An Official Multi-Society Statement: The Role of Clinical Research Results in the Practice of Critical Care Medicine

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CONTENTS

Background: **While the results of clinical research are clearly valuable in the care of critically ill patients, the limitations of such information and the role of other forms of medical knowledge for clinical decision making have not been carefully examined.**

Methods: **The leadership of three large professional societies representing critical care practitioners convened a diverse group representing a wide variety of views regarding the role of clinical research results in clinical practice to develop a document to serve as a basis for agreement and a framework for ongoing discussion.**

Results: **Consensus was reached on several issues. While the results of rigorous clinical research are important in arriving at the best course of action for an individual critically ill patient, other forms of medical knowledge, including clinical experience and pathophysiologic reasoning, remain essential. No single source of knowledge is sufficient to guide clinical decisions, nor does one kind of knowledge always take precedence over others. Clinicians will find clinical research compelling for a variety of reasons that go beyond study design. While clinical practice guidelines and protocols based upon clinical research may improve care and decrease variability in practice, clinicians must be able to understand and articulate the rationale as to why a particular protocol or guideline is used or why an alternative approach is taken. Making this clinical reasoning explicit is necessary to understand practice variability.**

Conclusions: **Understanding the strengths and weaknesses of different kinds of medical knowledge for clinical decision making and factors beyond study design that make clinical research compelling to clinicians can provide a framework for understanding the role of clinical research in practice.**

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EXECUTIVE SUMMARY

Within critical care medicine, a debate has arisen over how best to utilize the results of clinical research in clinical practice, particularly related to the relative weight to be given such information compared with other kinds of medical knowledge. The leadership of three professional societies serving critical care providers brought together clinicians, researchers, philosophers, and a patient representative, representing a variety of views on the subject in an attempt to add clarity to the debate and to develop a framework that would be useful for clinicians and academics in discussing these issues.

The group reached consensus in several areas.

- The results of clinical research, pathophysiologic reasoning, and clinical experience represent different kinds of medical knowledge crucial for effective clinical decision making.
- Each kind of medical knowledge has various strengths and weaknesses when utilized in the care of individual patients.
- No single source of medical knowledge is sufficient to guide clinical decisions.
- No kind of medical knowledge always takes precedence over the others.
- Patient and/or family preferences and features of the system in which care is delivered also represent important considerations.
- Explicitness is a hallmark of sound clinical reasoning.
- Clinical research will be more or less compelling to clinicians based on a variety of features (elucidated here) independent of study design and statistical robustness.
- Variability in practice may be acceptable when based upon different weighting of conflicting medical knowledge or different patient or clinician values.
- Explicit reasoning is necessary to assess the causes and appropriateness of variability in clinical practice.
- Clinical practice guidelines and protocols derived from clinical research are most likely to be useful under specific and defined circumstances.

- Clinical practice guidelines and protocols are not prescriptive, and clinicians must understand and be able to articulate appropriate reasons to adhere to or diverge from them in particular cases.

INTRODUCTION

Within the field of critical care medicine, a debate has arisen regarding the relative value of the results of clinical research for guiding clinical decision making, particularly with regard to use of tools derived from such research, such as clinical practice guidelines and protocols. Other forms of medical knowledge, including pathophysiologic principles and clinical experience, are acknowledged as crucial for determining the best course of action for individual critically ill patients, though integration of such knowledge with clinical research results has been left largely unexamined. Each form of medical knowledge has particular strengths and weaknesses, and all must be considered to arrive at a reasonable clinical judgment. No single form of medical knowledge always takes precedence over the others, meaning that no hierarchy of knowledge can be uniformly applied to clinical decisions. In weighing knowledge of various kinds, clinicians should strive to make such deliberations explicit, which will help us to understand some of the reasons for variability in practice. Furthermore, clinicians invoke a wide variety of factors beyond study design and rigor for finding the results of particular clinical research studies compelling. Understanding these factors will help to explain some variability in practice. In summary, acknowledging the strengths and limitations of clinical research for the practice of critical care medicine will help in the design and implementation of clinical practice guidelines and protocols and also in identifying an appropriate process for adopting or rejecting them in the care of individual patients.

METHODS

This document represents a multi-society project. The initial executive committee for this project included the President of each of the three societies in 2009 (J.R.C., M.M.L., K.K.G.) and the chair of the writing committee (M.R.T.). The executive committee chose experts in critical care research and education who represented a spectrum of viewpoints on the role of clinical research results in clinical practice based upon their prior writings and lectures at national and international meetings. The group also included a philosopher and an individual chosen to represent the views of patients.

The project members had a series of meetings that began with a day-and-a-half meeting in 2009 focused on defining the primary questions and terms of the debate. Four 90-minute meetings at four successive international conferences for the three societies followed in 2009 and 2010. Successive drafts of the resulting document were sent electronically to all participants for comment. The group continued deliberations and revisions in person, electronically, and by phone until achieving full and unanimous consensus on the final document.

PURPOSE

In their effort to provide optimal medical care to patients, clinicians have been aided by the increasing availability of clinical research designed to answer important questions regarding the safety and efficacy of diagnostic and therapeutic medical interventions. Such research can take a number of forms, including controlled trials or observational studies, and it generally reports measurable outcomes from human subjects or patients. While this kind of information is clearly of value, a debate has arisen over how best to utilize the results of clinical research in clinical practice, particularly related to the relative weight to be given such information compared with other kinds of medical knowledge. In critical care medicine, for reasons examined in more detail below, the debate is particularly acute. The leadership of three major professional organizations serving critical care clinicians (American College of Chest Physicians, American Thoracic Society, Society for Critical Care Medicine) identified an opportunity to move the debate forward, both by adding clarity to the discussion and by offering a conceptual framework for clinicians regarding the incorporation of the results of clinical research into the practice of critical care medicine. Leadership of these three organizations brought together a group of clinicians and researchers representing many viewpoints to discuss the issues and strive for consensus.

While this effort necessarily deals with many issues central to the notion of "evidence-based medicine," (1, 2) it does not represent a statement for or against that school of thought. Rather, the approach taken here involves a careful analysis of the optimal practice of critical care medicine, particularly focused on clinical decision making and specific tools designed to improve patient care. The aim is not to resolve current controversies regarding the value of specific interventions or practices, but rather to provide clinicians with a conceptual background and framework for evaluating discordant information and conflicting claims when caring for the critically ill.

THE PRACTICE OF CRITICAL CARE MEDICINE

While questions regarding the value and use of the results of clinical research in bedside practice are relevant to all fields of medicine, they are arguably more pressing and complex in the care of unstable and critically ill patients. Critical care medicine is, in large part, defined by the careful monitoring of many physiologic variables. Care of critically ill patients requires real-time analysis of these variables and adjustment of therapeutic measures, resulting both in a large number of clinical decisions with respect to each patient as well as the need to make decisions in a rapid fashion. In addition, the vulnerability of critically ill patients, their general inability to participate directly in medical decision making, and the high risk of poor outcome all serve to amplify the clinician's responsibility.

The use of clinical research in critical care is also complicated by several factors. Critically ill patients are often classified as having complex syndromes (e.g., sepsis or acute lung injury) rather than particular diseases defined by a specific test or single etiology (3). The lack of reliable syndrome definitions, the heterogeneity of patients' risk factors for critical illness, and attendant co-morbidities make performing, interpreting, and applying clinical research particularly challenging (4). In addition, as compared with many other disciplines such as cardiology and oncology, there is a relative paucity of large, randomized trials to inform practice in critical care medicine (5).

In sum, questions regarding the interpretation and use of clinical research results, while not unique to critical care medicine, are particularly pressing to intensivists, providing motivation for our professional organizations to address these issues.

FRAMING THE PROBLEM

Defining the role of clinical research for the practice of critical care medicine requires both an understanding of the primary responsibility of the critical care clinician as well as the elucidation of the kinds of knowledge and reasoning that should influence clinical decisions.

While the traditional goal of clinical medicine has been defined in terms of providing benefit to an individual patient, there has been recognition over the last several decades that clinicians also have a responsibility to larger populations and society at large, particularly regarding the just use of resources (6). The balance between good stewardship of limited resources and

advocacy for the individual patient can be challenging in critical care medicine (7). The primary duty of the clinician, however, remains the provision of benefit to the patient at hand.

Central to assessing the role of knowledge gained from clinical research in the care of individual patients is the question of what other kinds of knowledge or beliefs and what kinds of reasons and reasoning may properly be brought into clinical decision making. While much emphasis has been placed on the results of clinical research, other kinds of medical knowledge remain valuable for clinicians (8). Experiential knowledge, gained from the personal practice of medicine, as well as theoretical knowledge, based upon the principles derived from the life sciences, may legitimately serve as the grounds for medical decisions. The source of experiential knowledge may be the individual clinician, but may also be derived from other expert clinicians. Knowledge gained from the life sciences may take the form of fundamental physiologic principles that can help guide clinical decisions or be derived from specific basic or translational research studies that can be useful for understanding pathophysiology in individual patients. Clinical research, personal experience, and pathophysiologic understanding, then, constitute the broad categories of medical knowledge relevant to the care of individual patients.

Medical knowledge alone, however, is insufficient to arrive at the best decision for a particular patient, as the importance of eliciting and understanding the goals and values of the patient is universally acknowledged. The influence of relationships with family, friends, and community must be considered in medical decision making as well, particularly in the ICU, where patients are seriously ill and generally unable to participate directly in decisions about their care. Preservation of life may not always be an appropriate goal for some critically ill individuals, such as those with an extremely poor prognosis or severe and permanent loss of cognitive function. Therefore, while all three kinds of medical knowledge (clinical research-based, experiential, and pathophysiologic) might point toward treatments that may aid in preserving life, deciding to implement those treatments could be inappropriate if not consistent with the patient's goals of care.

In addition, the system in which care is provided may facilitate or limit the provision of specific interventions, based on legal, religious, financial, or logistic considerations. Behavioral and economic incentives that shape clinician practice are built into all health care delivery systems (9). But while patient goals and values as well as health care systems all play important and valid roles in medical decision making, these issues will not be explored further here. Instead we will focus on the implementation of medical knowledge.

Clinical decision making aimed at benefiting individual patients ought to incorporate all relevant medical knowledge regardless of kind or source (10). How various kinds of knowledge should be utilized, particularly when discordant or conflicting, is central to the notion of clinical judgment (11).

CLINICAL DECISION MAKING IN CRITICAL CARE MEDICINE

Strengths and Limitations of Kinds of Medical Knowledge

No single kind or source of medical knowledge is sufficient to fully inform clinical decision making; each has particular strengths and limitations when invoked in the care of critically ill patients.

Clinical research. The results of well-designed and well-executed clinical research studies provide medical knowledge that is valued, among other reasons, for its potential to reduce bias, the systematic error that results in an incorrect estimate of the association between an exposure (or treatment) and a disease (or outcome) (12). Clinicians, like all people, are prone to a variety of biases when making decisions, biases that may result in incorrect inferences and lead to erroneous, and potentially harmful, conclusions (13). Utilizing knowledge gained through techniques designed to minimize bias may provide a more sound footing than reliance on personal experience alone (14, 15). In addition, large clinical trials can often find clinically significant effects that are not easily detected when caring for individuals or small groups of patients. Knowledge gained from clinical research is subject to peer review and can easily be disseminated, providing for a shared body of knowledge for the profession.

It is important, however, to understand the limitations of using knowledge gained from clinical research in the clinical practice of medicine. Knowledge gained from populations cannot be directly and indiscriminately applied to the care of individuals (16, 17). This problem is particularly challenging when clinical features of an individual patient do not closely resemble those included in a clinical trial or meta-analysis (16). Knowledge gained from clinical research, by its very nature, remains fixed in both time and place; applicability to a new time and a different place is not assured. Clinical research may produce conflicting results, leaving clinicians uncertain regarding the relative value of such knowledge to an individual case. Finally, even rigorous clinical research remains fallible (18) and, at times, untrustworthy (19).

Pathophysiologic rationale. Reasoning from the principles of biology, biochemistry, and physiology served as the standard methodology of scientific medicine over most of its history, with mixed results (20). However, such reasoning serves several important roles. Pathophysiologic reasoning provides a check upon questionable findings from clinical research, such as the apparent effect of homeopathic remedies (21) or retroactive intercessory prayer (22). Biologic plausibility, a description of the purported mechanism of action for a particular therapeutic intervention, supports arguments of causality and increases the likelihood that the result of an observational study represents a meaningful association (23).

Pathophysiologic rationale also remains valuable in the care of individual patients, particularly in critical care medicine (24). Differences in physiology at presentation often provide a sound reason to alter decisions regarding the rapidity and intensity of initial diagnostic and therapeutic interventions (25). Recognizing relevant physiologic differences between individuals may guide initial choice of therapy. For instance, antibiotic choice may be determined in part by whether the patient is sick enough to warrant an ICU admission (26). As not all patients respond to interventions in a like manner, monitoring and responding to physiologic changes can provide early assessment of the likelihood of success of a therapy. A rising P_{CO_2} after initiating noninvasive ventilation, for example, suggests that intervention will likely not be successful in avoiding the need for invasive mechanical ventilation. In the ICU, pathophysiologic rationale often offers a compelling reason to alter treatment plans, for short-term goals are generally defined in terms of physiologic endpoints, such as organ function.

Clinical reasoning from scientific principles also has significant limitations. Most important, therapeutic strategies based on physiologic goals, such as suppressing arrhythmias after myocardial infarction (27) or improving oxygenation in acute lung injury (28), do not always lead to better outcomes, such as survival. In addition, reasoning from scientific principles can only be as good as our scientific understanding, which, despite great progress, remains far from complete. Although contemporary physiologic understanding falls short of providing a reliable guide for clinical decisions, pathophysiologic mechanisms ultimately underlie the processes of illness and recovery. Further exploration of these mechanisms, through animal and human studies, is essential to continued progress in critical care medicine.

Experiential knowledge. Experiential knowledge gained through the thoughtful practice of clinical medicine is widely acknowledged to be both necessary and fallible in clinical practice (29). The personal knowledge gained through primary experience is distinct from the kind of processed and indirect knowledge derived from clinical research (30), offering the experienced clinician a rich set of cases to which a new case can be compared (31). The value of primary experience has been more easily demonstrated in diagnosis, where sound conclusions are often reached through nonanalytic approaches (32). Therapeutic decisions can also be informed by clinical experience, particularly when assessing whether an individual patient differs in a meaningful way from those subjects enrolled in a clinical trial (16). Therapeutic decisions and performance may also be improved by experience, as studies revealing better outcomes for specific surgical procedures in high volume centers abound and high patient volumes are also associated with better outcomes of mechanical ventilation (33). Clinical observations are also crucial for detecting new disorders (e.g., AIDS) or changing manifestations of others (e.g., age-related severity of illness in the 2009 H1N1 influenza epidemic).

Reliance on clinical experience for clinical decision making, however, is likely to be influenced by a number of biases (13). Even when educated and trained to be aware of these potential biases, clinicians cannot hope to avoid them completely (34–36). Relying on experience may also make practice patterns more static, as reasons to change practice may not be directly evident. Experience does not guarantee expertise, nor does an experienced clinician alone mean better outcomes for patients (37).

Given the strengths and limitations of each kind of medical knowledge, no single type, by itself, is sufficient for clinical decision making. While good clinical research produces knowledge that minimizes bias, that knowledge cannot be deductively or mechanically applied to the care of individual patients. While pathophysiologic rationale and clinical experience allow for the incorporation of important differences in individual patients, reasoning from these alone may introduce bias or result in a focus on the wrong outcome. Ideally, clinicians will incorporate all available and relevant medical knowledge into a clinical decision to arrive at the best choice for a particular patient. Often the decision will be straightforward, but at times knowledge of different kinds may produce incomplete, inconsistent, or conflicting support for clinical decisions, creating difficulty and controversy.

Negotiating between Various Kinds of Medical Knowledge

No set hierarchy of knowledge to guide clinical decision making in all situations is possible (38, 39). While there have been many hierarchies suggested to aid experts in developing clinical practice guidelines or clinicians in providing care to individual patients, it is now recognized that a ranking based on study design or quality measures cannot be directly applied to clinical decisions; exceptions will always exist and must be acknowledged (39, 40). Clinicians, then, must continue to rely on sound clinical judgment to negotiate between potentially conflicting facts and reasons when attempting to reach a decision regarding the best course of action for an individual patient. Acknowledging this uncertainty and the inability of any predetermined hierarchy to resolve it does not make clinical judgment arbitrary nor mean that it cannot be improved upon. Encouraging consistent, mindful, and reflective practice on the part of critical care clinicians has the potential to improve the care of patients and to help advance the field (34).

Explicitness is to be greatly valued in improving clinical decision making. While there may be important elements of clinicians' knowledge that are tacit (10, 41), clinicians should be able to identify and articulate the sources and kinds of knowledge that are being invoked in support of a particular clinical decision. The initial step in arriving at a clinical decision is the identification of the medical knowledge pertinent to the case, including that derived from clinical research, pathophysiologic understanding, and clinical experience. Since no kind of knowledge is always superior or most compelling, simply relying upon the results of a relevant randomized controlled trial or meta-analysis will be insufficient. Clinicians are obligated to consider information and knowledge that might suggest action that would run counter to that suggested by clinical research. Table 1 provides some clinical examples in which clinicians may reasonably differ from a course of action more generally supported by clinical research. Sound clinical judgment in critical care medicine requires consideration of a variety of reasons and approaches to reasoning (42). Further examination and potential resolution of differences of opinion on the part of practitioners can only occur if they are clearly articulated. A clinician ought to be able to concisely outline and justify the process of clinical reasoning, elucidating the facts and reasoning supporting a particular decision, such as in the assessment portion of a clinical note, in a presentation to a colleague or trainee, or in discussion with the patient or family. This allows for the reasons and reasoning to be subject to challenge, rebuttal, and revision.

VARIABILITY IN CLINICAL PRACTICE

The weight given to particular facts and reasons invoked for a clinical decision can be expected to differ between clinicians, resulting in variability in practice (43). Variability and disagreement can stem from many sources (44), but can be related to how compelling individual clinicians find particular information, knowledge, or reasoning. One of the primary limitations of ranking clinical research solely on the basis of study design has been the fact that many other aspects of such research rightly contribute to whether clinicians find those results compelling enough to change practice. We have enumerated factors beyond a strict focus on study design and execution that make clinical research results more compelling in critical care medicine. These are summarized in Table 2. No particular clinical study can be expected to satisfy all criteria. When clinicians do not find the results of clinical research compelling, they will be more likely to weight experiential or pathophysiologic knowledge more heavily. Clinicians can therefore reasonably come to a different clinical conclusion in managing individual cases even though they are considering the same clinical research results (43, 45). It remains important, however, that individual clinicians attempt to apply a consistent and transparent approach to incorporating medical knowledge pertinent to the care of similar patients. Such an approach could help to minimize the effect of various cognitive biases on practice variability.

Differences in clinician assessments regarding the implementation of clinical research results may derive from differing professional values and prior knowledge (43). Values that may influence clinical decisions include concerns regarding cost, the importance of avoiding harm, belief in the value of standardization for the sake of standardization, or a tendency to employ unproven interventions in cases with extremely poor prognosis. Clinicians may reach different conclusions regarding patients with similar illnesses and preferences for care not because of ignorance or misunderstanding of the relevant clinical research, but by weighing that information in the context of different personal and professional values (46).

Making the clinical decision-making process explicit will aid in identifying the sources of variability in practice. Variability

TABLE 1. CLINICAL EXAMPLES IN WHICH CLINICIAN VALUES, CLINICAL EXPERIENCE, OR REASONING BASED ON PATHOPHYSIOLOGY MAY REASONABLY RESULT IN DIVERGENCE FROM PRACTICE SUGGESTED BY EMPIRICAL EVIDENCE

Treatment	Unique Patient Scenario	Explicit Rationale for Diverging from Empirical Evidence
Low tidal volume ventilation for severe ARDS	Nonsustained but hemodynamically significant episodes of ventricular tachycardia at low tidal volume that improves with higher tidal volume	Clinician experience prompts decision to use higher tidal volume than clinical research supports
Low tidal volume ventilation for severe ARDS	Elevated plateau pressures in the context of abdominal compartment syndrome	Pathophysiologic reasoning about transpulmonary pressures supports a decision to allow higher plateau pressures
Inhaled nitric oxide for severe ARDS	Single organ failure and severe life-threatening hypoxia	Pathophysiologic reasoning leads clinician to implement therapy without proven benefit for improving hospital survival
Use of blood transfusion in early goal-directed therapy for sepsis	Postoperative patient with breast cancer develops pneumonia and sepsis	Pathophysiologic reasoning emphasizes potential harm of allogeneic blood over potential benefit
Induced hypothermia after cardiac arrest	Witnessed in-hospital cardiac arrest with pulseless electrical activity as initial rhythm	Pathophysiologic reasoning extrapolating from out-of-hospital arrest leads to inducing hypothermia

Definition of abbreviation: ARDS = acute respiratory distress syndrome.

based upon knowledge deficits or faulty application of knowledge to decision making is unacceptable, while variability based upon different weighting of relevant knowledge is to be expected. Identifying sources of variability and determining what constitutes acceptable variation is an important challenge in this era in which strategies to improve quality of care often focus on reducing variability, including many "pay-for-performance" initiatives (47).

TOOLS DESIGNED TO AID CLINICAL DECISION MAKING

While much of the discussion thus far has focused on individual decision making on the part of clinicians, a great deal of the current controversy regarding the proper role of clinical research in the practice of critical care medicine centers upon the use of tools, such as clinical practice guidelines and protocols, largely derived from clinical research with expert clinician input. Guidelines and protocols can decrease variability in practice and in some cases improve the care and outcomes of critically ill patients (48, 49). But the application of clinical practice guidelines alone does not guarantee benefit and may even result in unintended consequences that might harm some patients (50, 51). Clinicians have also raised concerns that guidelines and protocols can be constraining, eroding clinical judgment and compromising medical education and professional development (17).

Clinical Practice Guidelines

Clinical practice guidelines (CPGs) seek to aid clinical decision making by recommending specific interventions for common clinical conditions or problems. When well chosen and properly implemented, CPGs may result in improved patient outcomes (52, 53). In aspiring to be "evidence-based," CPGs developed over the last decade have usually been based on a synthesis of available clinical research, though generally authored by groups containing individuals with significant clinical experience in the field (48). As efforts have been made to minimize bias in CPGs, development has increasingly depended upon the analysis of statisticians and methodologists in addition to the expert opinion of clinicians. Such a shift likely does decrease bias, but may also significantly reduce the clinical relevance and applicability of resulting CPGs (54). Ideally, development of CPGs would include both content experts and methodologists to ensure clinical relevance in addition to precision and consistency.

While CPG development has relied heavily upon hierarchies related to the strength and quality of clinical research studies, more recent efforts have acknowledged that other factors are also important for determining the strength of a recommendation (55). Several of these factors, including safety, cost, effect size, relevance of outcome, and the absence of conflicts of interest among authors, are identical to those we identified as factors relating to how compelling clinicians are likely to find research results. These factors are largely intrinsic to the specific study and intervention and, therefore, can be evaluated independently. Several CPG development groups now incorporate these considerations. But other factors that would make a particular research result or CPG compelling rest in a specific clinical context. The generalizability, applicability, acceptability, and ease of implementation of study results may depend on local factors that cannot be fully anticipated by developers of CPGs. Furthermore, attempts to incorporate these multiple factors into a single summary expression of "strength" of a recommendation is difficult, if not impossible (56).

CPGs are generally designed to assist with treatment decisions involving typical presentations of relatively common disorders. Individual patients, however, often present with a variety of conditions or atypical manifestations, making guideline application

TABLE 2. FACTORS BEYOND STUDY DESIGN AND EXECUTION THAT MAY MAKE CLINICAL RESEARCH COMPELLING TO CLINICIANS (IN ALPHABETICAL ORDER)

Biologic plausibility: coherence with principles of biochemistry, pharmacology, and physiology
Confirmatory: reproduces the results of another clinical research study
Consistency: coherence with other results of clinical or experimental research
Cost: inexpensive
Ease of implementation: simple to incorporate into practice, including local availability, acceptance and appropriate technical expertise
Effect size: large magnitude of treatment effect
Generalizability/applicability: similarity of patient population studied to that in one's own clinical practice
High value outcome: outcome meaningful and desired by patients
Objectivity: lack of conflict of interest on the part of researchers, authors, and sponsors
Prior knowledge/belief: consistent with clinician's current understanding
Safety: unlikely to cause significant harm
Time to effect: results in immediate or rapid response

TABLE 3. FACTORS DETERMINING SUITABILITY FOR ICU PROTOCOL IMPLEMENTATION

Favors Use of Protocol	Example
Need for frequent monitoring and adjustment	Serum potassium replacement with diuresis
Easily measured therapeutic goal	PTT during heparin administration
Set process improves outcomes	Sterile technique for CVC placement
Decisions must be made in rapid sequence	Advanced cardiac life support
Easy to implement	Stress gastritis prophylaxis
Narrow therapeutic window	Warfarin dosing
Impedes Use of Protocol	**Example**
Competing goals of intervention	Oxygenation, respiratory mechanics, and cardiac function for titrating PEEP in ARDS
Process not clearly associated with improved outcome	Tight glucose control
High variability in individual response to therapy	Specific vasopressor use in sepsis
Complicated and difficult to implement protocol	The Fluid and Catheter Treatment Trial (FACTT) fluid protocol

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CVC = central venous catheter; PEEP = positive end-expiratory pressure; PTT = partial thromboplastin time.

problematic (57). Whether a CPG applies to an individual patient remains a matter of clinical judgment. Virtually all guidelines explicitly recognize that clinicians need to continue to exercise clinical judgment regarding the relevance of the guideline to individual patients. Decisions not to utilize CPGs and protocols in particular cases are examined in more detail below.

Protocols

Protocols differ from clinical practice guidelines in that, after a decision to initiate, the protocol prescribes a specific series of behaviors (e.g., for central venous catheter placement) or changes in treatment (e.g., for heparin dosing based on partial thromboplastin time) without the requirement of further clinician input (49). Protocols may be adopted directly from a specific research study, although this approach is not always appropriate, as many research protocols are designed for specific methodological reasons not relevant to clinical practice (e.g., separation of groups to increase signal and power). Modification of research protocols for clinical practice may make sense when such protocols are complex or when there are good reasons to believe not all elements are necessary.

Well-chosen protocols and standing orders offer advantages. In the ICU, protocols may help avoid errors of omission, improve unit efficiency, decrease cost, and maintain standard of care (58). Protocols, however, are not always superior to expert clinician-directed care (59). Protocols are particularly useful for setting "default" actions in common decisions. Protocols that minimize harm to patients and have little attendant risk, such as deep venous thrombosis and stress ulcer prophylaxis, promise to improve long-term outcomes and decrease costs. "Non-thinking" tasks, those that clearly and uniformly are best done in a set fashion and where variation is harmful (e.g., dialysis circuit set-up), should be prime targets for the use of protocols. Protocols are likely to be less valuable when applied to highly variable clinical processes, particularly those with multiple and competing endpoints. Factors affecting the suitability of protocols for critical care interventions, along with examples, are summarized in Table 3.

INDIVIDUALIZED CARE

Protocols and guidelines attempt to synthesize, codify, and operationalize medical knowledge, primarily that generated from clinical research. As such, they may be useful in deliberations regarding patient care, but are not prescriptive and do not determine the best possible care of an individual patient. Little attention, however, has been focused on when and how clinicians should alter care from that dictated by a protocol or suggested by a clinical practice guideline (60). At times, pathophysiologic reasoning or clinical experience may suggest a course counter to that outlined in a CPG or a protocol. Protocols and guidelines do not necessarily trump decisions based upon experiential or pathophysiologic rationale. How guidelines and protocols are formulated and whether they consider factors unrelated to study design but important to clinicians (such as cost, safety, and ease of use), will ultimately determine how compelling clinicians will find them. The more compelling the guideline, the fewer the circumstances in which clinicians will feel the need to depart from it. When clinicians do decide to take action contrary to that recommended by well-established guidelines, they should be able to make explicit their reasons and reasoning for that action, just as they should be able to make explicit their reasons for adherence to the guideline. Clinicians should be able to offer publicly the facts and reasons supporting their decisions, making that reasoning subject to challenge or endorsement. Some clinical research suggests that conscious departures from clinical practice guidelines on the part of clinicians are not uncommon and, reassuringly, overwhelmingly represent appropriate clinical decisions (61).

CONCLUSIONS

Focusing on whether clinical practice guidelines and protocols are essential to improving patient outcomes may obscure the more important questions of when and how guidelines and protocols can be best developed, implemented, and adapted to acknowledge and account for the individuality of patients. Advocates for the implementation of protocols and guidelines have not always paid enough attention to the limitations nor delineated how and when it is appropriate for clinicians to disregard those recommendations. Here we have offered some specific suggestions regarding the design and use of such tools as well as a rationale and method for departing from them in the care of individual patients.

Relevant clinical research must be incorporated into clinical decision making: ignorance of or wholesale disregard for the results of clinical research represents an abrogation of clinician responsibility. Clinical research, however, should not be applied to individual patients without incorporation of other kinds of medical knowledge. Critical care medicine requires the application of research-based, experiential, and pathophysiologic knowledge to the care of an individual patient in an effort to improve the health of that particular individual. Even with more and better clinical research focused on the critically ill, the optimal practice of critical care medicine will remain dependent upon the practical wisdom of intensivists negotiating between occasionally conflicting facts, knowledge, and reasons relevant to specific medical decisions. By making this process more explicit, both in general terms and in the care of individual patients, we can hope to continue to improve outcomes for this extremely vulnerable group of patients, one patient at a time.

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