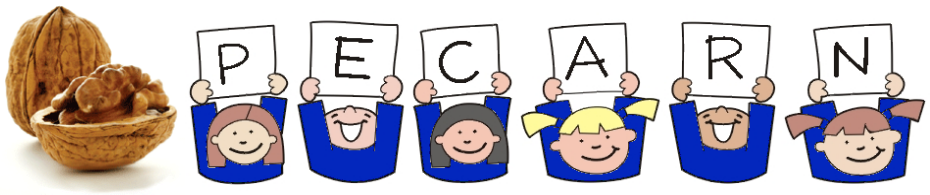
PECARN Newsletter

Winter 2010



In a nutshell

What's Inside?

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SALE: Buy One, Get One Free!

"What if I told you that we can sometimes do two trials for the price of one?"

Submitted by Charlie Casper, PhD (CDMCC)

Randomized clinical trials can be staggeringly expensive. What if I told you that we can sometimes do two trials for the price of one? Sounds too good to be true. However, this is the idea behind a factorial design. I am going to discuss the advantages and disadvantages of using a factorial design in randomized trials. I will use the simple and common two-by-two factorial design as an example throughout.

Suppose we wish to test the effects of two different drugs for pain. One is a pill and one is a liquid. We will randomize each study subject into one of four groups: sugar pill and water, active pill and water, active liquid and sugar pill, or both active pill and liquid. We will allocate approximately 25% of randomized subjects to each group. There are three scientific questions that are of primary interest. Does the pain pill have an effect on the primary outcome? Does the liquid have an effect on the primary outcome? Is the effect of the pill modified by the liquid (or vice versa)?

The third question deals with what is called an interaction. For example, suppose that the pill, by itself, decreases pain by 2 points on some scale. Suppose, further, that the same is true of the liquid. We might expect that pill and liquid together would decrease pain by 4 points. This may not be true. The combination of treatments might result in a 6-point decrease. This would be called a "synergistic" interaction. On the other hand, what if the pain score actually *increases* when the two are combined? This is sometimes called a "crossover" interaction. Another, less extreme, example occurs when there is little or no additional benefit in using both over just one or the other. For example, the combination of both treatments could result in a 2-point decrease. A possible explanation for this interaction is that both drugs work on the same pain receptor. Once either one of them has done its job, the other does nothing further.

Continued on page 2…

Next PECARN meeting: April 13 - 14, 2010 in San Antonio, TX Mark your calendars

Supported by Grant U03MC00008, Maternal and Child Health Bureau, Health Resources and Services Administration, Department of Health and Human Services

Continued from page 1 -"SALE: Buy One, Get One Free!" ...

At first glance, one may assume that, if there is an interaction, we need to perform some fancy statistical analysis to test the overall effect of the pill (or the liquid). On the contrary, we can actually ignore the interaction and the liquid entirely and perform a statistical test of the pill's effect as if we had a simple, two-arm trial. Why? Well, we can just think of the liquid as a potential effect modifier or risk factor, like age or duration of pain. These are always present in clinical trials and rarely accounted for in the primary analysis because randomization makes the groups equal (statistically, that is).

Although the usual statistical test for treatment effect is still valid in the presence of an interaction, some power can be lost. In other words, the chance of actually showing the treatment works can be diminished. Unless the interaction is huge, however, power loss will be very small. Power is also lost when the alpha level is adjusted. For example, if there is one hypothesis being tested we usually declare significance when the resulting p-value is less than .05. If we are testing each of the two treatment effects and wish to maintain an overall alpha of .05, we could use a correction and test each with an alpha of .025. This will result in a loss of power and a need for a greater number of subjects. There are also statistical tests for interaction. However, these have much lower power than the tests for the main treatment effects. The sample size required to detect an interaction can be over four times that required for main effects. This means that if we power a factorial-design study to see an interaction, we may be getting one study for the price of four or five, rather than two studies for the price of one. I prefer the original deal.

Two examples of factorial designs that are relevant to PECARN come to mind. One is the Pediatric Emergency Research Canada (PERC) CanBEST trial. In this trial there was some evidence (though not statistically significant) of a synergistic interaction between epinephrine and dexamethasone for the treatment of bronchiolitis. PECARN and PERC investigators are currently planning a new trial to verify this. The other example is a trial that has been approved in PECARN looking at fluid therapy in Pediatric Diabetic Ketoacidosis (DKA). This study has a factorial design in which subjects will be randomized to four groups that are defined by two rates of administration and two levels of sodium content of intravenous fluids.

Before designing a trial as a factorial, one should consider many possible scenarios. The presence of an interaction may change the interpretation of the results, create the need for further study, and decrease statistical power. However, in many cases, what is lost in power is minimal compared to what is gained by essentially doing two trials at once.

***Dr. Casper** is Assistant Professor of Pediatrics and biostatistician for the Data Coordinating Center at the University of Utah. He is currently involved in the design, implementation, and analysis of clinical trials and other projects for PECARN.*

Research Coordinator of the Year Award

As PECARN approaches its 9th year, it seems an appropriate time to institute a formal process for recognizing some of the most important members of PECARN – the site Research Coordinators (RCs). Without the hard work of the RCs, PECARN could not function. To honor their commitment and contribution to the success of our network, we would like to introduce the first annual PECARN Research Coordinator of the Year Award. The RC award will be presented at the January PECARN meeting in San Francisco.

NRC Welcomes New Program Associate, Kelly Johnson

The National Resource Center is pleased to announce its new program associate, Kelly Johnson. Kelly graduated Phi Beta Kappa from the University of Virginia in May of 2008, with degrees in English and Spanish as well as a specialization in pre-med. She has spent the past year working in the fields of public health, healthcare policy, and disaster preparedness with the US Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response in the Emergency Care Coordination Center (ECCC). In the future she plans to study pediatrics as a dual MD/MPH candidate. Kelly can be reached via email at **KyJohnso@cnmc.org** or at (202) 476-6840.

The EMSC National Resource Center Welcomes New Director

Ian Weston has more than 10 years of EMS experience and six years of experience in the health policy arena. Ian has been a volunteer firefighter and EMT for the Manhasset-Lakeville Fire Department in Long Island, NY, since 1999 and also serves with the Falls Church Volunteer Fire Department in Arlington, VA.

Most recently, Ian served as the senior director of government affairs and policy and chief financial officer at Jeffrey J. Kimbell and Associates, a health care/life sciences policy firm. In this capacity, Ian was responsible for developing legislative strategies and advising clients on health-related congressional legislation and activities. Prior to that, Ian served as a health policy advisor to U.S. Congressman John Sweeney (R-NY).

Ian holds a Masters Degree in Public Policy (Global Medical and Health Policy) from George Mason University in Virginia and received his Bachelor of Arts in Public Policy and Political Science from Syracuse University in New York.

At the NRC, Ian will lead the State Partnership Technical Assistance Team. Ian can be reached via e-mail at **iweston@cnmc.org** or via phone at (202) 476-6890.

EMSC Legislative Update:

On November 7, 2009, the House of Representatives passed their version of health care reform legislation, H.R. 3962, the Affordable Health Care for America Act. The Senate followed suit and passed their version of such legislation, H.R. 3590, the Patient Protection and Affordable Care Act, on December 24, 2009. The House and Senate will have to work out the differences between the legislation and vote on a final, compromise bill before health care reform can become law.

EMSC Appropriations: Although fiscal year (FY) 2010 began on October 1, 2009, Congress did not pass all of the FY 2010 appropriations bills before the start of the year. Therefore, in December 2009 Congress released the FY 2010 Consolidated Appropriations Act (H.R. 3288), which combines several different funding measures, including the Departments of Labor, Health and Human Services, and Education appropriations bill, into one. The bill includes $21.5 million for the EMSC Program. This is a $1.5 million increase over the fiscal year 2009 funding level.

On December 10, the House of Representatives approved H.R. 3288 by a vote of 221-202, and on December 13, the Senate passed the bill by a vote of 57-35. The President signed the measure into law on December 16.

EMSC Reauthorization: In January 2009, Congressman Jim Matheson (D-UT) introduced HR 479, the Wakefield Act, to reauthorize the EMSC Program for five years, from FY 2010 through FY 2014. In March of the same year, the House of Representatives passed HR 479 by a vote of 390-6. In February 2009, Senator Daniel Inouye (D-HI) introduced the Wakefield Act, S 408, in the Senate. Both bills authorize a funding level for the EMSC Program starting at $25 million in FY 2010 and ending at approximately $30.5 million in FY 2014.

In addition, on December 24, 2009, the Senate passed H.R. 3590, the Patient Protection and Affordable Care Act, by a vote of 60-39. The bill, which is the Senate's version of health care reform legislation, includes a provision to reauthorize the EMSC Program. As of press time, next the House of Representatives and the Senate will have to reconcile the differences between their respective versions of health care reform legislation and vote on a final, compromise bill.

EMSC Targeted Issues Grants:

The EMSC Program is seeking approval for a FY10 competition that would fund 4 new Targeted Issues grants. The award amount would be $300,000 a year for 3 years for each grant. The project start dates are anticipated to be September 1, 2010. For Further information please contact Dan Kavanaugh at **dkavanaugh@hrsa.gov** or 301-443-1321.

Recent EMSC Related Articles:

TI Grantee Joel Fein, MD – whose article "Patients' and Caregivers' Beliefs About Depression Screening and Referral in the Emergency Department" appeared in the November 2009 issue of *Pediatric Emergency Care* (Vol.25, Issue 11) – examined patient and caregiver beliefs about the acceptability of universal depression screening in the emergency department, and their perception of barriers to referrals following a positive screen.

An article in the *Annals of Emergency Medicine* (Vol.54, Issue 2), titled "A Statewide Model Program to Improve Emergency Department Readiness for Pediatric Care," reviews the Illinois EMSC's facility recognition program that may serve as a model to meet one of HRSA's performance measures for federal EMSC Program grantees.

The July 12 edition of *USA Today* featured the article "Your Health: Being Open Can Be Critical to Help Injured Children Heal." The article features the work of TI Grantees Nancy Kassam-Adams and Flaura Winston, MD, PhD, and their recently completed project "Evidence-based Secondary Prevention of Traumatic Stress: Practical Tools to Help Parents Help Their Children. "

Biosignatures Study

The second year of enrollment in the Biosignatures study ended on December 31, 2009 with over 850 samples collected during 2009. Year 3 enrollment began on January 1, 2010 and will continue through December 2010. A minor protocol amendment was disseminated and sites are in the process of obtaining IRB approval. A training was held in conjunction with the January PECARN Steering Committee Meeting in San Francisco.

C-Spine Injury (CSI) in Children

Case-control analysis: We have completed abstraction and eligibility verification for 540 cases and 2,774 controls. Two secondary analyses were presented at AAP: Presentation for Utility of Plain Films in the Diagnosis of CSI in Children, and a poster for Spine Immobilization Among Children Less than 2. The former analysis won the award for Overall Best Paper Presentation in Pediatric Emergency Medicine. Abstracts were submitted to the 2010 PAS and SAEM meetings: EMS care and CSI outcomes; AARS: Incidence, Associated mechanisms, Associated Clinical findings; and Sports -related CSI: A Description of Mechanism and Injury Patterns. The main manuscript which presents the results of the case-control analysis is currently under review.

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 to limit immobilization to children who are at non-negligible risk for C-spine Injury. Focus groups and focused interviews with all echelons of EMS leadership were completed in St. Louis, Milwaukee, Salt Lake City, Buffalo, Rochester, DC and Baltimore. All transcripts were reviewed and comments were categorized into topics such as qualities, beliefs, barriers, motivators and suggestions. We are currently reviewing these categorizations and writing the manuscript.

IAF Appendix Study

The IAF-Appendix study aims to examine the role of intra-abdominal fat in CT imaging with IV contrast in visualizing the appendix and to determine if it is possible to predict which patients will have adequate intra-abdominal fat (and so forgo oral contrast).

This study has begun across 16 participating sites. Patient screening for eligibility should be completed shortly. All sites are anticipated to move onto the Radiologist Abstraction Phase by the end of December 2009, and study completion is projected for early 2010.

IAI

The Intra-abdominal Injury (IAI) study was funded by the Centers for Disease Control (CDC) in October 2006. The goal is to develop a clinical decision instrument to determine the indications for abdominal CT use in children with blunt torso trauma.

Patient enrollment began on May 21, 2007 and ended on January 8, 2010! We enrolled over 12,000 patients with a capture rate of 81.3%. This includes over 770 patients with IAI. Data review is on-going and the CDMCC continues to generate queries to ensure top data quality. Please continue to work on data entry and query resolution as we wrap up the study. Great work, everyone!

Patient Safety and New York State Patient Safety

We have been making great progress in the chart review upload for the NY Patient Safety study. As of January 11, 2010, an impressive 1149 eligible charts have been uploaded for review into the eRoom. We are now 8 months into the study. The overall goal is 3285 charts over 12 months. This breaks down to 1095 charts per site. We are 35% of the way to our goal. We are 88% complete on incident report reviews and expect to have 100% completion before the PECARN meeting in San Francisco.

PECARN Core Data Project

Please plan for 2009 PCDP data to be submitted to the CDMCC by April 1, 2010. We will be happy to help in any way to streamline the submission process. Reports for data validity checks will be generated after data submission. Please review your site's report in a timely fashion.

All locked PCDP Data for 2002 – 2008 are now available in the cubes. For preliminary analysis of PCDP data, you can use the cubes or complete a data request form (found in the PCDP eRoom). The cubes can be accessed at https://www.utahdcc.org/reportportal. Contact **andrew.demarco@hsc.utah.edu** to obtain or reset your cube login and password.

For any questions, please contact Libby Alpern at **alpern@email.chop.edu.**

PECARN

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

Performance Measures

Our performance measures work continues into the new year on many fronts. A survey to EMSC stakeholders was administered in December of 2009 and analysis is ongoing. Another survey, assessing the data availability for measures is planned for early in 2010. These results will be integrated into the final project deliverables over the next 8 months.

Pre-hospital Infrastructure

We have collected data for 521,239 runs from fourteen EMS agencies for the years of 2004-2006. Data submission ended on April 17, 2009 and all questions with the agencies regarding their data have been completed. Since that time work has continued on preparing the data for analysis. These fourteen submitted data sets consist of varying size, amount of missing data, and format. Twenty-two EMS agencies ultimately participated in the study, with eight unable to submit data.

Seizure

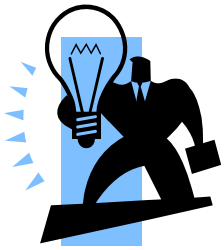
The Pediatric Seizure study (officially titled The Use of Lorazepam for Pediatric Status Epilepticus: A Randomized, Double-Blinded Trial of Lorazepam and Diazepam) is currently ongoing with 9 of the 11 participating sites actively enrolling. Children's Hospital Dallas has a site initiation visit scheduled for early February and Children's Boston is awaiting final IRB approval; both sites are set to begin enrolling shortly. With a total of 54 patients enrolled, we have now met 22% of our projected enrollment numbers.

TBI

The TBI project continues to move ahead at a brisk pace. Ten TBI abstracts were presented at the 2008 and 2009 PAS, SAEM, and AAP meetings, and four more were submitted for the 2010 PAS/SAEM meetings. This brings the total to 17 completed and submitted abstracts, on top of 3 published manuscripts. As you know, the main Prediction Rule manuscript was recently published in *The Lancet*, one of the highest impact factor journals in the world! We are finalizing and submitting 4-6 sub-study manuscripts in the coming months and are currently working on approximately 10 more manuscripts / TBI sub-studies. We hope to have all sub-studies submitted for publication over the next 1-2 years. The next TBI projects being prepared are: 1) knowledge translation of the prediction rule, and 2) progesterone for serious TBI!

Good Clinical Practice Tip:

Q: Can a monitor review photocopies of medical records, also called "shadow charts", instead of the originals?



A: As a general rule, site monitors should always review original medical records – for example; actual physician's office notes, clinic notes and hospital medical records. Monitors often ask site staff to photocopy original records for their review. Unfortunately, this request has been made for the convenience of the monitor – either the monitor does not want to spend the time reviewing the medical records or is not able to navigate through the documentation to find pertinent data. A fundamental problem in relying on photocopies is that the monitor cannot be certain that the documentation is complete. That is, data may have been advertently or inadvertently deleted from pages (e.g., in the margins or on the back page of the original record). In addition, there may be data in other parts of the record, however small, that may not have been photocopied. When a specific original record cannot be made available, a certified copy of the original record may be used. A record is considered "certified" when a qualified individual attests that the copies are accurate and complete.

Submitted by Kym Call, BA, CCRP
CDMCC Clinical Research Coordinator

THAPCA

The Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA) Trials began enrollment on September 1, 2009. The study has screened 257 total subjects; 31 were eligible but not randomized for various reasons and 17 have been randomized and enrolled into the trial. The protocol has been amended since September to allow co-enrollment with other interventional studies. A second amendment is pending that would remove the exclusion criterion that disqualifies a subject if they have multiple arrests prior to randomization. Starting in January, all sites will be trained on the use of OpenClinica, the new electronic data capture system being used by the DCC which should make data collection and query resolution more efficient. Thanks to all the THAPCA sites for their hard work and commitment to this important trial!

New Faces to PECARN

ACORN would like to welcome our new UCD HEDA Research Coordinator, **Kyle Pimenta.** Kyle completed dual Bachelor's degrees at UCD in Biochemistry and Philosophy in 2005. He then worked briefly for a private site monitoring company and for several years at the UC San Diego Antiviral Research Center. Among his many and varied interests (we'll let him tell you about these), Kyle is an avid futbol player. Please extend Kyle a warm PECARN welcome.

CDMCC congratulates **Alecia Peterson** - who recently married William Heaton on **December 7, 2009.** They eloped in Las Vegas.

Julie Smith graduated from Saint Joseph's University in 2008 with a B.S. in Sociology and Spanish. She worked on secondhand smoke research before joining the **CARN** team. She will be working on whatever projects are thrown her way at CNMC. When she isn't at work, she is hanging out with friends and family, and planning her wedding for this August.

Julie & Samira

Samira Shahzeidi recently joined the **CARN** team as a research assistant working simultaneously on a variety of studies at CNMC. She graduated from Northeastern University with a B.S. in Behavioral Neuroscience this summer, and has since moved back to the Washington D.C. area where she is originally from. She is eager to be getting more exposure in a hospital setting before applying to medical school. In her free time, she enjoys her life everyday, being a firm believer of 'work hard play hard'. Her three favorite things are food, travel, and family.

PEDNET welcomes **Genie Roosevelt** MD, MPH who is an Associate Professor and the PEM Fellowship Director at The Children's Hospital, Denver/ University of Colorado. She recently became the Site PI for Biosignatures.

New Jr. Faces to PECARN

CDMCC congratulates Heather Gramse and her husband, Craig. They welcomed a baby girl on November 11, 2009. Her name is **Sadie Muse Ella Gramse,** she was 7 lbs 4 oz, and 20.5" long.

PEDNET congratulates Brooke Lerner on the birth of her son **Lucas**, who was born June 25, 2009.

Cianna Azul Kuppermann Born in Peten, Guatemala on August 21, 2007. Cianna arrived at her "forever home" with the Kuppermann Family on June 6, 2009.

Nodal News

ACORN

Emily Kim completed a half Marathon in November 2009. We would publish her time, but don't want to scoop Runner's World! Congratulations, Emily!

PEDNET:

We would like to congratulate Sara Deakyne on her academic promotion. She received her MPH in May 2009, and was promoted to Instructor/ Research Coordinator in the Section of Emergency Medicine/Department of Pediatrics at the University of Colorado School of Medicine.

This newsletter was compiled by Heidi Niitsuma, Executive Secretary of the CDMCC