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More than Just EBM: Teaching How to Interpret Clinical Guidelines

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In the 1990s, Evidence-Based Medicine (EBM) emerged as a standard in clinical training, supplanting textbooks and expert reviews which were criticized for their too frequent reliance on an individual author's personal experience and opinion. Nowadays, you can expect your trainees to know the basics of how to interpret a randomized controlled trial (RCT), and many are already capable navigators through other basic methodologies such as meta-analysis. Critically appraising clinical practice *guidelines*, however, is more difficult.

In the typical EBM "pyramid of evidence," expert opinion and case series are considered low levels of evidence while RCTs and systematic reviews reside at the apex. In contrast, clinical practice guidelines occupy a plane of their own outside this construct, a mix of evidence, practicality, science, and judgment. As such, trainees require a different set of skills to deal with them.

The ability to readily interpret clinical practice guidelines is critically important as these directly impact the way we practice at the bedside. Consider the issue of when to recommend lipid-lowering therapy. A glance at the ACC/AHA's 2013 lipid guidelines reveal no fewer than 51 RCTs and meta-analyses supporting their recommendations.[1] Therefore, from a practical standpoint, we must rely on guidelines to some extent—we simply cannot read every RCT and SR that paves the roads of general medicine.

So how do we evaluate the clinical guidelines themselves? Not surprisingly, guidelines about guidelines already exist to support this agenda. The Appraisal of Guidelines, Research, and Evaluation (AGREE) II tool contains 23 items grouped into 6 categories.[2] These complex tools may seem daunting at first glance, but are certainly worth a read if you want to learn more. You do not need such tools, however, to get started. As a practical approach to teaching about clinical guidelines, here are some questions to ask:

1. What framework did the guideline authors use?

Ideally, clinical practice guidelines should be fully transparent regarding their scope, intent, and methodology. While the methodology section often is included at the beginning of a guideline, it may otherwise be hidden in an appendix or even online. For example, let's look at a few different lipid guidelines: The ACC/AHA's lipid guideline states that "Independent contractors conducted the systematic review" and followed "most" of the Institute of Medicine standards (called "Clinical Guidelines We Trust").[3] In contrast, the VA/DoD lipid guideline[4] and the United Kingdom's NICE guideline[5] each employed an independent system for guideline creation. Those systems are found in separate documents. While you may not be familiar with these different guideline development processes, you should at least look for evidence that the authors applied a known methodology in development of the guideline.

2. Who wrote the guideline?

This can affect both perspective and bias.

Perspective: Different perspectives may all be valid depending on the situation. For instance, as a non-profit advocacy group, the American Cancer Society often prioritizes cancer screening in individuals while the U.S. Preventive Services Task Force (USPSTF) as a governmental organization may have another population-based perspective. A specialty group that treats certain cancers may yet have a different point of view.

Bias: Bias is more than a different viewpoint—it renders the recommendations suspect. Look for sources of bias, such as industry or other financial ties that may influence a guideline's recommendations. While transparency is expected in developing clinical guidelines, such disclosures may still be housed deep in an appendix or online. It's worth looking for it.

3. When was the guideline written?

A guideline several years old may still be quite valid—the question is whether any new relevant data has emerged since the last guideline or guideline update. One quick way to address this is to find the guideline reference on PubMed, and then look on the right side of the Web page for similar articles and other articles that reference the guideline—newer guidelines will often appear here. Updated guidelines are often penned by new writing committees from previous editions, thus broadening the perspectives represented.

4. Look at the differences in strength and evidence for individual recommendations within a guideline.

This is a key point, and not always obvious: Not all recommendations

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within a guideline have the same weight. The major society guidelines usually contain multiple recommendations. Guidelines should use a rubric indicating the strength of each recommendation. Often the strength of the recommendation and the level of evidence supporting it are given separate ratings. Let us again look at the ACC/AHA lipid guidelines as an example. For patients with diabetes, they recommend moderate intensity statin therapy, and high intensity statin therapy if these patients are at higher estimated risk. But these recommendations do not carry the same weight: the first is assessed as a Class of Recommendation of "I" with a Level of Evidence of A, while the second is a Class of Recommendation of "IIa" with a Level of Evidence of "B".

It is impossible to know what I/A versus IIa/B really means unless you read the recommendation rating scheme. We must teach our learners to examine these differences carefully—they may not appear on the pictorial treatment algorithm, but are often of clinical importance: there is a subtle difference between recommending physicians "should" do something rather than "could".

Other guidelines such as the JNC-8 for hypertension or the CHEST guidelines for venous thromboembolic disease offer their own rating systems. To further complicate matters, in 2016 the ACC/AHA has since updated its Level of Evidence system to A, B-R, B-NR, C-LD, C-EO[6] making the recommendations of newer ACC/AHA guidelines more difficult to compare to their predecessors. This confusing alphanumeric salad of recommendation rubrics will likely continue to change—many authors are moving toward the GRADE system[7]—in the effort to make clearer just what is a "strong" versus "weak" recommendation.

5. Where is the "art" in the guideline?

At some point, there must be a transition from evidence to recommendation. This threshold may be a tentative toe in the water or a large leap of faith. For the lipid guidelines, moving from evidence that statins lower cardiovascular risk to *recommending* a percentage risk threshold—that is judgment. Did the authors explain how they reached these recommendations? How were potential benefits and harms weighed against one another? Were costs and real-world implementation considered? What about effect size? An intervention may "work," but is it "worth it?"

To be fair, this act of judgment must happen in a clinical guideline—that is what makes a guideline different than a systematic review. The whole purpose of the guideline is to interpret the evidence and translate it into a practical recommendation. This transition to interpretation may not always be explicitly stated—finding the art among the tables and IAs and 2Cs is our task. Well written guidelines should point out what clinical questions appear to be settled, which data is lacking, and where a need for additional research exists.

Thoughtful guideline authors are working to improve the guideline process. For example, the MAGIC (Making GRADE the Irresistible Choice) project employs a separate research team to analyze evidence, reduce time from evidence to recommendation, and provide point-of-care resources.[8]

Until guideline development processes become more reliably standardized and transparent, clinicans and educators may use these questions as a starting point to assist learners with varying levels of experience in assessing clinical practice guidelines.

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