea that ‘less is more’ with respect to data collection. In this article, we address three important justifications:

Cost
Collecting data is a costly venture, not just in terms of data entry and storage but also from the resolution of data queries. The increase in cost is not linear and it becomes even more costly when multiple sites, repeated measurements, or complex derived data (e.g., many variables derived from collected data elements) are involved. The assurance of data integrity is a requirement for FDA clinical trials and is expected for other research studies as well. The cost is worthwhile when it is clear that the data elements are directly related to study questions and measurable outcomes.

Good Scientific Practice
Most statistical reviewers of NIH and foundation proposals look for a direct connection between specific aims and methods. Included in the methods section is the expectation of outcome measures, possible covariates of interest, and discussion of timing, storage, access, and use of all data that is collected during the course of the study.

The International Conference on Harmonization (ICH): E9 Statistical Principles for Clinical Trials documents, gives detailed recommendations for how to specify both primary and secondary variables. Specifically, it states that there should be one pri-
mary variable for randomized clinical trials (RCTs) an efficacy variable, that the relationship between the primary and secondary variables should be clearly described, and this should be the variable, “capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial.” Further, with respect to secondary variables, the ICH guidelines assert that “the number of secondary variables should be related to the limited number of questions to be answered in the trial.”

While the strategies for RCTs may be arguably too rigorous for alternative experimental designs or trials (e.g., observational studies), the basic principles are the same. Data should relate to a priori, focused hypotheses for all clinical studies to ensure consistency, maintain patient safety, and ensure accurate discussion of trial results.

Methodological

There are a number of possible theoretical problems in the collection and analysis of data that are not specifically tied to the stated research questions. The most problematic is multiplicity. Multiplicity, in this setting, refers to the testing of multiple hypotheses. Generally, it comes about when you are trying to run too many statistical tests under one general question. The philosophy is that the level of significance (usually 0.05) is not actually 0.05 when there are multiple hypotheses being tested. This is called type I error or “false positives”; the more tests you run the more likely it is that you will reject the null hypothesis when it is in fact true. The problem of controlling overall type I errors associated with multiple primary outcome variables has been discussed for years. The most rigorous criteria related to multiplicity are applied to RCTs, however, the issues are relevant for any study evaluates specific research hypotheses.

There are many papers that discuss the theoretical implications related to multiplicity and specifically the importance of prespecification of primary endpoints in clinical trials (Moye, 2001a, 2001b). Dr. Moye’s claims are generally accepted by established researchers in clinical trials, and are further expounded upon with methods for adjusting the overall statistical significance when more than one endpoint (or secondary endpoints that are not directly related to the primary endpoint) are tested (D’Agostino, 2000).

Another potential dilemma that is often attributed to mis specification, or not clearly defined, primary and secondary variables within a trial study is subset analysis. Subset analysis is when analysis is performed on subsets of the data within a study trial. For example, a trial is conducted to look at efficacy of a new drug but an analysis is also done on only those patients that are below a certain age. If the protocol did not specifically address this analysis then it is possible that the study does not have adequate power to detect a difference; further, this practice also brings us back to the multiplicity problem. Both of these examples, multiplicity and subset analysis, highlight the theoretical considerations that must be taken into account to decide what data should be collected, and what study questions should be asked to ensure the scientific validity of the study.

Hints for Ensuring Collected Variables are Appropriate for Your Study Question

Given the previously described rationale, the next question is, how do we guarantee we are collecting the proper (and important) data for our study? The suggestions given below are not exhaustive, but might help in the determination of data elements, as well as co-ordinating protocols for research studies.

Outlining the tables that you are planning to use to demonstrate the projected outcome of your study is a great way to evaluate the data being collected. Not only can missing variables be identified in this way, but these can be used to focus the specific aims (or research questions) as well as assist in the descriptions of potential papers that will be submitted on the research. Statistical Analysis Plans (SAPs) generally include such tables because they help demonstrate the analyses that will be used to answer specific research question, and demonstrate how data that will be collected are to be used. A useful guide to laying out these tables can be found in The Consolidated Standards of Reporting Trials (CONSORT). These guidelines encompass various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of RCTs.

Another useful approach for guarding against collecting too much, or not enough, data is the use of pilot testing. Creating a data collection tool and conducting a small pilot study can be useful in pointing out potential problems and extraneous information. The use of pilot studies is especially useful in multi-site trials, where data definitions can be different across institutions. Even for single site studies, pilot testing outside of your institution can be a useful way to discover potential data collection, problems, and a way to define important data elements that will answer your research questions.

Good study design and planning are essential in clinical research of any kind. By collecting the most parsimonious set of variables to answer a well-defined research question(s) the study protocol will be strengthened and trial conduct will be simplified. Additionally, cost of the trial and time to generate manuscripts can be reduced when appropriate planning is done before the research begins. A well-thought out research study will be more convincing both for funding agencies as well as colleagues who will benefit from our research.

References


PECARN Listserv
The EMSC National Resource Center launched the PECARN “Listserv” in April. Each monthly listserv message covers a topic relevant to the network, funding notices and other news of interest. Topics covered include bio-banking repositories and a series on translational research. To receive the Listserv messages, e-mail pecarn@emscnrc.com with SUBSCRIBE as the subject and your name, e-mail address, phone number, job title and your institution in the body of the message. Suggestions for topics can also be sent to the same e-mail address using “TOPIC” as a subject.

New Targeted Issue Grants Awarded
Targeted Issue (TI) grants are intended to address specific needs or concerns in EMSC that typically result in a new product, resource or demonstrate the effectiveness of a model system component or service of national value. Nine new TI grants were awarded starting in Fiscal Year 2007 including two PECARN studies: Quality Performance Measures for Pediatric Emergency Care and Diagnostic Signatures in Febrile Infants. A fact sheet for the new TI grants is available from the NRC.

Federal Legislative Update
Fiscal Year 2008 (FY08) Funding
In June the Senate Appropriations Committee considered the FY08 Labor-Health and Human Services-Education appropriations bill. The committee recommended an appropriation of $20 million for the EMSC Program, the Senate has yet to act on this bill.

In July, the House Appropriations Committee considered its version of the FY08 Labor-Health and Human Services-Education appropriations bill (HR 3043). The committee recommended an appropriation of $19.8 million for the EMSC Program. The House of Representatives also considered HR 3043 and approved an amendment to the bill offered by Congressman Dave Reichert (WA) to increase funding by $2.5 million. HR 3043 was passed by a vote of 276 to 140; therefore, as approved by the House, $22.3 million would be provided for the EMSC Program in FY08.

EMSC Reauthorization
Legislation to reauthorize the EMSC Program was introduced in both the House of Representatives and Senate earlier this year. The Wakefield Act was introduced in the Senate by Senator Daniel K Inouye (HI) and in the House by Representative Jim Matheson (UT). Currently, the Senate version of the bill, S 60, has 7 cosponsors while the House version of the bill, HR 2464, has 24 cosponsors. To date, neither the House nor the Senate has acted on their respective version of the legislation.

2007 Annual EMSC Grantee Meeting Highlights
The NRC hosted its annual grantees meeting in June in Silver Spring, Maryland with over 200 attendees. Updates were provided on Targeted Issue grants by principal investigators Drs. David Jaffe, Brian Johnston, Lee Pyles and Robert Sapien. PECARN members participated throughout the meeting. Four PECARN posters were presented the first day. Drs. Nate Kuppermann and Ron Maio represented PECARN by presenting “But I Have a Great Idea: Integrating Priorities and Personal Passions in EMSC Research.” Also, a thank you to Helena Rincon, Mike Tunik and Sally Jo Zuspan for moderating sessions.

EMSC Website Offers a New “Toolbox” - Facility Categorization
The NRC will release a new “toolbox” on Facility Categorization this Fall on the EMSC program website, http://mchb.hrsa.gov/emsc.

National Meetings
AAP National Conference & Exhibition
October 27-30, 2007, San Francisco, CA
www.aap.org/nce

NASEMSO Annual Meeting
Oct 28-Nov 2, 2007, Minneapolis, MN
www.nasemso.org/Meetings/Annual/

135th APHA Annual Meeting
November 3-7, Washington, DC
www.apha.org/meetings

2008 NAEMSP Annual Meeting
January 10-12, 2008, Phoenix, AZ
www.naemsp.org

The new federal Grant Manager Specialist at HRSA for the NDDP and the CDMCC cooperative agreements is Mr. Jose Aviles. (See contact information below).
PECARN Study UPDATE

C-Spine Injury in Children

Case-control analysis: We have completed 95% of the abstraction needed to meet our sample size of 550 cases and their associated controls. More than 3000 queries have been sent and 90% have been resolved. Several sites will undergo a systematic review of the coding of substantial injuries during September. We anticipate data cleaning and the preliminary analysis to be complete by December 1st with a goal of presenting the findings during the spring academic meetings.

EMS Focus Groups: This aspect of the study aims to use focused interview and focus group methodology to identify the barriers and facilitators to EMS participation in research aimed at limiting immobilization to those children who are at non-negligible risk for c-spine injury. We have undergone IRB review and approval at Washington University and the first focus groups are being conducted in St. Louis.

Diagnostic Grouping System

The investigative group has worked with the CDMCC to make the Diagnosis Grouping System available to researchers and others interested in grouping diagnosis codes. Both an Excel and a SAS program have been created that will report 4 different groupings for ICD-9 codes entered into the programs. Three groupings are related to the DGS and one is related to the Severity Classification System. These groupings are also available in the cubes of the PCDP. The Excel and SAS programs are being tested now for clarity and ease of use. Please let us know if you are interested in testing either version of the grouper. We anticipate the programs will be available later this fall on the PECARN website. The Severity Classification System was presented as a platform presentation in the Health Services Research Session II at the Pediatric Academic Societies meeting in Toronto in May of this year.

Bronchiolitis Study

The results of the Bronchiolitis study were published as the leading article in the New England Journal of Medicine on July 26, 2007. The article has generated a substantial amount of media coverage in the Utah and Sacramento markets. The study was also picked up by PR Newswire and HealthNewsDigest.com.

Traumatic Brain Injury

TBI patient enrollment ended in September, 2006 after successful enrollment of 34,000 patients for the derivation phase of the study and an additional 9,000 patients for the validation phase. Data cleaning and query resolution are in their final phases for the main analysis; sites should expect to receive a query of physician certifications shortly.

The study PIs continue to travel frequently to the CDMCC for data cleaning, analysis and preparation for subsequent subanalyses. Two abstracts were presented at the PAS and SAEM meetings - one abstract on the epidemiology of TBI in PECARN and another on the inter-rater reliability of variables for the decision rule. We look forward to completion of data analysis for the decision rule, and drafting of the main manuscript by then end of the summer. Several other manuscripts are being prepared, and we hope to have several presentations at the 2008 PAS/SAEM meetings.

Prehospital Working Group

Sixteen of the original EMS surveys were collected and analyzed. Two additional surveys were submitted. There are three outstanding surveys that are currently being completed. Dr. Kathy Brown is facilitating the completion of Hopkins and Holy Cross’ surveys while Dr. Ellen Crain is working to complete the survey at Jacobi, the newest HEDA site. Once the remaining surveys are complete, the data will be cleaned and reanalyzed. We expect to reanalyze the data in September and then work on writing up the results.

Intra-abdominal Injury

Data collection began in May 2007, and all participating sites are enrolling patients. As of early August, more than 950 subjects have been enrolled. We will continue enrollment for approximately 24 total months.

Thank you to all sites for your outstanding responsiveness in preparing for the study start and for successfully initiating the study. Special thanks to those sites who have submitted site specific tools to be shared among the group.

PECARN Core Data Project

All sites have submitted 2006 data, and most have already approved their final data. Once data cleaning is complete, we will add 2006 data to the cubes and analysis tables. Currently the data cubes are in a new, more flexible format and include all available data for 2002-2005. For preliminary analysis of PCDP data, you can either use the cubes or complete a data request form. The cubes can be accessed at http://reports.pecarn.org/reportportal

Contact Andrew.demarco@hsc.utah.edu to obtain or reset your cube login and password. The data request form can be found at https://www.ndercssl.org/eRoom/NDDP/PECARNCoreDataProject/0_a670. For any questions, please contact Libby Alpern at: Al-
PECARN Study UPDATE

Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA)

The Hypothermia investigative team will be having a conference call with a group from the NHLBI on September 20, 2007 to discuss the future RCT. A study overview and study budget will be submitted to the NHLBI prior to November 15, 2007. If the study concept and budget is accepted, a full R01 application will be submitted to the NIH in February 2008. This study is a collaborative effort with the Collaborative Pediatric Critical Care Research Network and other external sites.

Seizure

Eight of the ten participating sites have received formal approval from their IRBs to begin community consultation. Some have needed approval from the EMS agency’s IRB. Two of those are still waiting for approval. A total of 17 EMS agencies have joined the network. Three HEDAs in New York City have partnered with FDNY, and four HEDAs in Maryland have partnered with MIEMSS. Most partners have completed the agency survey and provided a data dictionary. The investigators have finalized the variable list for patient data and are currently developing directions for submitting data.

Patient Safety

HEDA Site PI surveys and ED department staff surveys are complete and have been submitted to the CDMCC by all participating sites. Data verification and analysis is ongoing. All sites received IRB approval for the incident reporting phase of this study and are in the process of collecting 1 month of incident reports to submit to the CDMCC.
Documenting IRB Approvals

The number of PECARN projects that require documentation of IRB approval has continued to increase in both volume and complexity. New IRB submissions must be documented and older projects often require ongoing renewals that extend past enrollment and analysis. IRBs often change their requirements from year to year and this can cause confusion from both the site and data center perspective.

Electronic IRBs can eliminate problems with paper copies, but new problems have emerged as a result of electronic submission and approvals. We have experienced a variety of issues that can cause delays in posting and documenting approval, or can cause confusion in determining if an IRB has actually given approval to a project. Below I have listed some recommendations to make the documentation of IRB approval easier.

### Don’ts:
- Don’t send an email with a link that the data center cannot access.
- Don’t send a full IRB submission, we only need the IRB approval.
- Don’t send an approval without the hospital name.
- Don’t send an approval by an ED or internal review board.
- Don’t send an approval without an expiration date.
- Don’t send an approval without the study name.
- Don’t send documents that list a deadline instead of an expiration date.
- Don’t send a document stating the intention of the IRB (to expedite, exempt, etc) we only need the final approval.
- Don’t send a continuation letter without an expiration date or other details.
- Don’t send IRB communication stating the status of your application if not actually approved.
- Don’t send an email from the IRB, site PI or RA promising approval will come very soon.
- Don’t send a letter from the IRB chair congratulating you on the approval, then listing outstanding conditions.

### Do’s:
- Do send an approval that contains a clear statement that the study is approved by the IRB.
- Do send an approval with an approval date.
- Do include an expiration date.
- Do reference an approval that has the complete protocol name.
- Do include the protocol version number and date.
- Do send an approval that has the hospital’s name.

### Documenting Submission Dates

The report card now scores sites based on submission of a new IRB protocol within a specified time limit. CDMCC records the submission date for each site. It is important that the date of submission be documented in the most official way possible. IRB submission dates for new protocols can be documented in the following ways:

* Email or letter from IRB personnel documenting the date the submission was received.
* Stamped copy of protocol submission document (submit only the page with the receipt stamp and the name of the protocol).
* Electronic notification indicating the date the protocol was submitted.

### Making It Clear

It is important that you do not send us your approval in pieces or strings of emails, as often these emails and faxes do not refer to the protocol and they can in no way be linked to an actual protocol. Pasted emails or documents cut off by printing will not do either.

Remember, it is the responsibility of the PI to review IRB approvals and add the necessary required information before the current approval expires. We understand that each IRB works differently, but please remember that the PI can clarify in writing what the IRB is issuing. A sample copy of the IRB approval clarification letter can be found at: https://www.nedarcssi.org/eRoom/NDDP/CDMCC/0_1533a
I have been a statistician with the Intermountain Injury Control Research Center (IICRC) since March 2006. I have been involved in several collaborative PECARN research projects including the Bronchiolitis study, TBI, PCDP, and Psych working group. My expertise is in the manipulation of large data sets, statistical programming, multivariate statistics and survival analysis. Prior to joining PECARN, I worked as a Research Assistant and Biostatistician at the Myeloma Institute for Research and Therapy at the University of Arkansas. I worked with clinical investigators on all aspects of study design. I served as sub-investigator for a Myeloma Institute protocol, and co-authored several peer-reviewed publications.

Before I came to the U.S. to join my husband, I worked as an Orthopedist back in Beijing, China. I received my Master’s degree in Statistics from the Mississippi State University in 2003. To me, working with PECARN has been a great experience as I can use both my clinical experience and statistical knowledge to contribute to the well-being of patients. I have a lovely daughter, Catherine, and she will turn one year old in October. My husband and I really enjoy being parents.
**New Faces**

**ACORN**

Clara Ramirez is our new Intra-Abdominal Injury (IAI) study coordinator at UC Davis. Clara has worked for several years on the Sacramento Area Latino Study on Aging (SALSA)- a study tracking the incidence of physical and cognitive impairment, as well as dementia and cardiovascular disease, in elderly Latinos in the Sacramento region.

Rosemarie (Rosie) Molinaro, new UC Davis PECARN Coordinator. Rosie comes to us from the pharmaceutical company Genentech, where she has coordinated multiple sites in various pharmaceutical trials over the past seven years.

**CARN**

Emily Mulvey, RA, CARN

I am the new coordinator for the seizure study at CNMC. Yay Me! My husband Matt and I just moved here from North Carolina with our two dogs, Bodie and Kiya. However, I am an original Californian and I miss it dearly. My BA is from UC Santa Barbara in Film and French. Oo La La! And my MA from CSU Long Beach is going to be in Research Psychology if I can just get my thesis completed. I am studying the personal and situational factors that may aid military spouses in coping with deployment. Oh ya, my husband is a Marine and we are training for the Marine Corps Marathon. It will be my first and hopefully not my last. I look forward to working with the PECARN team on such a fascinating study.

**CDMCC**

Heather Gramse, BA, CDMCC Study Coordinator

I am the new Study Coordinator for the Patient Safety study and the upcoming Biosignatures study here at the CDMCC. I received my Bachelor’s of Science degree from Utah State University in beautiful Logan, Utah. I am a newlywed, living just outside of Salt Lake City with my husband, Craig. I am not new to the IICRC. I briefly worked in the PECARN network developing the eRoom IRB tracking system. I returned to the IICRC about a year later to work part-time on a study that is evaluating the effectiveness of the shaken baby prevention program in Utah. Now full-time in PECARN, I am enjoying working, being married and occasionally going camping in the great outdoors.

Bonnie LaFleur, Ph.D., MPH, CDMCC Statistician

Bonnie hails most recently from the department of biostatistics at Vanderbilt University. She received a Ph.D. in Biometrics from the University of Colorado Health Sciences Center in August of 1999 and a MPH in biometry from San Diego State University in 1996. She has over fourteen years of experience in biostatistical consulting. She has spent the last 7 years in collaboration with researchers in the development and the application of statistics to biologic data (specifically in the areas of genomics, cancer biology and developmental and cell biology), as well as enjoying the continuation of involvement with clinical research.

Cody Olsen, MS, CDMCC Statistician

Cody began working as a statistical analyst for the CDMCC at the University of Utah in April. He is currently working with the C-spine and Patient Safety studies. Cody recently graduated from Oregon State University with an M.S. in Statistics. He and his wife are originally from Utah; their son Parker was born in Corvallis, Oregon.

**Nodal News**

**ACORN**

We would like to congratulate Halim Hennes and Evie Alessandrini who both recently received EMSC TIG awards- Halim for the prehospital pain management study and Evie for her study of quality measures. Congratulations also to Duke Wagner, research coordinator at Medical College of Wisconsin, who successfully earned his CCRC certification this quarter.

**GLEMSCRN**

Congratulations to Dr. Alex Rogers in his promotion to Assistant Professor at the University of Michigan effective 9/1/07.

Publications:

**Stanley RM.** Teach SJ, Mann NC, Alpern ER, Gerardi MJ, Mahajan PV, Chamberlain JM. Variation in Ancillary Testing among Pediatric Asthma Patients Seen in Emergency Departments. Acad Emerg Med. 2007 Apr 19; [Epub ahead of print]