

## FOUNDATIONS OF EVIDENCE-BASED PRACTICE: CRITICAL CARE TRIAL NETWORKS

By Peter E. Morris, MD, and Kathleen Dracup, RN, DNSc



**C**ritical care management involves not only a struggle to sort through alarms, tubes, and catheters, but a struggle to find the right scientific evidence upon which to base our management decisions. Our teachers and mentors urge us to deliver an “evidence-based” decision as often as possible. But, in fact, careful examination of our evidence-based medicine decisions suggests that practices in the intensive care unit (ICU) are based on a blend of local, national, and international opinion from thought-leading experts in specific areas of critical care.

These opinions often come to us in the form of consensus statements, which are important roadmaps for evidence-based practice. Practice guidelines from consensus statements are forged from available data and experience. Often the only available literature for these guidelines derives from retrospective observations or single-center efforts.

### Shortage of Randomized Controlled Trials in Critical Care

Patient care decisions are complex interpretations of sometimes unrelated literature that we tie together to address unique patient conditions. Possibly the most powerful tool to promote evidence-based medicine is the well-designed, multicenter, randomized controlled trial (RCT). How these RCTs come into existence is an interesting interplay among medical, social, and financial priorities. Creation of RCTs—particularly

nonindustry RCTs—is a difficult process, especially when one considers all the deserving topics within critical illness that exist, as well as the overall scarcity of funds. Often we find ourselves and our patients in situations in which there is no multicenter trial from which to pull information to use in bedside decisions. Although there may not be a multicenter study to address every condition that a critically ill patient exhibits, still we must decide on a plan of action that will reflect all of that patient’s problems.

There are various attributes of a multicenter study that are important to consider. In weighing data from a multicenter RCT versus other types of study formats, we tend to hold the RCT’s findings in higher esteem because of the multicenter design, which generally displays fewer biases than do retrospective or single-center studies. Theoretically, results from a properly conducted multicenter trial should be given more weight and be more accepted than results from other types of studies. The RCT has been credited as yielding the highest level of scientific clinical credibility.<sup>1</sup>

Multicenter RCTs are certainly expensive, and conducting them requires considerable time and collaboration. Funding of a trial’s protocol development, database development and maintenance, training of bedside staff in care management interventions, statistical analysis, and publishing all present challenging financial hurdles.

RCTs are by no means perfect, and there’s still controversy about them. One debate focuses on

## “ Critical care societies, health organizations, funding agencies, and individual bedside caregivers share the responsibility of translating RCT data into practice. ”

whether the population of patients studied in RCTs is representative of everyday ICU populations. In critical care RCTs, comorbidity and mortality within the study arms are usually lower than they are in the overall ICU population. A study's inclusion and exclusion criteria affect the mortality rate in this way. Critically ill patients are heterogeneous with respect to illness severity and type of illness. These patients can receive many therapies simultaneously: ventilator support, antibiotics, renal replacement therapies, tube feedings, intravenous fluids, sedation, analgesia, pressor agents, and possibly antiarrhythmic agents.

Very tight or narrow inclusion-exclusion criteria of these illnesses or therapy requirements create a more homogeneous study population, thereby fueling controversy over adequate representation of the general ICU. Because ICUs display a mixture of illnesses and severities, studies that use tight criteria to draw patients from ICU populations achieve a more homogeneous population (a “good” factor), facilitating group comparisons. At the same time, these narrow criteria affect the study's results, possibly making them less applicable to real-life circumstances (a “bad” factor), which in turn makes it more challenging to apply RCT findings across ICUs. These are very difficult practice issues to resolve in light of the heterogeneity of ICU populations.<sup>2</sup>

### What Is a Critical Care Trial Network?

A critical care trial network is an organization composed of health care centers, typically with a government agency or a professional society providing oversight. The critical care network's goal is to produce a result that clarifies patient care. These networks are often organized to produce multicenter RCTs.

There are prominent critical care networks worldwide (Table 1). Currently, the National Heart, Lung, and Blood Institute is sponsoring a critical care network that focuses scientific questions of care on the acute respiratory distress syndrome and acute lung injury (the ARDS Network). This network has produced several RCTs that have been incorporated into

**Table 1**  
**Critical Care Trials Networks**

Network	Web address
Australian and New Zealand Intensive Care Society's Clinical Trials Group	<a href="http://www.anzics.com.au/ctg">http://www.anzics.com.au/ctg</a>
Canadian Critical Care Trials Group	<a href="http://www.ccctg.ca/index.php">http://www.ccctg.ca/index.php</a>
European Society of Intensive Care Medicine–European Critical Care Research Network	<a href="http://www.esicm.org/Data/ModuleGestionDeContenu/PagesGenerees/05-research/0B-eccrn/40.asp">http://www.esicm.org/Data/ModuleGestionDeContenu/PagesGenerees/05-research/0B-eccrn/40.asp</a>
National Institutes of Health–National Heart, Lung, and Blood Institute–Adult Respiratory Distress Syndrome Network	<a href="http://www.ardsnet.org/front">http://www.ardsnet.org/front</a>
PALISI: Pediatric Acute Lung Injury and Sepsis Investigators	<a href="http://pedscm.org/PALISI_network.php">http://pedscm.org/PALISI_network.php</a>

consensus statements, as have other critical care trial networks' RCTs. (See the Web site of the ARDS Network<sup>3</sup> for a listing of their publications.)

Despite the ARDS Network's successes in focusing our practice attention within lung injury, there exist other critical care issues—such as those concerning trauma, neurology, infectious disease, or appropriate blood product administration—that may fall outside the scope of the ARDS Network. These critical care topics also may warrant the attention of a network trial because of the numbers of patients involved, their illness severity, and the cost to patients and society resulting from these types of critical organ dysfunctions.

Recently, an initiative called the US Critical Illness and Injury Trials Group (USCIITG) received a conference grant from the National Institute of General Medical Sciences.<sup>4</sup> In collaboration with other National Institutes of Health (NIH) institutes, the USCIITG (Table 2) will sponsor a series of meetings to focus attention on critical care research and care delivery issues. The purpose of these meetings will be to foster dialogue exploring network architecture and trial design within critical care, facilitating investigator-initiated clinical trials. The inaugural meeting of the USCIITG will be held November 18 and 19, 2008, on the Bethesda NIH campus. The meeting has an open registration. (See

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“ Individual caregivers and critical care societies have a responsibility to help form the agenda and topics upon which critical care trial networks act. ”

**Table 2**  
**US Critical Illness and Injury Trials Group<sup>a</sup>**

**Background Information**

The US Critical Illness and Injury Trials Group (USCIITG), funded by a grant from the National Institute of General Medical Sciences, will create a clinical research framework that will reduce barriers to investigation using an investigator-initiated, evidence-driven, inclusive approach that has been successful elsewhere.

The USCIITG will not fund clinical trials, but will promote development of evidence-based protocols and the preparation of applications for funding to test hypotheses. The group's specific aims are as follows:

- Establish a nationwide network of experts to review data, establish national priorities, vet hypotheses, write clinical protocols, and generate pilot data
- Promote interactions and synergy across established academic and nonacademic programs to improve the power of clinical trials and to test hypotheses in US populations across the patient age continuum
- Provide a venue to discuss education and training in the science of clinical trial design, including conduct, analysis, and reporting for critically ill or injured patients
- Ensure patient protection and privacy by addressing the ethical, legal, and social implications of research in the specialized circumstances of critical illness or injury

**The inaugural meeting of the USCIITG will be held on the Bethesda campus of the National Institutes of Health on November 18-19, 2008.**

<sup>a</sup> Adapted from: National Institutes of Health Web site.<sup>5</sup>

page 194 in this issue for a formal announcement from the NIH.)

### How Results of RCTs Are Brought Back to the Bedside

Critical care societies, health organizations, funding agencies, and individual bedside caregivers share the responsibility of translating RCT data into practice. Funding institutes and associations certainly wish to see their funds produce meaningful data at the bench or in a clinical trial. They also wish to see results of their funded studies translated back into bedside practice. But networks have scarce resources and typically maximize these resources within the design of the RCT and publication of the RCT's findings. Comparatively little funding is designated for the delivery of information to the bedside practitioner beyond presentations at society meetings and publications.

Although the process is inexpensive, passive dissemination of a study's findings (ie, the idea that publishing the RCT itself will cause bedside practice to change) may not be the most powerful way to alter bedside practice.<sup>6</sup> RCT data are important, of course, but as we struggle to make our bedside practice evidence based, the interplay between RCTs and the critical care societies who interpret RCT data for bedside practice also becomes increasingly important. Within the "evidence-based cycle" of data generation, publication, and dissemination to the bedside, critical care societies and individual caregivers play a particularly important role. The multisociety Surviving Sepsis Campaign is one example of this type of effort.<sup>7</sup>

### A Cyclical (Not a Linear) Relationship Among Bedside Caregivers, Societies, and Trial Networks

An important interrelationship exists among individual caregivers, critical care societies, and critical care networks because there is considerable giving and receiving from all parties. Some may see these relationships as linear, but they are more accurately described as a circular interaction. An easy part of the evidence-based cycle to follow is the pathway from the network's conduct of the RCT to the publication of the RCT results and, eventually, promulgation of society-sponsored practice guidelines based on the RCT.

An interesting but sometimes unappreciated aspect of the cycle is the role of the bedside caregiver. He or she ultimately interprets the RCT's information into bedside practice, and it is the bedside caregiver who, by identifying care issues, raises the awareness of the new care concerns at the society level. So when the question is asked, "Who tells the critical care trial networks what to study?," the cyclical relationship of evidence-based medicine becomes clear. The voices of bedside caregivers are the driving factor in the selection of what a critical care trial network decides to study. Our shared responsibility to foster dialogue and data that drive evidence-based practice begins with priorities such as participation in hospital committees, medical writing, and attending meetings of local and national critical care societies.

Bedside caregivers influence what becomes new evidence by speaking at these venues, serving as patients' advocates, and raising awareness of the day-to-day problems encountered in critical care delivery. Individual caregivers and critical care societies have a responsibility to help form the agenda and topics upon which critical care trial networks act.

As an academic field, critical care is relatively young. Due to the horizontal nature of critical care delivery,<sup>8</sup> it may be challenging for nonprofit and government agencies to identify our field as a distinct discipline worthy of scarce funding capital. After all, critical care is provided across many disease states. But critical care is a necessary hospital support line—a unique entity with its own research needs. An organizational approach to focus these needs comes about through growth of critical care networks. And individual medical and nursing professionals—represented by health care organizations and critical care societies—ought to aid in the development of research priorities.

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

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**FINANCIAL DISCLOSURES**

None reported.

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