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Value and limitations of clinical practice guidelines in neonatology

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SUMMARY

Given the overwhelming size of the neonatal literature, clinicians must rely upon expert panels such as the Committee on Fetus and Newborn in the USA and the National Institute for Healthcare and Excellence in the UK for guidance. Guidelines developed by expert panels are not equivalent to evidence-based medicine and are not rules, but do provide evidence-based recommendations (when possible) and at minimum expert consensus reports. The standards used to develop evidence-based guidelines differ among expert panels. Clinicians must be able judge the quality of evidence from an expert panel, and decide whether a recommendation applies to their neonatal intensive care unit or infant under their care. Furthermore, guidelines become outdated within a few years and must be revised or discarded. Clinical practice guidelines should not always be equated with standard of care. However, they do provide a framework for determining acceptable care. Clinicians do not need to follow guidelines if the recommendations are not applicable to their population or infant. However, if a plan of care is not consistent with *apparently* applicable clinical practice guidelines, the medical record should include an explanation for the deviation from the relevant practice guideline.

1. Introduction

(Ghostbusters Columbia Pictures 1984)[Dana is possessed]

Dr. Peter Venkman: I make it a rule never to get involved with possessed people.

[Dana starts passionately making out with him]

Dr. Peter Venkman: Actually, it's more of a guideline than a rule…

The *art and science* of medicine are often viewed as competing interests. In truth, the practice of medicine in the newborn intensive care unit (NICU) is a synthesis of science and art. The fundamentals of anatomy, physiology, microbiology, genetics and biochemistry are learned in medical school and then applied to everyday practice. The "art of medicine" is integrated into patient care as we begin to apply those fundamental teachings to a newborn patient under the supervision of those considered expert in a given area. This mode of education is time-honored and valuable because it uses the immediacy of the spoken word applied directly to the care of the individual infant at hand. "Wise clinicians," however, may not be as wise as we hope, the spoken word may be misinterpreted or incorrectly recalled, or the information may be outdated. Almost all teachings become obsolete with time. The limited half-life of information is best exemplified in the quote of Sidney Burwell (Dean of Harvard Medical School 1935–49) who said, "Half of what you are taught as medical students will in 10 years have shown to be wrong. Unfortunately, none of your teachers know which half" [1]. Therefore, clinicians must constantly rely on other sources of more contemporary information (medical journals, conferences, postgraduate courses, expert panels, and even the Internet) to determine if they are practising in an acceptable fashion.

One of the greatest challenges, especially for younger practitioners, is the filtering of the immense body of clinical information and choosing what seems reasonable and practical to incorporate into daily practices. Most neonatologists are willing to accept information that seems authoritative and generally in line with their own practices. By default, many clinicians accept the conclusions of systematic analyses as authoritative and the final word on evidence-based practices in the NICU. Indeed, systematic reviews are at the pinnacle of the evidence-based pyramid [2] (Fig. 1). However, as discussed below, systematic analyses are subject to

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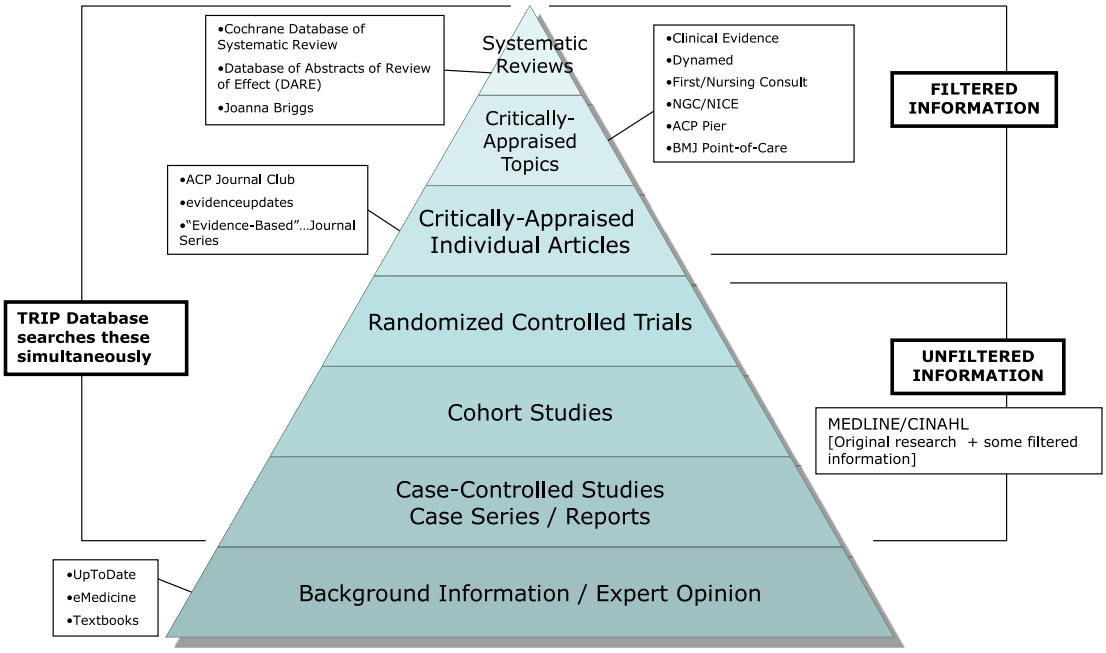

Fig. 1. Levels of evidence pyramid.

methodological problems. The alternative — reading dozens of articles or papers and trying to synthesize the material themselves — is not practical, nor within the expertise of most clinicians. Therefore, practitioners have relied upon national committees of experts (e.g., Committee on Fetus and Newborn of the American Academy of Pediatrics in the USA and the National Institute for Health and Care Excellence in the UK) for guidance.

This chapter addresses the following questions as they relate to guideline development: (i) What are the levels of evidence that guide practice? (ii) How do organizations develop guidelines? (iii) Must practitioners follow clinical practice guidelines (CPGs)? (iv) Do guidelines equate with standard of care?

2. Levels of evidence which inform clinical practice guidelines

As discussed below, CPGs should specify the quality of evidence on which they are based. The Institute of Medicine's evidence-based medicine pyramid [2] (Fig. 1) is widely used to illustrate the different levels of evidence supporting recommendations for clinical practice. Each ascending level in the pyramid represents a different kind of study design, and corresponds with increasing quality of evidence. The pyramid is most useful for comparing the relative effectiveness of therapeutic interventions. However, in addition to judging the comparative effectiveness of therapeutic interventions, there are also clinical questions that must be evaluated. These are addressed in Table 1, which is reproduced from the Oxford Centre for Evidence-Based Medicine [3]. Note that for any given evidence level, the type of evidence may vary according to the clinical question. It is also important to recognize that there may well be variations in the quality of the evidence within an evidence level. As examples, consider factors that impact the quality of the evidence at the various levels of the evidence pyramid.

2.1. Systematic reviews

In a *systematic review*, peer-reviewed publications that address a specific question are assembled, clinically appraised, and synthesized in a manner that limits bias. A systematic review may or may not include a *meta-analysis*, in which the results of separate studies are statistically integrated [4]. Although a meta-analysis should always include a systematic review, not all systematic reviews include a meta-analysis because pooling of data may not always be appropriate. This issue is discussed in more detail in *Meta Analysis* on pages 403–409 of this issue but a few points deserve emphasis regarding whether systematic analyses should be considered CPGs.

The quality of systematic reviews depends in large part on the rigor, standardization, and objectivity of the methods for selecting and appraising studies. Additionally, the quality of meta-analysis depends on (i) the objectivity of the methods for standardizing the outcome and extracting the data, (ii) critical examination of the data for the possibility of publication and other biases, (iii) evaluation of the degree of heterogeneity among studies, and (iv) the appropriateness of the model (fixed effects versus random effects) used to calculate the weighted (for sample size) average, and confidence interval of the measure of effect. Because there may not be consensus about the "correct" method of performing a particular meta-analysis, the robustness of the results to different assumptions should be tested with sensitivity analyses. If effect sizes are similar, then results of the meta-analysis are robust.

Experience has shown that meta-analyses of relatively small studies tend to overestimate effect size (especially when meta-analyses are dominated by small trials[*]). In some cases, subsequently performed large randomized trials have failed to confirm a significant effect [5]. Moreover, whereas reviews may eliminate studies of poor methodological quality from consideration, and evaluate the methodological quality of studies included in the review, evaluation of the quality of the meta-analysis itself may be not be possible, either for lack of information or because such an evaluation is beyond the capability of the reader. Thus, caution

[*] Unfortunately, small studies dominate many meta-analyses. Turner et al. [6] reported that in 70% of 14,886 meta-analyses in the Cochrane Database of Systematic Reviews in 2008, all of the studies included in the meta-analysis had a power to detect a 30% reduction in relative risk of <50%.