New practice guidelines: Constrained or enhanced by the evidence?

Recent guidelines have revisited the management of two major modifiable risk factors for cardiovascular morbidity: hypercholesterolemia and hypertension. The authors of each purposefully emphasized high-grade evidence in generating their recommendations. But, as pointed out by Thomas et al in this issue of the *Journal*,[1] the authors of the hypertension guidelines still resorted to "expert opinion" in five of their 10 recommendations.

The authors of the new hypertension guidelines from the Eighth Joint National Committee (JNC 8),[2] as well as the new cholesterol guidelines[3] discussed by Raymond et al in the January 2014 issue of the *Journal*,[4] relied on interventional clinical trial evidence for their recommendations. The good news in the context of pay-for-performance metrics is that both of these new guidelines are easier to adhere to than the previous ones. But will the new guidelines really help us achieve better patient outcomes?

Concerns about these guidelines spring directly from their assumed major strength—ie, that they are based on interventional trial data. Well-run, randomized, controlled trials are the brass ring of evidence-based medical practice, presumably providing the cleanest demonstration of therapeutic efficacy. But with "clean" data potentially come sterile, non-real-world conclusions that may advise but should not limit our practice decisions. Most of our patients do not fit neatly into trial inclusion and exclusion criteria, nor do they exactly match the demographics of trial volunteers. Patients who participate in clinical trials are *not* the same as the patients who populate our clinics. Nor, unfortunately, is the blood pressure measurement technique likely the same in the clinical trial setting as in many of our offices.

In the clinic, it seems obvious not to be overly zealous about blood pressure control in an elderly, frail, hypertensive patient. But at the same time, aiming for a systolic pressure lower than 150 mm Hg (which is looser than in the last set of guidelines) as a target for those over age 60 is incredibly arbitrary, given that physiology and biologic risk rarely act in a step-function manner. Biologic metrics tend to behave as a continuum. If we recognize that the blood pressure can be readily and safely reduced further in a given patient, and if there are observational data to support the concept that risk for cardiovascular events roughly parallels the systolic blood pressure in a continuous manner to lower than 150 mm Hg, why aim to lower it only slightly? Trial-based guidelines are valuable, but they should not replace sound physiologic reasoning and common sense (also known as "expert opinion"). Yet we must temper this logical reasoning with lessons learned from trials such as ACCORD,[5] which showed that overly vigorous efforts at reaching theoretical therapeutic targets may be fraught with unexpected adverse outcomes.

Our challenge is to appropriately individualize therapy, usually in the absence of relevant comparative efficacy studies. Trying to apply homogenized clinical trial data

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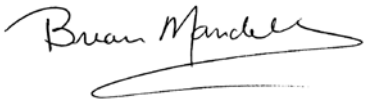
to the individual patient in the examination room is not always reasonable. Treating a 59-year-old who has a slowly escalating systolic pressure of 142 mm Hg is not the same as treating a 32-year-old who has a chronic pressure of 138 and an audible S4.

The new hypertension guidelines should be easier to implement than the previous ones in JNC 7. I like some of the specificity of the new recommendations and the disappearance of beta-blockers from the list of recommended early therapies. Yet I think that in the presence of comorbidities and end-organ damage, they may be too lax. And certain groups are left relatively undiscussed, such as patients with cerebrovascular disease, known hypertensive vascular injury, and obstructive sleep apnea, as there were limited trial data to provide guidance (although for some clinical subsets we do have very suggestive observational and experiential data). We can't always wait for the perfect trial to be done in order to make clinical decisions.

To paraphrase Thomas et al,[1] for these guidelines, one size fits many, but we still must do significant custom tailoring in the office. In the months ahead, we will try to provide some guidance on how to effectively deal with those situations where robust trial evidence is insufficient to direct clinical decision-making.



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