

## APEX Study Design Refined

Following three conference calls with a panel of experts, the subcommittee for the Achievement of Perinatal Excellence (APEX) study identified five outcomes that will be used in assessing the quality of obstetrical care at participating hospitals in the Network: uterine hemorrhage, infection, thromboembolism, maternal third and fourth degree tears, and term neonatal trauma and HIE.



Study PIs, Drs. Grobman, and Bailit have been working closely with the BCC to revise the protocol to reflect the corresponding statistical considerations and analysis plans for determining outcome rates across designated hospitals and patient characteristics and process measures associated with the risk of each outcome. Meeting at the BCC in June, the study PIs and BCC staff delineated a list of variables to capture the data

required for these measurements. Data forms are being designed to be as streamlined and functional as possible, keeping in mind the accessibility of data in hospital charts.

Because the amount of data collected will be immense, several options are being considered that will decrease the quantity of data but still give a statistically accurate portrayal of patient characteristics and care. The APEX subcommittee will discuss these at their July meeting and at the steering committee meeting. The study design still includes a pilot study, during which data related to these measures will be abstracted from charts for one month of 25% of all eligible deliveries in designated hospitals (about 2500 patients). In addition, hospital characteristics, such as volume of deliveries by day and shift, nurse-to-patient ratio by shift, whether or not there is a hemorrhage protocol and location of septic workups for infants will be collected. These data then will be analyzed to assess their adequacy to

measure quality of care, and, if required, revisions to the data collection tool will be made before the study officially starts.

The BCC is developing a web-based data entry system, that will allow data to be entered from multiple computers at the centers. Nurses will be allowed to abstract data straight from the medical chart into the web system without first completing data forms. However, those who prefer to complete data forms prior to data entry may still do so. The processing of data will be similar to the current system, utilizing concurrent on-line data editing as data is entered, with further editing and auditing done at the BCC after the data is uploaded onto its mainframe. It is anticipated that this web data entry system will be the start of web entry for future studies.



## News from the Publications Committee

For the first time in the Network's history, two manuscripts resulting from analyses done for the same annual meeting of the Society for Maternal-Fetal Medicine have been accepted for publication by the *New England Journal of Medicine*: 1) the results from the twin cohort of the STTARS trial and 2) the results from the two-year follow-up of infants born in the repeated corticosteroids trial (BEARS). As of April of this year, four other manuscripts have been published and, as of May, another eight manuscripts have undergone revisions in the publication process.

Seventeen analysis proposals were approved by the Publications Committee earlier this spring and targeted for presentation at SMFM in 2008. Two of these will be the primary results of the BEAM and Omega-3 trials. Four of the proposals relate to the FOX trial and five others are from the STTARS trial. Analysis of some of the SMFM proposals is dependent upon the completion of laboratory assays or other analyses.

## DQ and R Committee Posts Slides

The newly formed Network Committee on Data Quality and Recruitment has been making presentations on relevant subjects at recent steering committee meetings. The power point slides from two of these presentations, *Loss to Follow-up in Randomized Trials* and *Protocol Adherence in Randomized Trials*, are posted on the internal MFMU web site, under Useful Network Information. The slides explain the importance of patient retention and reasons why protocols must be followed as designed. It is highly recommended that the nurse coordinators share these slides with their research staff.

A slide presentation on data verification (edits and audits) will be made by the Committee at the July Steering Committee meeting.



## Study Updates

### SCAN Trial

Centers are still in the process of completing their certification requirements in order to begin the SCAN trial. As of mid-June, two thirds of the Network centers had been certified to start.



One cause for the delay is that the ultrasound scans which have been submitted for certification have not been de-identified, requiring that they be sent back to the center prior to verification.

As of June 20, 129 patients had given their consent to be screened for eligibility, with seven identified with a cervical length less than 30 mm by transvaginal ultrasound. Three patients have successfully passed compliance and been randomized.

At the time that the SCAN neonatal outcome data forms were being designed, it was recognized that some of the data points commonly collected on neonates are no longer being used or have been updated and a number of procedures formerly done in the NICU are now being done in the newborn nursery. Following discussions with Dr. Rose Higgins, Project Scientist for the NICHD Neonatal Research Network, the Neonatal Baseline and NICU Summary forms are being revised and new definitions written in the manual of operations. These should be released for use shortly.

### TSH Trial

Twelve of the Network centers are certified and working on

the TSH trial. While screening is going well (over 2,100 patients in April and May, out of the anticipated 3,000 per month), randomization into both strata, hypothyroxinemia (H) and subclinical hypothyroid (S), is proceeding more rapidly than expected. As of June 20, more than 10,500 patients had been screened, with 98 patients randomized into the S stratum and 70 patients into the H stratum.

Bayley III training for the follow-up examiners will be held on October 15<sup>th</sup> at the Bolger Center in Potomac, Maryland. Dr. Sherry Eyre, Clinical Measurement Consultant at Harcourt Assessment will provide a half-day overview of the differences between the Bayley II and the Bayley III, covering all three areas of the test: cognitive, language and motor. In the afternoon, Terri Leach, the “gold standard” examiner for MFMU Network trials, will show a video demonstration of a 12-month exam and discuss techniques for conducting a successful evaluation. Throughout the day, examiners will learn specifics about the TSH trial and requirements for initial and ongoing certification.



If not already experienced with the Bayley III, all examiners should acquire the Bayley III kits and practice the exam prior to attending the training session.

### CAPPS

The CAPPS chart review teams have gained three new nurse coordinators, Allison Northen, Jo-Ann Tillinghast and Joan Moss. With their assistance, a total of four teams now

review 90 charts each month. Review members have shown their dedication in many ways, including holding calls while on vacation. Recently, Karen Dorman called in for a chart review while she was on the ferry to Martha's Vineyard! We greatly appreciate all of the time and effort that all of the review members have provided!

CAPPS recruitment continues to roll along. As of June 20, 8,803 patients have been randomized to the RCT and 1,921 also have been enrolled in the Prediction study. We are in the final stretch and urge everyone to continue recruiting patients so that we can complete the sample size of 10,000 by the end of the year.

As a reminder, on Thursday afternoon (July 12) of the next Steering Committee meeting, the CAPPS subcommittee is welcoming all interested parties to attend a meeting immediately following the main meeting to discuss markers that will be evaluated for the Prediction study.

### GDM Trial

Recruitment picked up this Spring (47 patients were randomized in May!) and, if tradition holds, should maintain momentum through the summer months. The trial has reached 92% of its sample size, with 1753 of 1900 patients enrolled.

It is anticipated that recruitment will end in mid-September. Specimen collection has also improved over the past three months, reaching 84.4% of the total expected. Overall, 78.7% of specimen samples have been collected.

## Quarterly Status Reports for Centers now Standard

Several years ago, Dr. Cathy Spong, the NICHD Project Scientist for the MFMU Network, instituted a reporting mechanism that ranks each center's performance with the others. The main categories of performance include number of patients recruited to studies and retention/completion of study procedures, protocol adherence, number of data queries, timeliness of data entry, and length of time to begin a new study.

Since centers have been part of the Network and participating in ongoing studies for varying periods of time, it has been difficult to accurately reflect rankings. However, beginning in October 2007, the performance reports will incorporate the two new centers that joined the Network in April 2006 and will use all relevant data starting as of October 2006.

Initially used infrequently, the performance data now is presented to the centers at their quarterly Steering Committee meetings. Meeting individually with the PI and Network Coordinator from three or four centers each quarter, Drs. Spong and Thom discuss reasons for how the center is ranked and how the center could improve its performance. Follow-up conference calls or site visits to assist with specific issues often are a result of these open discussions.

It is hoped that these evaluations will lead to tighter scrutiny of issues and more creative problem-solving strategies. Because many of the problems are discussed centrally, suggestions for potential solutions then are able to be shared by Drs. Spong and Thom with the other centers.

## Advisory Board Confers on Newest Approved Studies

On June 18<sup>th</sup>, the Network's Advisory Board met by conference call to discuss the scientific merit and potential impact of the two studies most recently approved by the Steering Committee: the STAN Trial and A Randomized Study Comparing Vaginal Progesterone and 17-OHPC in the Prevention of Preterm Birth.

Major issues were raised for both studies and will be discussed at the upcoming steering committee meeting. For

the STAN trial, the Board proposed making significant perinatal morbidity the primary outcome. This would require increasing the sample size and add to the cost of the trial which in itself was an issue since the machines each cost about \$38,000. The Board discussed the results of recent vaginal progesterone and whether the design of the Network's study should be an equivalence trial and even whether a placebo arm can be added. The Board members' reviews have been provided to the PIs of these two protocols.

## VBAC Calculator Available

The calculator developed by Dr. William Grobman, Alternate PI at Northwestern, to predict vaginal birth after cesarean delivery is now available on the web. The website, Perinatology.com, has posted a link, under its list of calculators, to the location on the MFMU Network's website



<http://www.bsc.gwu.edu/mfmu/vagbirth.html>. One also can just type in this address in any search engine or go straight to the MFMU Network's public website and click on VBAC Calculator.

The calculator uses the following data to give the predicted chance for vaginal birth after cesarean, along with the 95<sup>th</sup> confidence interval: age, BMI, race, whether or not the woman has had a previous vaginal delivery or a vaginal delivery since last cesarean, and whether the indication for the prior cesarean was arrest of dilation or descent.

The calculator is based on the equation published in the article, authored by Dr. Grobman and the MFMU Network, "Development of a nomogram for prediction of vaginal birth after cesarean delivery," *Obstetrics and Gynecology*, 109:806-812. The calculator is posted with the following disclaimer: "It is designed for educational use and is based on a population of women who received care at the hospitals within the MFMU Network. Responsibility for its correct application is accepted by the end user."

*Best Wishes for a Happy, Relaxing Summer with Family and Friends*

## People in the News

**Caroline Cobb**, research assistant at the BCC, is leaving her position to attend the graduate program in experimental psychology at Virginia Commonwealth University. Her special interest is in drugs and behavior and she will be doing specific research in the area of tobacco use. Thanks, Caroline, for your work on the GDM trial. We wish you the best!

A warm welcome is extended to **Bilen Getachew**, who has as been hired to replace Caroline. Bilen was born in Boston, grew up in Ethiopia, and then returned to the U.S. to attend Franklin and Marshall College where she earned a B.S. in Biology. Prior to joining the BCC, she worked at the Immune Tolerance Network in Bethesda where



she supported clinical trial data on research involving Type 1 diabetes. Previously, she worked in several organizations devoted to promoting healthcare, especially in third world countries, pursuing her passion to help people live healthier lives. These included providing logistical and program support at the American International Health Alliance in Addis Ababa, Ethiopia, and working on management initiatives and medical translation at a Clinton Foundation hospital site, also in Addis Ababa. Following college, she was an intern at the Global Health Council in Washington, DC. She plans to pursue her MPH in the near future and enjoys reading, traveling, playing basketball and volunteering.



### MFMU CALENDAR

#### Steering Committee Meetings

July 12 – 13, 2007  
 October 11 – 12, 2007  
 January 10 – 11, 2008  
 April 10 – 11, 2008  
 July 10 – 11, 2008  
 October 23- 24, 2008

#### Publications Deadlines

July 15 – SGI analysis proposals due to protocol subcommittees  
 August 3 – SMFM Abstracts due at [MFMUPROP@biostat.bsc.gwu.edu](mailto:MFMUPROP@biostat.bsc.gwu.edu)  
 August 7 – Call to review final SMFM abstracts  
 August 10 – Deadline for SMFM submission

#### Professional Meetings

January 28 – February 2, 2008, SMFM Annual Meeting, Dallas  
 March 26, 2008 – March 29, 2008 , SGI Annual Meeting, San Diego

## On the Light Side: Another Brain Teaser Contest

The first person to submit the correct answer will receive special recognition. Please submit to: [Lucy\\_L@biostat.bsc.gwu.edu](mailto:Lucy_L@biostat.bsc.gwu.edu).

On the Philadelphia to Detroit Amtrak train there are three passengers named Smith, Jones and Brown. By coincidence, the engineer, dining car operator and the conductor have the same last names as those three passengers (but not necessarily in that order).

1. Passenger Smith lives in Philadelphia
2. The conductor lives in Pittsburgh, exactly half way between Philadelphia and Detroit
3. The passenger with the same last name as the conductor lives in Detroit
4. The passenger who lives nearest to the conductor earns a monthly salary that is *exactly* three times that of the conductor
5. Passenger Jones earns \$5000 a month
6. Brown (a member of the crew) recently beat the dining car operator at billiards

What is the engineer's last name?