RESEARCH BASED EVIDENCE CLINICAL TRIALS

Marc Peters: What are the relevant outcome in PICU trails. Presentation was a summary of an editorial that was published in ICM --- please pull that. Consort statement on outcomes was reviewed. Primary outcome and power obviously linked. Mortality is front loaded in sepsis study and coupled with enrollment window may decrease available sample. Can enrich sample to decrease the signal-noise ratio. Increase target pool. Move to morbidity – alive plus something. Use a spider plot to evaluate a template of outcomes. Pragmatic design. Learn from every trial.

Martin Kneyber: Protective Lung ventilation: What do we know? What would we need to know? Martin reviewed physiological challenges in study design. Low Vt study – classic study. Issues with comparison group. Issues with heterogeneous lung (over and underinflation). Titrating TV to body weight is likely short sighted. Results of low Vt studies are inconsistent. The young may be less susceptible to volutrauma. (We wish that we were still young.) Still need to know "optimal" Vt. It may be useful for trials to focus on pressure (PIP or plateau). See Amato paper in the NEJM on driving pressure. Need better bench science.

Martha Curley: The time from idea to completion of a clinical trial is often long and extremely expensive and translation of the findings to clinical practice takes even longer. And the number of unfunded yet meritorious applications, particularly by junior investigations is concerning and often frustrating and demoralizing to our future generation of investigators. It might, thus, be time to rethink this paradigm. One such strategy is to take advantage of big data. Taking advantage of qualitative and mixed methods approaches to categorize and acceptance of alternative approaches including adaptive modeling could also be important. It is also likely that we need to unpack our traditional syndromes to achieve smarter, targeted and precise enriched designs. In addition, we need to closely follow how these approaches are working in ongoing adult trials. We also need to carefully monitor the quality of each of our clinical trials—to what might be viewed as an "industry standard." Finally, we need to network to achieve these goals and create a research agenda with maximal translation potential and work to keep research teams that have been established intact since they represent important resources.

Michael Agus: Glycemic Control: What we know and what we need to know. We have never been categorized as being too sweet. Michael review the history of endocrine research in the field. Glucose story started before Greet then Greet then NICE sugar then Chip now Half-Pint. November 8th – BIG DAY for the NEJM! Normalize an abnormal value? Devil in the details of study design. There seems to be a signal for potential benefit of glucose control but the major issue/confounder is hypoglycemia. There appears to be benefit on mortality and secondary infections in adults but this effect on infections may be age dependent with a potentially opposite effect in children. Another concern is that a number of patients in the trials did not have hyperglycemia. Need to know if it works and why it works?

Robert Tasker: Brain Injury: What do we know, what would we need to know.

Go to Mark Duffett's website for RCT is PCCM. (Critical Care2013**17**:R256). The Adapt trial now at 830 subjects. It's cool to have a British accent. Pediatric TBI hypothermia data. Difficult to make a clinical decision based on existing research. Need to think about enrichment designs and risk stratification. Abandon the RCT – clinical effectiveness research. Need a population where the outcomes are different and the "Standard" Rx are different. New series in the NEJM on various methods of CE RCT. Can you ask the questions or embed within EMR? Tea and crumpets must be protective against pediatric stroke in the UK and thus an RCT is not feasible.