

# The Evidence Supporting Cardiovascular Guidelines

## Is There Evidence of Progress in the Last Decade?

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**For more than 3 decades**, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines has contributed substantially to the quality of cardiac care by developing guidelines pertaining to virtually all areas of cardiovascular disease. The intent is to provide health care professionals inundated by an ever-expanding medical literature with the evidence required for optimal patient care. ACC/AHA guidelines are revised and updated periodically, often in collaboration with other professional societies, to keep the documents current and relevant as new knowledge emerges. The purpose of guidelines is to inform clinical practice through a series of recommendations that codify the body of evidence on the disease in question according to the strength (class) of the recommendation and its underpinning level of evidence (LOE).

Because randomized controlled trials (RCTs) provide the highest standard of evidence regarding the benefit or lack thereof of a diagnostic test or treatment, ACC/AHA recommendations supported by at least 2 confirmatory high-quality RCTs or meta-analysis of high-quality RCTs are accorded the highest LOE ranking (LOE A). Recommendations stemming from less rigorous data—such as a single RCT or nonrandomized observational studies—have less quality of evidence (LOE B), while those with limited data or derived from expert consensus have even lower quality ranking (LOE C). The European Society of Cardiology (ESC) publishes its cardiovascular guidelines using a similar ranking methodology.

In 2009, Tricoci et al<sup>1</sup> published an analysis summarizing the level of evidence supporting all recommendations in the 16 ACC/AHA guideline recommendations that existed at that time. Among the 2711 total recommendations, only 314 (11%) were classified as LOE A, including only 245 (19%) of the 1305 recommendations in the strongest, class I (“should do”) category. The distribution of LOE A recommendations varied widely among the various guidelines and was highest in topics that have been the most frequent focus of RCTs, such as heart failure, secondary prevention, and unstable angina; however, even in these areas, less than 33% of class I recommendations received LOE A designations.<sup>1</sup>

The surprising findings of Tricoci et al were similar to those from subsequent analyses of guidelines in other fields of medicine.<sup>2,3</sup> In 2011, recognizing the importance of guidelines, the Institute of Medicine (now the National Academy of Medicine) updated its 1990 mandate for guideline development<sup>4</sup> and called for recommendations based on formal and systematic reviews of evidence using transparent processes that minimize conflicts of interest.<sup>5</sup> The ACC/AHA task force responded

by revising its guidelines methodology to include a more rigorous and systematic review of the literature, standards for assessing individual studies, and constitution of guideline writing committees to include a broader multidisciplinary panel of experts and key stakeholders.<sup>6,7</sup>

Whether these changes, and continued research efforts in cardiology, have resulted in guidelines that are now more substantively evidence-based is unknown. In this issue of *JAMA*, Fanaroff and colleagues<sup>8</sup> reevaluated the evidence unpinning the ACC/AHA guidelines. The results are remarkably similar to those reported by Tricoci et al a decade ago.<sup>1</sup> Despite the proliferation of guideline revisions and expansion of the guideline portfolio to additional topics of interest, still only a minority of recommendations are supported by rigorous data. Less than 10% of all current recommendations merit an LOE A ranking. Even among the class I recommendations, only 14.2% are considered LOE A, meaning that the other 85.8% of class I recommendations were based, by definition, on “usefulness or effectiveness” of the diagnostic or therapeutic strategies evaluated. As noted in the previous analysis, the distribution of LOE A recommendations varies widely among subspecialty areas and disciplines, but even among the relatively RCT-rich areas of general cardiology (eg, hypertension, hypercholesterolemia), coronary artery disease, and heart failure, less than 30% of class I recommendations are accorded LOE A support.

Fanaroff et al also provide an analysis of ESC guidelines that mirror the results of the US data, although with slightly higher percentages of recommendations with LOE A designation. In the ESC guidelines, LOE A rankings are given to less than 15% of all recommendations, less than 25% of all class I recommendations, and less than 33% of class I recommendations in general cardiology, coronary artery disease, and heart failure.<sup>8</sup>

A potential limitation of the current analysis, as noted by the authors, is that it includes only the major full guideline revisions and does not consider the guideline updates published when new data emerge that warrant changes in a few selected recommendations. It is possible that new RCT evidence might elevate a recommendation from LOE B to LOE A. However, even in recent guideline updates only a minority of the new recommendations are LOE A.<sup>9-11</sup>

Additional analyses of note by Fanaroff et al<sup>8</sup> are the trends in composition of the recommendations since 2008. The revised methodology of the ACC/AHA guidelines has led to the desired result with fewer recommendations based only on expert consensus (LOE C), resulting in a higher percentage of recommendations based on moderate-quality evidence (LOE B). Such rankings are now further characterized as B-R (moderate-quality

evidence based on 1 or more RCTs or meta-analyses of such RCTs) or B-NR (moderate quality evidence from well-designed nonrandomized data or their meta-analyses). Future guidelines could move the field forward by indicating what is needed in trials, registries, and observational studies to elevate specific recommendations from LOE B to LOE A status.

There will never be enough time, effort, or funding to implement RCTs to address all clinical scenarios that confront physicians. Moreover, RCTs are usually confined to patients of specific ages with single conditions. It should be understood that guidelines are not rules but are what the word implies—guides. Individual patients are unique and many differ from those enrolled in the RCTs on which the guidelines are based, but consistent deviation should be explained. Elderly individuals with multiple comorbid conditions, who constitute an increasing number of patients seen in clinical practice, are excluded from most RCTs. This results in the common need to extrapolate guideline recommendations built on ideal patients to the real patients seen in practice, which has elevated cardiovascular registries to a higher level of prominence. Despite the imperfections of registry data, which are often derived from administrative information embedded in electronic health records and with the potential for confounding inherent in nonrandomized databases, registries have the potential to confirm results of RCTs or to extend them to individuals with more complex, comorbid conditions. The revised ACC/AHA methodology now allows for class I, LOE A status for data derived from high-quality registry data. Because “high quality” is in the eye of the beholder, this is a step forward but one that needs careful surveillance.<sup>12</sup>

However, a contentious point of ongoing concern is the persistence of many class I, LOE C recommendations in both the current US and the European guidelines; 37% of ACC/AHA and

49% of ESC class I recommendations are considered LOE C, based principally on consensus opinion. In the absence of any real evidence, can such class I recommendations be justified?

A strong argument can be made that the majority of class I, LOE C recommendations should be downgraded to class II—from “should do” to “reasonable to consider.” However, there are certain class I, LOE C statements that populate most guidelines that need to keep the class I designation, as they remind physicians and other clinicians that the purpose of a guideline is improved patient care. For example, it is unlikely that there will ever be RCTs confirming that a history and physical examination should be performed in patients with symptoms of heart failure (LOE C), that an electrocardiogram should be performed in a patient with suspected acute coronary syndrome (LOE B), and that a multidisciplinary team is beneficial when making management decisions for patients with complex coronary artery disease or valvular heart disease (LOE C). The primacy of these recommendations ensure that guidelines remain patient-centric and do not evolve to a just-the-facts recitation of data distilled from RCTs of tests, treatments, and devices.

Patients and physicians interact in complex medical systems and deal with a bewildering amount of information with the potential for both benefit and harm. Because of guidelines’ important effect on clinical practice, industry sponsors have become intensely interested in guidelines and often plan their developmental phase for products to advance to class I, LOE A status whenever possible.

Although guidelines are imperfect and are a work in progress, they remain the cornerstone for informing clinical decisions. The important observations of Fanaroff et al are reminders that some progress has been made in a decade of evolution of cardiovascular guidelines but that there is still considerable work to do.

#### ARTICLE INFORMATION

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