Systematic Reviews and Evidence-based Critical Care Medicine: A Step in the Right Direction

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Medical decision making in critically ill patients is often challenging. Although sound decision making should be grounded in the best available scientific evidence, busy critical care practitioners who seek to apply best evidence at the bedside may encounter obstacles along the way. Many of us have neither the time nor the skills to locate, evaluate, and synthesize the results of the relevant clinical trials. Because of this, many clinicians rely on summary information provided by review articles to keep abreast of new developments and to guide their practice decisions.

In recent years, attention has focused on the strengths and weaknesses of traditional narrative review articles (1,2). Narrative reviews are usually broad in scope, summarizing the epidemiology, pathophysiology, diagnosis, and treatment of a given condition. Although their broad perspective provides a reader with an excellent introduction to a topic, information about specific clinical questions is often incomplete. In addition, narrative reviews often mix evidence with the expert opinion of the authors, which may be biased (3). New methods have been developed to overcome these limitations. Many readers are likely familiar with meta-analysis, which is one method for summarizing evidence, but may not be aware that meta-analysis belongs to a larger family of systematic review methods.

Systematic reviews differ from traditional narrative reviews in several important ways (2). They usually address a specific clinical question, in contrast to the broad scope of narrative reviews. Unlike narrative reviews, systematic reviews follow planned methods that are described in sufficient detail so as to be reproducible. Authors of systematic reviews attempt to identify all potentially relevant articles through a comprehensive literature search. Articles are selected according to prespecified criteria, and are critically appraised for methodological quality. In systematic reviews, data may be synthesized either qualitatively or quantitatively, as in a meta-analysis (4). Because systematic reviews use methods to minimize random error and bias, they are more likely to produce valid, evidence-based conclusions than narrative reviews. That discrepancies exist between the results of systematic meta-analyses and the recommendations found in traditional review articles points to limitations in the validity of narrative reviews (1,5). Systematic reviews are also potentially useful for highlighting and exploring sources of variation in study results, prompting the observation that meta-analyses and other systematic reviews are "method[s] for studying studies" (6).

In this issue of the *Journal,* Saint and Matthay (7) review the epidemiology and prevention of three common, potentially serious, and often preventable nosocomial complications of critical illness: venous thromboembolism, upper gastrointestinal bleeding, and catheter-related vascular infection. Their article illustrates and clarifies some of the differences between narrative and systematic reviews. By embracing some of the methods of systematic reviews, the authors have taken an important step in the direction of evidence-based critical care medicine.

Saint and Matthay selected a broad perspective for their article, and thus, it is fundamentally a traditional narrative review. Focusing on two aspects (epidemiology and prevention) of three complications, the authors do not cover any single complication in great detail. For many of their recommendations, clinicians will still need to consult and critically review the primary literature before they can be certain that the cited evidence is valid and applicable to a particular clinical situation.

As in a systematic review, Saint and Matthay describe their methods for identifying potentially relevant studies. However, other aspects of their article are more characteristic of a narrative review. In a formal systematic review, we would expect a complete description of methods for selecting or excluding studies, and a detailed appraisal of each study's methodological quality. These omissions do not necessarily invalidate their recommendations, but do make it more difficult for the reader to render judgment.

In the scale employed by Saint and Matthay, evidence from at least one randomized controlled trial in patients admitted to the intensive care unit (ICU) is designated grade A evidence. We certainly agree that evidence from a well designed and conducted randomized trial is better than evidence from an observational study or case report. But methodological quality varies among randomized

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trials. Many factors influence study quality, such as the randomization procedures, double-blinding, and complete patient follow-up. Randomized trials that do not meet these standards may produce biased estimates of treatment effects (8).

Study methodological quality is not the only factor that must be considered when grading evidence. Equally important is whether the study's findings are applicable to a particular patient's situation. Thus, Saint and Matthay have correctly favored evidence from trials in ICU patients over trials in other patients. But ICU patients are a heterogeneous group, and important differences in risk and treatment response are likely. Thus, data regarding venous thrombosis risk obtained from critically ill patients with respiratory infection may not apply to patients with heart failure. The successful practice of evidence-based medicine requires that studies be appraised for both internal validity and generalizability before their findings are applied in practice.

Saint and Matthay offer many sensible recommendations for preventing critical care complications. The best studied (and most extensively reviewed) complication that they address is stress-related upper gastrointestinal bleeding. Pooled results suggest that when compared with placebo, histamine-2 (H2) receptor antagonists significantly reduce the incidence of clinically important bleeding, but have no significant effect on mortality. However, nonsignificant trends favor prophylaxis with sucralfate rather than H2-blockers when the outcomes are pneumonia and mortality (9). Thus, Saint and Matthay state that the best choice for prophylaxis may depend on the anticipated duration of mechanical ventilation, since pneumonia risk increases greatly after 4 days of ventilatory support. This compelling argument warrants further study.

Another problem that warrants additional attention is the prevention of venous thromboembolism, which has been extensively studied, and found to be effective, in postoperative patients. Saint and Matthay do not present any convincing evidence that indicates that prophylaxis yields clinically important benefits in critically ill medical patients. In the absence of data from well-designed, prospective randomized trials, they cite retrospective studies, nonrandomized or nonblinded trials, studies with endpoints of questionable clinical importance, and studies in general medical patients. We believe that the most appropriate conclusion is that well-designed, relevant trials are needed.

Relevant trials have been performed to evaluate several technologies for preventing catheter-associated vascular infection. Good evidence supports the use of catheters impregnated with antiseptic or antibacterial agents (10,11). In contrast, current best evidence argues against the common practice of routine catheter changes, either over a guidewire, or at a new site. This practice should be abandoned, unless future clinical trials can identify patients in whom benefits occur.

Evidence from well-designed and applicable clinical trials is not, in itself, sufficient for high-quality critical care decision making, which should also integrate the clinical experience and judgment of the physician, and the preferences of the patient. It might be argued that cost effectiveness should also be considered. Although formal cost-effectiveness analysis is a valuable aid to medical decision making, especially at the institutional or policy level, most published cost-effectiveness studies are not structured from the patient's perspective, and applying such studies to decision making at the bedside is often inappropriate.

ICU practice often fails to incorporate new scientific knowledge. Effective technologies are sometimes accepted reluctantly or not at all (such as antibiotic or antiseptic impregnated venous catheters), while other technologies of questionable value diffuse rapidly (for example, routine prophylaxis for stress-related gastrointestinal bleeding). Other practices (such as routine changes of central venous catheters) persist despite no evidence of benefit. For 25 years, we have recognized wide variations in medical practices (12), suggesting that many patients have received insufficient, unnecessary, or low yield care. Systematic reviews will certainly not solve these problems, but they will help to summarize, clarify, and explain discrepancies in the critical care medicine literature. Much additional primary research is also needed, so that nosocomial complications of critical illness can be prevented effectively. Saint and Matthay are to be commended, above all, for reminding us that our first responsibility is to do no harm.

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