

# Editorial

## ADVANCING CRITICAL CARE THROUGH INTERDISCIPLINARY RESEARCH

By Cindy L. Munro, RN, PhD, ANP, and Richard H. Savel, MD



This issue of the *American Journal of Critical Care* presents a pivotal report from the Multisociety Strategic Planning Task Force for Critical Care Research that outlines an agenda for research to improve outcomes in critically ill patients. The report lists 4 crucial themes for advancing critical care research and identifies research priorities in 5 broad categories (basic/cellular, translational, clinical, outcomes, and education). The 4 themes address the counterproductive nature of the traditional approach to conducting research in “silos,” the need to link diverse research approaches (such as basic and translational research), the importance of disease complexity and patient heterogeneity, and a need to improve research infrastructure.

The task force is a joint effort of the Critical Care Societies Collaborative (CCSC), which is a formal collaboration among the American Association of Critical-Care Nurses, the American College of Chest Physicians, the American Thoracic Society, and the Society of Critical Care Medicine. It includes experts from each of the CCSC member societies as well as the US Critical Illness and Injury Trials Group. In order to provide the widest exposure to critical care

practitioners, the executive summary and/or recommendations are being published concurrently in the journals of the CCSC member societies (the *American Journal of Critical Care* and *Critical Care Nurse*, *CHEST*, the *American Journal of Respiratory and Critical Care Medicine*, and *Critical Care Medicine*).

### Improving Outcomes

Improving outcomes for critically ill patients is an overarching goal for all practitioners. Individual practitioners are responsible for maintaining currency, acquiring new knowledge, and becoming proficient at clinical skills. Additionally, practitioners must evaluate the evidence upon which they base their practice and continually refine their care based on new findings. Practitioners are not just end users of new research—they generate clinical questions, identify interventions to be tested, and are actively involved in efforts to build the knowledge base for critical care.

Progress has been made in understanding the underlying pathophysiology of many conditions associated with critical illness and in testing and validating interventions. Advances in basic and laboratory science have opened new avenues for clinical and translational research. Conversely, bedside investigations have provided fertile research

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avenues for basic science. As an example, the understanding of the central role of inflammation in the development of sepsis developed as a result of a variety of approaches to the problem. The interaction between bench and bedside led to examination of biomarkers with the potential to guide early identification of sepsis and to direct therapy in the future.

Better understanding of outcomes related to genotypes and application of pharmacogenetics will enhance and personalize therapies for the critically ill. Outcomes research, which introduced questions about the safety and efficacy of blood transfusions (reviewed in Collins<sup>1</sup>), has spawned laboratory investigations of the properties of stored blood that might be associated with adverse effects. Basic research can suggest avenues of investigation and offer explanations of phenomena associated with critical illness, whereas clinical and outcomes research can determine effects of interventions at the bedside. Translational and educational research move critical care practice forward by enabling the application of new knowledge. Approaches to knowledge generation are synergistic, not substitutable.

### A Continuum of Research

A continuum of research approaches is necessary to challenge current practice and to hone our practice using interventions that work. Elbert Hubbard might have been speaking directly to critical care practitioners when he wrote, “The recipe for perpetual ignorance is: Be satisfied with your opinions and content with your knowledge.”<sup>2</sup> Much of our current practice remains untested, and what we do at the bedside is often based on anecdote, opinion (personal or expert), and imperfect science. In examining the knowledge base for nursing care of patients with sepsis, an expert panel of the World Federation of Nurses concluded, “Multiple areas of nursing care have either no evidence to inform practice or the level of evidence is confined to expert opinion.”<sup>3</sup>

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Paucity of evidence continues to afflict all disciplines and most patient problems.

Critical care research continually evolves. Even issues that appear to have been settled must always be open to further examination and revision. Mark Twain had wisdom applicable to critical care: “It ain’t what you don’t know that gets you into trouble. It’s what you know for sure that just ain’t so.”<sup>4</sup> This is particularly true regarding complex bundles of interventions in which the contribution of individual elements is not well demonstrated. One example of ongoing controversy fueled by new research is related to the Surviving Sepsis Campaign. The sepsis bundle was first published in 2004 and updated in 2008.<sup>5</sup> It focused on early goal-directed therapy and has been widely credited with improving outcomes for patients with sepsis and septic shock. Adherence to the sepsis bundle is frequently included as a quality indicator for critical care practice.<sup>6</sup>

However, recent research studies related to 3 of the elements of the sepsis bundle—recombinant human activated protein C (rhAPC), red blood cell transfusion, and tight glycemic control—have produced data that question the benefit of these components. Continued inclusion of rhAPC (drotrecogin alfa, marketed as Xigris by Eli Lilly and Company) in the 2008 Surviving Sepsis guidelines was based on 3 studies that showed better outcomes for those patients with sepsis at high risk of death. Two were randomized controlled trials, the PROWESS (Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis) trial and the ADDRESS (Drotrecogin Alfa [Activated] for Adults with Severe Sepsis and a Low Risk of Death) trial, and one was an open-label observational study called ENHANCE (Extended Evaluation of Recombinant Activated Protein C).

Interestingly, both trials were stopped early—PROWESS for efficacy, ADDRESS for futility—and there was controversy regarding subgroup analyses. Additional research was conducted because of ongoing concerns about safety and a need for better understanding of subgroups most likely to benefit from rhAPC. In the most recent large randomized trial (PROWESS-SHOCK), rhAPC failed to show survival benefit for patients with severe sepsis and septic shock, and Eli Lilly voluntarily withdrew Xigris from the market on October 25, 2011.<sup>7</sup> Critical care practice is littered with interventions discarded in light of knowledge gained from new research.

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Clearly, ongoing research is needed to guard patients against “what you know for sure that just ain’t so.”

## Conclusion

The overarching themes and research priorities identified by the task force move critical research forward in important ways. Breaking the barriers to multidisciplinary research is vital. Creating interdisciplinary research, in which individual disciplines transcend boundaries to create new meaning, is imperative. At its best, critical care research is a shared endeavor, focused on patient success instead of individual or disciplinary advancement. It focuses on highly significant problems affecting morbidity, mortality, and patient and family satisfaction with processes and outcomes. Research that arises from interdisciplinary attention to patient problems will be highly innovative, practice-changing science.

In order to expand our arsenal of effective interventions, we must continue to question current practices and seek validation of interventions. We must embrace interdisciplinary research to improve patient outcomes. The report of the task force provides direction and encouragement toward that end.

The statements and opinions contained in this editorial are solely those of the coeditors.

## FINANCIAL DISCLOSURES

None reported.

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