Practice Guidelines

Belief, Criticism, and Probability

EVERY DAY, HEALTH CARE PROVIDERS AID PATIENTS in making decisions about their health. The process by which providers acquire, assimilate, and implement information to make decisions involves evaluation of published clinical research studies and reliance on early medical training, discussions with colleagues, local policies, personal clinical experience, and external influences.[1] Another important source of information is practice guidelines developed and published by professional medical societies.

Guidelines can serve a useful purpose for providers by presenting a compilation of available evidence in a given therapeutic area. Guidelines can also help the provision of care, because standardization may help streamline processes for implementation of interventions. In some circumstances, quasi-experimental studies show an association between following recommendations in guidelines and improved outcomes for patients.

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However, guidelines are not just summaries of the evidence. They are also interpretations of that evidence by guideline authors who bring to the process their own conscious and unconscious biases.[2] Recently, guidelines have come under scrutiny for lack of transparency in their development, conflicts of interest of guideline authors, and failure to include all interested parties in the development process, leading to recommendations for improvements in the process.[3] Some caregivers are opposed in principle to guidelines because they believe that they are not relevant to their patients and cannot address all clinical situations. Some caregivers believe that guidelines in general decrease caregiver autonomy. Multiple guidelines on the same topic with different recommendations based on different selection of studies (or different interpretations of the same studies) can prove more confusing than helpful.[4] Also, some caregivers may interpret guidelines as strict dictums or use them for purposes for which they were not intended, with unforeseen consequences. For example, a quality-of-care rule based on observational data that patients with community-acquired pneumonia receive antimicrobials within 4 hours of presentation was based on a recommendation in 2003 guidelines. One study showed that implementation of this rule resulted in an approximately 20% increase in the misdiagnosis of pneumonia and greater unnecessary exposure to antimicrobials with no decrease in mortality.[5]

More recently, researchers have appraised the average quality of the evidence that forms the basis for recommendations in guidelines. Sniderman and Furberg point out that "the anchoring authority of the guideline process is the belief that guidelines are evidence based, not opinion based, and therefore their conclusions flow directly from the conclusions of studies."[3(p429)] Some guidelines evaluate recommendations by assigning "strength" of recommendations based on the consensus of the guideline authors and the "quality" of the data that form the basis for recommendations. A recent study[6] of the quality of evidence in cardiology guidelines showed that of more than 7000 recommendations, a median of 11% were based on data from randomized controlled trials (RCTs) and 48% on expert opinion, case studies, or standards of care. In this issue of the *Archives*, Lee and Vielemeyer[7] report on a similar analysis of guidelines in infectious diseases. Their study shows that of more than 4000 recommendations, 14% were based on data from RCTs and 55% on opinion or case series. Both studies showed that although the number of recommendations increased across time, few of the new recommendations were based on RCT data.

What are providers to make of recommendations in guidelines if most of those recommendations are based on opinion? First, these data reinforce that absolute certainty in science or medicine is an illusion. Rather, evaluating evidence is about assessing probability. As Weed states discussing causal inferences, "Given that certainty is impossible, there are 3 alternatives: belief, probability, and criticism."[8] Appropriate clinical research allows us to make decisions with the greatest probability of providing more benefit than harm to patients. When we make decisions based on opinion, there is a greater probability of drawing incorrect conclusions than if we had valid and reliable evidence from clinical studies. This does not mean that opinion is always wrong, but, as Weed continues, relying on belief alone "makes it somewhat easier to conceal error."[8] Science is based on justifiable belief from evidence, while unjustifiable belief is based on opinion alone. Conclusions based on clinical experience draw associations between exposure to interventions and outcomes based primarily on a temporal relationship—we use an intervention and observe the outcome—usually backed by post hoc rational-sounding explanations of biological plausibility. However, history has shown that this type of evidence can be misleading, sometimes with major adverse consequences for patients. For this reason, in the United States, regulatory approval of drugs and biological interven-

tions is based on "substantial evidence" from "adequate and well-controlled" trials. Congress specifically held that the opinions of practicing clinicians was an insufficient standard for evaluating the safety and effectiveness of drugs and biologics.[9]

Second, the studies on quality of evidence reinforce that regulatory approval is the first step in an intervention's life cycle, and there is much more to learn about appropriate use, additional uses, how to use interventions such as dose and duration of therapy, and adverse events once interventions are widely applied in clinical practice. In addition, there is a place for studying interventions already shown effective from explanatory trials in a pragmatic way in clinical practice.[10] The absence of certainty or "perfection" is not an excuse for mediocrity. The importance of such studies is highlighted in recent health care reform legislation. The Patient Protection and Affordable Care Act included provision for a new Patient-Centered Outcomes Research Institute with funding of up to $500 million per year to perform comparative effectiveness research. The presence of recommendations in guidelines based solely on opinions or case series should spur future research to address those same problems rather than considering future research on the topic "unethical" merely because a recommendation exists. Instead, one could question the ethics of continuing to treat or withhold treatment from patients without an adequate controlled assessment of whether we are doing more harm than good. As Hippocrates noted, "Science is the father of knowledge, but opinion breeds ignorance." It is important that studies be designed to minimize bias and assess outcomes important to patients. The grading of evidence correctly places primacy on RCT evidence for evaluating the effects of interventions. Randomization controls for selection bias. In nonrandomized studies, it is difficult if not impossible to control for lack of baseline comparability on measured and unmeasured factors that can affect outcomes. However, the appropriate research design is based on the question under consideration. Observational studies may be appropriate when evaluating questions such as risk factors for disease or attributable mortality. In addition, poorly designed, executed, and analyzed randomized trials do not provide reliable evidence. New methods and updates in previous methods of grading evidence are taking into account aspects of trials in addition to randomization, such as the importance to patients of the measured outcomes and the amount of missing data.[11] A more uniform and transparent process for grading evidence would help caregivers understand the limitations of the evidence in guidelines.

Third, it is unclear whether and how providers use the quality-of-evidence indicators in guidelines when making decisions or offering advice. Once guidelines make a recommendation, it is unclear whether providers incorporate the uncertainty inherent in recommendations based on less evidence into their decision-making process or whether they communicate this uncertainty to patients. It is important to know when one must make decisions with greater uncertainty, since this allows providers to determine when it is more likely necessary to deviate from guidance in individual cases. It is important for patients to understand the limitations in the evidence for them to make decisions about their own health and to understand what to expect.

Perhaps the main point we should take from the studies on quality of evidence is to be wary of falling into the trap of "cookbook medicine." The existence of guidelines is probably better than no guidelines, but guidelines will never replace critical thinking in patient care. Although the evidence and recommendations in guidelines may change across time, providers will always have a need to know *how* to think about clinical problems, not just *what* to think. Guidelines may provide caregivers with the potential answers to clinical questions, but caregivers must still generate the right questions by history taking and performing physical examinations. Caregivers must also apply the recommendations in guidelines to individual patients whose circumstances may differ substantially from the conditions under which interventions were studied in clinical trials. Guidelines also take some time to complete and publish and can be outdated almost as soon as they are published. Given the explosion in medical information, now more than ever before, providers at all levels of training need to obtain the skills to critically evaluate evidence on an ongoing basis. As with individual research studies, providers should critically evaluate guidelines and the evidence on which they are based and how relevant recommendations are locally at their institutions and in their patients. Therefore, we should take to heart the conclusions of Lee and Vielemeyer[7] that we should exercise caution when using guidelines as the sole source guiding patient care decisions. Especially for subspecialists, guidelines may provide a starting point for searching for information, but they are not the finish line. The fact that many recommendations are based on opinion should also serve as a call to future researchers to critically evaluate and study the questions that need better answers. We would do well to remember Voltaire's admonition that "opinion has caused more trouble on this little earth than plagues or earthquakes."[12]

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