

Several very thought-provoking articles offered by Dr. Robbins for our consideration. Lee’s paper used an elegant graphic display to illustrate that 55% of over 4000 recommendations made by the IDSA are based on level 3 evidence – essentially just expert opinion. Only 14% were supported by an RCT (level 1). The authors point out that guidelines can only summarize the best evidence we have – sometimes expert panels are tasked with making recommendations regarding questions for which randomized controlled trials may be logistically or ethically difficult to perform. However, this study shows that simply following guidelines cannot always be equated with providing evidence-based practice.

In a related study, Kett and colleagues suggested that adherence with IDSA guidelines for the treatment of hospital-acquired (and related pneumonias) may actually increase mortality!

Kett’s study was a multicenter retrospective cohort with 303 patients suspected at risk for multi-drug resistant pneumonia. They used a propensity model to attempt to control for variables that might bias or confound their results. A Kaplan-Meier analysis showed that survival in the group of patients treated in adherence with guidelines was significantly worse than in patients whose treatment was noncompliant - 65% vs. 79% (p<0.004). This difference persisted after adjustment for severity of illness. Non-adherence was largely due to failure to double-cover pseudomonas, and to empirically cover MRSA. Yet, once cultures and sensitivities were analysed, patients in the non-
adherent group were actually slightly more likely to have received active empirical antibiotics.

The authors contention that toxic side effects of potentially unnecessary antibiotics might explain the (huge) mortality difference doesn’t seem plausible. Antibiotic complications would have to have killed 1 out of every 7 patients in the adherence group to explain these results. It’s more likely that the retrospective study design and statistical analysis did not generate adequate internal validity to answer this complicated question.

The author’s conclusion is sound. An RCT is needed. Although we doubt that adhering to IDSA guidelines actually kills patients, these two studies taken together suggest that physician’s should not necessarily be villainized for failure to comply with guidelines that are sometimes based on little more than expert opinion.

**Biostatistics:** *Propensity scoring* is a statistical technique used to adjust for bias and confounding in cohort studies. It is akin to multiple linear and multiple logistic regression in that it allows the researcher to statistically adjust for differences between groups of non-randomized patients that might impact the outcome of interest. For instance, in Kett's study, suppose that physicians were more likely to adhere to IDSA guidelines in sicker patients. Since severity of illness is likely related to mortality, this might make it falsely appear that adherence increases mortality. However, inclusion of an Apache severity score in a propensity model allows the researcher to essentially match subjects and controls for severity of illness. All variables that might effect the propensity for the physicians to adhere to the guidelines can be included. However, unrecognized factors cannot be adjusted for. This is one reason a randomized controlled trial is a stronger general study design than a cohort study regardless of what statistical analysis is employed.
Levy et al. Vascular hyporesponsiveness to vasopressors in septic shock: from bench to bedside. Intensive Care Med 2010;36:2019-29. and...


These reviews took some effort to get through, but were full of good information. Although much is known about the mechanisms of vascular hyporesponsiveness in septic shock, it hasn’t translated yet into the development of any new effective therapies. Specifically, pharmacological inhibition of nitric oxide, prostaglandin synthesis, or K\textsubscript{ATP} channels, and substitutive doses of vasopressin have all failed to improve clinical outcomes.

Some interesting physiology was brought forth by the authors in regards to resuscitation. Studies suggest that increasing arterial pressure does not necessarily improve microcirculatory perfusion in septic shock. In fact, pharmacological vasoconstriction can actually worsen microperfusion despite an increase in blood pressure. Additionally, vasopressors lower the capillary hematocrit (an interesting effect explained in Boerma’s paper), and worsen tissue oxygen diffusion, potentially diminishing cellular oxygen delivery. Norepinephrine has never been shown to improve mortality in septic shock. We’re not suggesting it shouldn’t be used, but it is disquieting to consider these arguments against a central tenet of hemodynamic support in the ICU. Maybe in the future, we’ll find more elegant ways to measure and support microcirculatory perfusion besides simply cranking up the MAP with norepinephrine.

This was another retrospective cohort study. Four-hundred six cardiac arrests lasting > 10mins were analyzed. The decision whether or not to perform eCPR was at the discretion of the physician running the code, observing specific contraindications. A portable self-priming ECMO unit was employed to rapidly initiate veno-arterial ECMO in 85. Propensity scoring was used to select 60 matched pairs from the study population for analysis. In each matched pair, one patient had undergone standard CPR, and one had undergone extracorporeal cardiopulmonary resuscitation (eCPR). The patients were matched based on a large number of variables that were related to the propensity for the patients to have received eCPR. These included age, comorbidities, cause of arrest, location of arrest, initial rhythm, and study period. The odds ratio for mortality before discharge or suffering significant neurological injury was significantly reduced in the patients receiving eCPR (OR: 0.17 95%CI: 0.04-0.68; p=0.012). Mortality benefit was also significant after 6 months of followup.

Retrospective cohort studies should be considered “hypothesis-generating”. This study provides strong rationale to support an RCT. As an aside, our fledgling ECMO program has been busy this winter with the onset of influenza season. We have yet to attempt eCPR, which obviously requires a well-coordinated system for rapid ECMO implementation.

**Brief mentions:**


In this prospective cohort study, 72 patients who had undergone tracheostomy after at least 3 weeks of mechanical ventilation were followed up by a psychologist. Five of 41 patients (12%) followed up 3 months after vent weaning were found to meet criteria for post-traumatic stress disorder. A post traumatic stress syndrome questionnaire (PTSS-10) performed within a week of vent weaning predicted eventual diagnosis of PTSD with a sensitivity of 100% and specificity of 76%.
Dr. Owen Reece pointed out that other studies have shown the rate of PTSD in patients who have experienced ICU care ranges from 10-50%. Significant flaws in this study include the 43% drop-out rate, and the ethically-questionable failure to provide treatment to patients predicted to be at risk for PTSD by the PTSS-10 questionnaire done before discharge.


This study employed an inexplicably bizarre and weak study design. Residents were randomized to learn central line insertion via video training vs video plus simulation center training. For reasons that are unclear, the line-related complication rate between simulation trained residents and controls were never presented. Instead, the researchers used a convenience control group (surgical residents not involved in the randomization) to show a difference in the rate of catheter-related blood stream infection.

If you are going to go through the trouble of performing a randomized controlled trial, you should analyze the main clinical outcome variable between the experimental and control groups. Failure to present this analysis seems so strange that it raises the suspicion that the results may have been omitted purposefully. We believe simulation center training is highly worthwhile, but this study does not add much support to that contention due to its weak study design.