Reassessment of Clinical Practice Guidelines
Go Gently Into That Good Night

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In 1990, the Institute of Medicine proposed guideline development to reduce inappropriate health care variation by assisting patient and practitioner decisions.[1] Unfortunately, too many current guidelines have become marketing and opinion-based pieces, delivering directive rather than assistive statements.

Current use of the term *guideline* has strayed far from the original intent of the Institute of Medicine. Most current articles called "guidelines" are actually expert consensus reports. It is not surprising, then, that the article by Tricoci et al[2] in this issue of *JAMA* demonstrates that revisions of the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines have shifted to more class II recommendations (conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment) and that 48% of the time, these recommendations are based on the lowest level of evidence (level C: expert opinion, case studies, or standards of care). This trend is especially disconcerting given the quantity of cardiovascular scientific literature published during the last decade.

The overreliance on expert opinion in guidelines is problematic. All guideline committees begin with implicit biases and values, which affects the recommendations they make.[3] However, bias may occur subconsciously and, therefore, go unrecognized. Converting data into recommendations requires subjective judgments; the value structure of the panel members molds those judgments.[4] Guideline consumers could adjust for these biases if guideline panels made their values and goals explicit, but usually they remain opaque.[5]

The most widely recognized bias is financial. Guidelines often have become marketing tools for device and pharmaceutical manufacturers. While the ACC and AHA receive no industry funding for guideline development, they do receive industry support to disseminate guideline products such as pocket guides. Financial ties between guideline panel members and industry are common. "Experts" on guideline panels are more likely to receive industry funding for research, consulting fees, and speakers' honoraria. In 1 study of 44 guidelines, 87% of the guideline authors had some form of industry tie.[6]

Other biases are also important. The specialty composition of a guideline panel likely influences guideline development. Specialty societies can use guidelines to enlarge that specialty's area of expertise in a competitive medical marketplace. Federal guideline committees may focus on limiting costs; committees influenced by industry are more likely to shape recommendations to accord with industry needs.

Guidelines have other limitations. Guidelines are often too narrowly focused on single diseases and are not patient focused. Patients seldom have single diseases, and few if any guidelines help clinicians in managing complexity.[7] Paradoxically, guidelines are also often too comprehensive, covering every possible intervention that could be appropriate for a patient with that single disease. Tricoci et al[2] found that in ACC/AHA guidelines with at least 1 revision, the number of recommendations increased 48% from the first guideline to the most recent version. If there is a main message in such guidelines, it is likely to be lost in the minutiae. Guidelines are not patient-specific enough to be useful and rarely allow for individualization of care. Most guidelines have a one-size-fits-all mentality and do not build flexibility or contextualization into the recommendations.[5,7] There are simply too many guidelines, often on the same topic. For instance, clinicians really do not need 10 different adult pharyngitis guidelines.[8] Moreover, guidelines are often out of date. The evidence base used to create guidelines changes quickly. Most guidelines become outdated after 5 years, and most guideline developers lack formal procedures for updating their guidelines.[9,10] The ACC/AHA guidelines are periodically updated, with updates taking a mean of 4.6 to 8.2 years until publication.[2]

As a result, many clinicians do not use guidelines. An even greater concern, however, is that some of these consensus statements are being turned into performance measures and other tools to critique the quality of physician care. This potential problem could be minimized if performance measures were derived from high-quality guidelines based on the highest level of evidence and applied to patients with a

See also p 831.

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single disease requiring little clinical judgment and no attention to patient preferences. Using multiple single disease–focused quality indicators to judge the quality of care provided to older patients with multiple comorbidities creates another level of difficulty.[7] These patients require collaborative efforts to balance each patient's overall health status with the burdens, risks, and benefits of complex care, something single disease guidelines and their resultant quality indicators do not address.

If guidelines continue to exist, they need to undergo major changes. Recently, Sniderman and Furberg[11] called for reforming the guideline development process. Their suggestions could be strengthened further by not only creating codes to "govern conflict of interest," as disclosure and governance alone will not ensure unbiased recommendations, but also by guideline panel membership limiting (if not excluding) those with financial or other potential conflicts of interest or at least being balanced by members having no conflicts of interest. Only when likely biases of industry and specialty societies have been either removed or overcome by countervailing interests can impartial recommendations be achieved.

The time has come for guideline development to again be centralized, for example under the guidance of the Agency for Healthcare Research and Quality or a group similar to the US Preventive Services Task Force. Such centralization should help reduce bias and redundancy and better guide the research agenda. The US Department of Health and Human Services seems best suited to fund guideline endeavors.

In addition, guideline development needs to be prioritized. Guidelines are not necessary for every disease but are needed for diseases having significant practice variability and for which a valid evidence base can guide recommendations. Within a guideline document, individual recommendations also need to be prioritized. For instance, recommending that a symptomatic heart failure patient with decreased ejection fraction should receive an angiotensin-converting enzyme inhibitor is clearly more important than repeatedly documenting left ventricular systolic function.[12]

Finally, guidelines need flexibility. Clinical guidelines are supposed to be guides, not rules, and one size certainly does not fit all patients. Recommendations should vary based on patient comorbidities, the health care setting, and patient values and preferences. If flexibility is to be taken seriously, the nearly automatic translation of guidelines into performance measures would require renewed attention.

These recommendations are not new but need to be heeded. However, it seems unlikely that substantial change will occur because many guideline developers seem set in their ways. If all that can be produced are biased, minimally applicable consensus statements, perhaps guidelines should be avoided completely. Unless there is evidence of appropriate changes in the guideline process, clinicians and policy makers must reject calls for adherence to guidelines. Physicians would be better off making clinical decisions based on valid primary data.

Financial Disclosures: None reported.
Additional Contributions: We thank Thomas Huddle, MD, PhD, Division of General Internal Medicine, and Stefan Kertesz, MD, MPH, Division of Preventive Medicine, University of Alabama School of Medicine, for their valuable comments on previous drafts of the manuscript. Neither individual received compensation for their contributions.

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Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

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Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.

Data Extraction The number of recommendations and the distribution of classes of recommendation (I, II, and III) and levels of evidence (A, B, and C) were determined. The subset of guidelines that were current as of September 2008 was evaluated to describe changes in recommendations between the first and current versions as well as patterns in levels of evidence used in the current versions.

Results Among guidelines with at least 1 revision or update by September 2008, the number of recommendations increased from 1330 to 1973 (+48%) from the first to the current version, with the largest increase observed in use of class II recommendations. Considering the 16 current guidelines reporting levels of evidence, only 314 recommendations of 2711 total are classified as level of evidence A (median, 11%), whereas 1246 (median, 48%) are level of evidence C. Level of evidence significantly varies across categories of guidelines (disease, intervention, or diagnostic) and across individual guidelines. Recommendations with level of evidence A are mostly concentrated in class I, but only 245 of 1305 class I recommendations have level of evidence A (median, 19%).

Conclusions Recommendations issued in current ACC/AHA clinical practice guidelines are largely developed from lower levels of evidence or expert opinion. The proportion of recommendations for which there is no conclusive evidence is also growing. These findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived.

JAMA. 2009;301(8):831-841 www.jama.com

CLINICAL PRACTICE GUIDELINES are systematically developed statements to assist practitioners with decisions about appropriate health care for specific patients' circumstances.[1] Guidelines are often assumed to be the epitome of evidence-based medicine. Yet, guideline recommendations imply not only an evaluation of the evidence but also a value judgment based on personal or organizational preferences regarding the various risks and benefits of a medical intervention for a population.[2]

For more than 20 years, the American College of Cardiology (ACC) and the American Heart Association (AHA) have released clinical practice guidelines to provide recommendations on care of patients with cardiovascular disease. The ACC/AHA guidelines currently use a grading schema based on level of evidence and class of recommendation (available at http://www.acc.org and http://www.aha.org). The level of evidence classification combines an objective description of the existence and the types of studies supporting the recommendation and expert consensus, according to 1 of the following 3 categories:

- Level of evidence A: recommendation based on evidence from multiple randomized trials or meta-analyses
- Level of evidence B: recommendation based on evidence from a single randomized trial or nonrandomized studies
- Level of evidence C: recommendation based on expert opinion, case studies, or standards of care.

The class of recommendation designation indicates the strength of a recommendation and requires guideline writers not only to make a judgment

See also p 870 and Patient Page.

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about the relative strengths and weaknesses of the study data but also to make a value judgment about the relative importance of the risks and benefits identified by the evidence and to synthesize conflicting findings among multiple studies. Definitions of the classes of recommendation are as follows:

- Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective
- Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
- Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy
- Class IIb: usefulness/efficacy is less well established by evidence/opinion
- Class III: conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

Thus, level of evidence C and class II indicate, respectively, recommendations lacking supporting evidence and those subject to uncertainties about the appropriate medical decision.

The significant increase in the quantity of scientific literature concerning cardiovascular disease published in recent years (along with the number of technical and medical advances)—if aimed to address unresolved issues confronting guideline writers—should have resulted in guideline recommendations with more certainty and supporting evidence. However, whether guidelines have truly evolved in this direction has not been systematically investigated.

Thus, we performed a systematic review of the ACC/AHA clinical practice guidelines issued from 1984 to September 2008, with intent of examining all guidelines published since 1984 for changes associated with the use of class of recommendation grading schema both for individual guidelines and categories of guidelines and evaluating the adequacy of evidence behind current guideline recommendations. Our ultimate goal was to elucidate possible gaps that may limit the evidence-based foundations of ACC/AHA guidelines and to highlight potential opportunities for improvement.

METHODS

All ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division to obtain the number of recommendations within each class of recommendation and the distribution of level of evidence designations across all guidelines. The recommendations are clearly displayed statements highlighted in each guideline document and separated from the remainder of the text. Each recommendation contains a specific designation reflecting the class of recommendation and the level of evidence. Therefore, the abstraction of the data performed for this analysis only reflected the content of the documents and was not subject to any judgment by the abstractors.

Current guidelines were defined as those posted on the ACC Web site on September 30, 2008 (http://www.acc.org/qualityandscience/clinical/topic/topic.htm#guidelines). The review included only comprehensive guideline documents; focused updates were not included because these represent an update on a limited number of recommendations and are not reflective of an entire topic. Guidelines were classified into the following categories: (1) disease-based guidelines; (2) interventional procedure–based guidelines; and (3) diagnostic procedure–based guidelines.

The aim of the analysis was to report the distribution of recommendations across classes of recommendation and levels of evidence. For current guidelines for which at least 1 previous version was available, changes in the use of classes of recommendation were evaluated by comparing the first version with the current version. Because levels of evidence were introduced only in 1998 and not consistently adopted after they were introduced, only 6 of 17 current guidelines have a previous version reporting level of evidence and were suitable to assess changes (atrial fibrillation, heart failure, stable angina, unstable angina, pacemaker, and percutaneous coronary intervention). We reported the use of class of recommendations and level of evidence in current guidelines, defined as above.

Because individual guidelines may vary widely in the numbers of recommendations, in order to weigh equally each guideline subject within each category (ie, disease, interventional, or diagnostic), the summary of the distribution of guideline recommendations within a category across the grading schemes is shown as the median of the percentage reported for each guideline subject in question. Median values are also reported to summarize the changes in each of the categories.

RESULTS

Historical Summary

From 1984 to September 2008, the ACC/AHA Joint Task Force issued 53 guidelines on 22 topics, including a total of 7196 recommendations.[3-55] Among the 53 guidelines, 24 were diseased-based, 15 were interventional procedure–based, and 14 were diagnostic procedure–based. In 1990, the class II recommendation was expanded to include classes IIa and IIb. As of September 2008, 17 of the 53 guidelines were listed as the current guidelines on the ACC Web site.

Observed Changes Over Time

The ACC/AHA guidelines are periodically updated. Among the current guidelines, 12 are revisions of previously issued documents. The mean time elapsing from the publication of a version to the update was 4.6 years (SD, 1.8 years) for disease-based, 5.4 years (SD, 2.1 years) for interventional procedure–based, and 8.2 years (SD, 2.4 years) for diagnostic procedure–based guidelines.

Considering only the current guidelines with at least 1 revision, the total number of recommendations has in-

creased from 1330 to 1973 (48% increase). The raw increase in number of recommendations was higher for diagnostic procedure–based guidelines (242 additional recommendations) than for interventional procedure–based (130 additional recommendations) or disease-based (101 additional recommendations) guidelines (TABLE 1).

Overall, the guidelines shifted to more class II recommendations and fewer class III recommendations, while the use of class I recommendations remained fairly constant over time (Table 1). Among disease and interventional guidelines, there was a definite trend toward more class II recommendations, while the proportion of class I recommendations decreased. In diagnostic guidelines, there was a greater increase in class I recommendations and a decrease in class II recommendations. In addition, the proportion of class III recommendations decreased among all guidelines, but especially for interventional guidelines.

Overall, among current guidelines, there were 1124 class II recommendations of 3044 total recommendations, with a median of 41% (interquartile range [IQR], 29%-51%) of recommendations in class II across the guidelines (TABLE 2).

Level of Evidence

From the introduction of levels of evidence in 1998 through September 2008, 33 guidelines have been released, of which 27 adopted level of evidence classification and 6 did not. Among current guidelines, only echocardiography guidelines[17] do not report level of evidence. The 16 current guidelines reporting levels of evidence, comprising a total of 2711 recommendations, classify 314 recommendations as level of evidence A (median, 11% [IQR, 6%-16%]), whereas 1246 have level of evidence C (median, 48% [IQR, 26%-57%]) (Table 2).

Among disease-based guidelines, which generally have a greater proportion of level of evidence A, there is great variability regarding the use of levels of evidence. Unstable angina/non–ST-segment elevation myocardial infarction,[51] heart failure,[28] and secondary prevention guidelines[44] have more than 20% recommendations with level of evidence A, whereas valvular heart disease guidelines[55] have only 1 recommendation (320 total; 0.3%) with level of evidence A (Table 2). Individually, most of the current guidelines include more than 50% level of evidence C recommendations, with valvular heart disease guidelines having the highest percentage at 71% (226/320).

Level of evidence A recommendations are mostly concentrated in class I (TABLE 3). Nonetheless, among all 1305 class I recommendations of guidelines reporting level of evidence, only 245 have level of evidence A (median, 19% [IQR, 11%-30%]); whereas 481 (median, 36% [IQR, 20%-50%]) have level of evidence C. Only 6 of 17 current guidelines have a previous version reporting level of evidence. Such guidelines were those updated more frequently. In this small subset, compared with the first versions reporting levels of evidence, there was a median of 6 additional level A recommendations (IQR, 5-11), 13 level B recommendations (IQR, 3-29), and 24 level C recommendations (IQR, 14-25).

COMMENT

The ACC/AHA guidelines—as an established guidance for management of cardiovascular disease—have progressively increased the number of recommendations, but these recommendations largely reflect a lower certainty of evidence. Furthermore, in current guidelines, level of evidence C—indicating recommendations based solely on expert opinion, case studies, or "standard of care"—is the most frequent designation. These findings point to consistent gaps in evidence about medical practices and the need to generate the research required to close gaps in knowledge.

Guidelines' Role and Evolution of ACC/AHA Practice Guidelines

There is a broad consensus that medical practice should be based on evidence about outcomes of therapies and interventions and in agreement with the values and preferences of the patient. This construct of evidence-based medicine is predicated on the existence of a body of evidence of benefits and risks that can be distilled into value judgments about reasonable actions that are expressed in clinical practice guidelines.[56]

During the last decade, the need for development of guidelines has increased because of advances in development of drugs and devices resulting in greater complexity for the diagnosis and treatment of cardiovascular diseases. Potential increases in health costs and risks due to marketing-driven, uncontrolled use of novel clinical options also make guidelines increasingly important.[57-60] Furthermore, the most solid evidence in guidelines is now used to develop performance measures, which are used, in turn, to judge the quality of practice, often in the context of differential payment or public reporting.

In this setting, the ACC/AHA guidelines have assumed a critical role in the establishment of standards of cardiac care and in providing benchmarks to define quality of care.[61-63] As such, it is important to recognize current limitations of the ACC/AHA guidelines to identify potential areas for improvement.

How Solid Is the Base of Evidence in Current ACC/AHA Practice Guidelines?

The considerable increase in the number of guideline recommendations across all guidelines through the current versions has not been uniformly supported by an increased volume of definitive evidence. In fact, while the overall proportion of recommendations labeled as class I has remained relatively constant, the greatest increase in guidelines recommendations has been among those subject to uncertainties, namely class II. Across guidelines, the median of recommendations in class II is currently 41%.

Level of evidence provides the link between recommendations and evidence base. Although there is significant variation among individual guidelines in

Table 1. Change in the Number of Recommendations and Distribution Across Classes of Recommendation Between First Guideline Version and Current Version[a]

Guidelines by Year of Publication	Class I		Class II		Class III	
	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
Disease guidelines						
Atrial fibrillation						
2001[6]	46/95 (48.4)		38/95 (40)		11/95 (11.6)	
2006[7]	41/111 (36.9)	–23.7	55/111 (49.5)	23.9	15/111 (13.5)	16.7
Heart failure						
1995[26]	73/127 (57.5)		33/127 (26)		21/127 (16.5)	
2005[28]	66/129 (51.2)	–11.0	44/129 (34.1)	31.3	19/129 (14.7)	–10.9
Perioperative evaluation						
1996[38]	8/28 (28.6)		8/28 (28.6)		12/28 (42.9)	
2007[40]	13/50 (26.0)	–9.3	27/50 (54.0)	88.8	10/50 (20.0)	–53.4
Stable angina						
1999[46]	67/162 (41.4)		62/162 (38.3)		33/162 (20.4)	
2002[47]	78/235 (33.2)	–19.7	98/235 (41.7)	9.0	59/235 (25.1)	23.2
Unstable angina						
2000[49]	86/139 (61.9)		38/139 (27.3)		15/139 (10.8)	
2007[51]	87/128 (62.8)	1.5	29/128 (27.5)	0.7	12/128 (9.7)	–10.2
Valvular heart disease						
1998[53]	152/321 (47.2)		114/321 (35.4)		55/321 (17.1)	
2008[55]	156/320 (48.8)	3.3	124/320 (38.8)	9.5	40/320 (12.5)	–26.8
Change in No. of recommendations	+9		+84		+8	
Change in distribution across classes, median (IQR), %		–10.2 (–17.5 to –1.2)		16.7 (9.1 to 29.5)		–10.6 (–22.8 to 10.0)
Interventional guidelines						
CABG						
1999[10]	26/56 (46.4)		19/56 (33.9)		11/56 (19.6)	
2004[11]	39/56 (46.4)	0	34/56 (40.5)	19.3	11/56 (13.1)	–33.3
Pacemaker						
1984[29]	27/87 (31.0)		29/87 (33.3)		31/87 (35.6)	
2008[14]	38/122 (31.1)	0.4	50/122 (41.0)	23.0	34/122 (27.9)	–21.8
PCI						
1988[34]	20/69 (29.0)		27/69 (39.1)		22/69 (31.9)	
2005[37]	39/136 (28.7)	–1.1	69/136 (50.7)	29.7	28/136 (20.6)	–35.4
Change in No. of recommendations	+43		+78		+9	
Change in distribution across classes, median (IQR), %		0 (–0.6 to 0.2)		23.0 (21.2 to 26.4)		–33.3 (–34.4 to –27.6)
Diagnostic guidelines						
Echocardiography						
1990[15]	58/116 (50.0)		37/116 (31.9)		21/116 (18.1)	
2003[17]	190/333 (57.1)	14.1	83/333 (24.9)	–21.9	60/333 (8.0)	–0.5
Exercise testing						
1986[23]	6/32 (18.8)		15/32 (46.9)		11/32 (34.4)	
2002[25]	15/71 (21.1)	12.7	37/71 (52.1)	11.2	19/71 (26.8)	–22.2
Radionuclide imaging						
1986[41]	14/98 (14.3)		78/98 (79.6)		6/98 (6.1)	
2003[43]	36/84 (42.9)	200.0	43/84 (51.2)	–35.7	5/84 (6.0)	–2.8
Change in No. of recommendations	+163		+33		+46	
Change in distribution across classes, median (IQR), %		14.1 (13.4 to 107.1)		–21.9 (–28.8 to –5.4)		–2.8 (–12.5 to –1.7)
Summary of all guidelines						
Change in No. of recommendations	+215		+195		+63	
Change in distribution across classes, median (IQR), %		0.2 (–9.7 to 5.7)		15.3 (6.9 to 25.4)		–16.4 (–28.4 to –2.2)

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; PCI, percutaneous coronary intervention.

[a]Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class III: conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

available evidence supporting recommendations, the median of level of evidence A recommendations is only 11% across current guidelines, whereas the most common grade assigned is level of evidence C, indicating little to no objective empirical evidence for the recommended action. The continued paucity of adequate evidence from randomized clinical trials is made most obvious by individual guidelines such as valvular heart disease,[55] which has only 1 level of evidence A recommendation and yet has 71% level C recommendations. Thus, expert opinion remains a dominant driver of clinical practice, particularly in certain topic areas, highlighting the need for clinical research in these fields. Interestingly, our findings are reflective of a specialty—cardiology—that has a large pool of research to draw on for its care recommendations. Guidelines in other medical areas in which large clinical trials are performed less frequently may have an even weaker evidence-based foundation.

Implications for Guideline Writing

The current format of the ACC/AHA practice guidelines aims to provide recommendations to a broad set of possible decision points for each disease or condition. But whether guidelines should result from knowledge only and should not contain recommendations such as those in class II or level of evidence C is a matter of debate. Another organization, the US Preventive Services Task Force, has a different policy in guideline writing that avoids issuing recommendations that are not supported by evidence.[64]

The main argument in favor of comprehensive documents is that patient care needs to be delivered and decisions made even in situations that have not been the subject of large randomized clinical trials. Physicians may need more guidance particularly in making decisions when extensive evidence is lacking. Alternatively, one might ar-

Table 2. Distribution of Class of Recommendation and Level of Evidence in Current Guidelines

		No./Total (%)						
		Class of Recommendations[a]			Level of Evidence[b]			
Guidelines	Year	I	II	III	A	B	C	None
Disease guidelines								
Atrial fibrillation[7]	2006	41/111 (36.9)	55/111 (49.5)	15/111 (13.5)	13/111 (11.7)	33/111 (29.7)	65/111 (58.6)	0/111
Heart failure[28]	2005	66/129 (51.2)	44/129 (4.1)	19/129 (14.7)	34/129 (26.4)	25/129 (19.4)	70/129 (54.3)	0/129
Peripheral artery disease[33]	2005	147/237 (62.6)	68/237 (28.1)	22/237 (9.4)	36/237 (15.3)	142/237 (60.4)	59/237 (25.1)	0/237
STEMI[45]	2004	248/422 (58.8)	123/422 (29.1)	51/422 (12.1)	57/422 (13.5)	167/422 (39.6)	199/422 (47.2)	0/422
Perioperative evaluation[40]	2007	13/50 (26.0)	27/50 (54.0)	10/50 (20.0)	6/50 (12.0)	28/50 (56.0)	16/50 (32.0)	0/50
Secondary prevention[44]	2006	38/48 (79.2)	10/48 (20.8)	0/48	11/48 (22.9)	33/48 (68.8)	4/48 (8.3)	0/48
Stable angina[47]	2002	78/235 (33.2)	98/235 (41.7)	59/235 (25.1)	15/235 (6.4)	92/235 (39.1)	128/235 (54.5)	0/235
Supraventricular arrhythmias[48]	2003	61/147 (41.5)	77/147 (52.4)	9/147 (6.1)	9/147 (6.1)	55/147 (37.4)	83/147 (56.5)	0/147
Unstable angina[51]	2007	187/298 (62.8)	82/298 (27.5)	29/298 (9.7)	70/298 (23.6)	139/298 (46.8)	88/298 (29.6)	0/298
Valvular heart disease[55]	2008	156/320 (48.8)	124/320 (38.8)	40/320 (12.5)	1/320 (0.3)	93/320 (29.1)	226/320 (70.6)	0/320
Ventricular arrhythmias and sudden cardiac death[52]	2006	103/217 (47.5)	100/217 (46.1)	14/217 (6.5)	21/217 (9.7)	69/217 (31.8)	127/217 (58.5)	0/217
Summary of disease guidelines, median (IQR), %		48.8 (39.2-60.7)	38.8 (28.6-47.8)	12.1 (8.0-14.1)	12.0 (8.1-19.1)	39.1 (30.8-51.4)	54.3 (30.8-57.5)	0
Interventional guidelines								
PCI[37]	2005	39/136 (28.7)	69/136 (50.7)	28/136 (20.6)	15/136 (11.0)	56/136 (41.2)	65/136 (47.8)	0/136
CABG[11]	2004	39/84 (46.4)	34/84 (40.5)	11/84 (13.1)	16/84 (19.0)	51/84 (60.7)	17/84 (20.2)	0/84
Pacemaker[14]	2008	38/122 (31.1)	50/122 (41.0)	34/122 (27.9)	6/122 (4.9)	45/122 (36.9)	71/122 (58.2)	0/122
Summary of interventional guidelines, median (IQR), %		31.1 (29.9-38.8)	41.0 (40.8-45.9)	20.6 (16.9-24.3)	11.0 (8.0-15.0)	41.2 (39.1-51.0)	47.8 (34.0-53.0)	0
Diagnostic guidelines								
Exercise testing[25]	2002	15/71 (21.1)	37/71 (52.1)	19/71 (26.8)	0/71	3/71 (4.2)	6/71 (8.5)	62/71 (87.3)
Echocardiography[17]	2003	190/333 (57.1)	83/333 (24.9)	60/333 (18.0)	0/333	0/333	0/333	333/333 (100.0)
Radionuclide imaging[43]	2003	36/84 (42.9)	43/84 (51.2)	5/84 (6.0)	4/84 (4.8)	58/84 (69.0)	22/115 (26.2)	0/115
Summary of diagnostic guidelines, median (IQR), %		42.9 (32.0-50.0)	51.2 (38.1-51.7)	18.0 (12.0-22.4)	2.4 (1.2-3.6)	36.6 (20.4-52.8)	17.4 (12.9-21.8)	43.7 (21.8-65.5)
Summary of all guidelines, median (IQR), %		46.4 (33.2-57.1)	41.0 (29.1-50.7)	13.1 (9.4-20.0)	11.4 (5.8-16.2)	39.4 (31.3-57.1)	47.5 (25.9-56.9)	0

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

[a] Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class III: conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

[b] Level of evidence A: recommendation based on evidence from multiple randomized trials or meta-analyses. Level of evidence B: recommendation based on evidence from a single randomized trial or nonrandomized studies. Level of evidence C: recommendation based on expert opinion, case studies, or standard of care. Summary statistics include only guidelines reporting level of evidence.

gue that in the absence of evidence, clinicians should make decisions mostly based on their personal clinical judgment—rather than on the consensus of a group of clinical experts—as well as on their direct knowledge of a specific patient's clinical situation. The possibility that an increase in recommendations in class II might lead to greater use of procedures or interventions in the setting of an uncertain benefit has not yet been widely studied. In 1 report from the ACC National Cardiovascular Data Registry, nearly 30% of percutaneous coronary interventions performed in the United States, accounting for more than 115 000 procedures, were done under a class II ACC/AHA indication.[65] In another study, 39.1% of cardiac catheterizations after an acute myocardial infarction, accounting for nearly 45 000 procedures, were classified as class II indications.[66]

The increase in number of recommendations included in the ACC/AHA guidelines is likely due to greater complexity of patient management decisions. The result has been longer documents. Recommendations with an absence of supporting evidence often require elaboration in the text to explain their rationale, which may be as extensive as the paragraphs reviewing the results of various clinical trials. Extensive documents including a large proportion of uncertain or non–evidence-based recommendations may make it increasingly difficult, when referring to a guideline, to locate the most important and/or evidence-based information relevant to an individual patient. Thus, they may reduce the implementation of evidence-based recommendations because the length of the documents may interfere with prompt access to guideline information.[67-69]

Table 3. Distribution of Levels of Evidence Across Classes of Recommendation

Guidelines	Year	Class of Recommendation–Level of Evidence, No. (%)[a]								
		I-A	I-B	I-C	II-A	II-B	II-C	III-A	III-B	III-C
Disease guidelines										
Atrial fibrillation[7] (n = 111)	2006	8 (7.2)	12 (10.8)	21 (18.9)	3 (2.7)	18 (16.2)	34 (30.6)	2 (1.8)	3 (2.7)	10 (9.0)
Heart failure[28] (n = 129)	2005	20 (15.5)	13 (10.1)	33 (25.6)	9 (7.0)	11 (8.5)	24 (18.6)	5 (3.9)	1 (0.8)	13 (10.1)
Perioperative evaluation[40] (n = 50)	2007	5 (10.0)	5 (10.0)	3 (6.0)	0	19 (38.0)	8 (16.0)	1 (2.0)	4 (8.0)	5 (10.0)
Peripheral artery disease[33] (n = 237)	2005	29 (12.2)	88 (37.1)	30 (12.7)	4 (1.7)	43 (18.1)	19 (8.0)	3 (1.3)	9 (3.8)	10 (4.2)
STEMI[45] (n = 422)	2004	45 (10.7)	95 (22.5)	108 (25.6)	5 (1.2)	50 (11.8)	68 (16.1)	7 (1.7)	21 (5.0)	23 (5.5)
Secondary prevention[44] (n = 48)	2006	10 (20.8)	26 (54.2)	2 (4.2)	1 (2.1)	7 (14.6)	2 (4.2)	0	0	0
Stable angina[47] (n = 235)	2002	12 (5.1)	34 (14.5)	32 (13.6)	1 (0.4)	39 (16.6)	58 (24.7)	2 (0.9)	19 (8.1)	38 (16.2)
Supraventricular arrhythmias[48] (n = 147)	2003	5 (3.4)	32 (21.8)	24 (16.3)	4 (2.7)	20 (13.6)	53 (36.0)	0	3 (2.0)	6 (4.1)
Unstable angina[51] (n = 298)	2007	57 (19.1)	82 (27.5)	47 (15.8)	5 (1.7)	52 (17.4)	25 (8.4)	8 (2.7)	5 (1.7)	16 (5.4)
Valvular heart disease[55] (n = 320)	2008	1 (0.3)	59 (18.4)	96 (30.0)	0	25 (7.8)	99 (30.9)	0	9 (2.8)	31 (9.7)
Ventricular arrhythmias and sudden cardiac death[52] (n = 217)	2006	19 (8.8)	32 (14.7)	52 (24.0)	1 (0.5)	35 (16.1)	64 (29.5)	1 (0.5)	2 (0.9)	11 (5.1)
Summary of disease guidelines, median (IQR), %		10.0 (6.2-13.9)	18.4 (12.6-25.0)	16.3 (13.1-24.8)	1.7 (0.4-2.4)	16.1 (12.7-17.0)	18.6 (12.2-30.1)	1.3 (0.2-1.9)	2.7 (1.3-4.4)	5.5 (4.6-9.8)
Interventional guidelines										
PCI[37] (n = 136)	2005	14 (10.3)	18 (13.2)	7 (5.1)	1 (0.7)	34 (25.0)	34 (25.0)	0	4 (2.9)	24 (17.6)
CABG[11] (n = 84)	2004	12 (14.3)	25 (29.8)	2 (2.4)	4 (4.8)	19 (22.7)	11 (13.1)	0	7 (8.3)	4 (4.8)
Pacemaker[14] (n = 122)	2008	4 (3.3)	15 (12.3)	19 (15.6)	1 (0.8)	18 (14.8)	31 (25.4)	1 (0.8)	12 (9.8)	21 (17.2)
Summary of interventional guidelines, median (IQR), %		10.3 (6.8-12.3)	13.2 (12.8-21.5)	5.1 (3.8-10.4)	0.8 (0.8-2.8)	22.6 (18.7-23.8)	25.0 (19.0-25.2)	0 (0-0.4)	8.3 (5.6-9.1)	17.2 (11.0-17.4)
Diagnostic guidelines										
Exercise testing[25] (n = 71)	2002	0	2 (2.8)	1 (1.4)	0	1 (1.4)	2 (2.8)	0	0	3 (4.2)
Radionuclide imaging[43] (n = 84)	2003	4 (4.8)	28 (33.3)	4 (4.8)	0	29 (34.5)	14 (16.7)	0	1 (1.2)	4 (4.8)
Summary of diagnostic guidelines, median (IQR), %		2.4 (1.2-3.6)	18.1 (10.4-25.7)	3.1 (2.2-3.9)	0	18.0 (9.7-26.2)	9.7 (6.3-13.2)	2.4 (1.2-3.6)	18.1 (10.4-25.7)	3.1 (2.2-3.9)
Summary of all guidelines, median (IQR), %		9.4 (4.4-12.7)	16.6 (11.9-28.1)	14.6 (5.1-20.2)	1.0 (0.3-2.2)	16.2 (13.2-19.3)	17.6 (11.9-26.4)	0.6 (0-1.7)	2.8 (1.1-5.7)	5.4 (4.6-10.0)

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

[a] Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class III: conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful. Level of evidence A: recommendation based on evidence from multiple randomized trials or meta-analyses. Level of evidence B: recommendation based on evidence from a single randomized trial or nonrandomized studies. Level of evidence C: recommendation based on expert opinion, case studies or standard of care. Summary statistics include only guidelines reporting level of evidence.

To address this problem, the ACC/AHA Task Force on Practice Guidelines has adopted a standard format by placing the recommendations in bolded format at the beginning of the discussion supporting the recommendations and by adding tables and publishing an executive summary. Other guideline writing committees may partially address these issues while still using the current format by separating the summary of clinical trial data from the interpretation of the trial data and the rationale used to justify the recommendations. The data of the present study should serve as a basis to evaluate whether the current format of the guidelines should be altered to achieve a better focus on recommendations supported by objective evidence.

The analysis presented in this article does not address cardiovascular guidelines released by other major societies, such as the European Society of Cardiology (ESC). However, it is likely that the ESC guidelines and other cardiovascular guidelines face similar challenges, particularly concerning the evidence base at the foundation of the recommendations. When guidelines address topics with limited or conflicting information, it would not be unexpected to find variation on specific recommendations between documents released by different societies. Indeed, differences between the recommendations of the ACC/AHA and ESC guidelines have been noted in recent guidelines.[51,70-72]

The presence of a large proportion of recommendations with no supporting data from randomized clinical trials requires careful judgment by guideline authors. In such circumstances, the potential for authors' conflicts of interest, real or perceived, may be important. Recommendations based only on expert opinion may be prone to conflicts of interest because, just as clinical trialists have conflicts of interests, expert clinicians are also those who are likely to receive honoraria, speakers bureau, consulting fees, or research support from industry.[73,74]

It is difficult to quantify the effect of conflicts of interest in a guideline writing process, but this was not the subject of the present study. Certainly, real or not, the perception among guideline readers that financial ties may introduce significant bias in guideline recommendations has been noted in 1 report.[69] A commonly adopted method to deal with conflicts of interest is adding disclosures, although it is not clear what effects such disclosures might have. Disclosing a conflict may make the authors wary about recommending products in which they may have an interest. However, it may also act in the opposite direction by increasing the authors' confidence in recommending such products once a conflict has been disclosed.

Major guideline-releasing organizations have recognized the importance of having a rigorous policy regarding conflicts of interest; such policies manage and balance potential conflicts rather than eliminating them. The ACC/AHA's code regulating potential conflicts of interest requires the collection and publication of relationships with industry by guideline-writing groups as well as peer reviewers. Relationships are orally disclosed at every meeting, votes are recorded for all recommendations, and members with significant conflicts abstain from voting, although they can participate in the discussion. In addition, the ACC/AHA task force now requires that 30 to 50% of writing group members have no conflicts of interest, and the guideline writing group must be chaired by someone with no conflicts of interest. Finally, there is no industry funding for guideline development, although the ACC and AHA do receive industry support for distribution of guideline derivative products such as pocket guides.

Implications for Research

The findings of this analysis indicate that the current system generating research is inadequate to satisfy the information needs of caregivers and patients in determining benefits and risks of drugs, devices, and procedures. The clinical research system in the United States has been described as a fragmented "nonsystem," with a lack of common goals, vision, and collaboration.[75] In addition, the current clinical research agenda in the United States is strongly influenced by industry's natural drive to introduce new products.[76] There is limited sponsorship of trials to address questions of comparative effectiveness or routine clinical practice. The problem of how to generate funding for research addressing practical clinical questions that do not involve a marketable product is currently unresolved. Parties with an interest include patients, health care practitioners, and payers. Frequently, patient advocacy groups are effective in raising funds or influencing congressional funding in this regard. There are examples of public-private partnerships addressing practical questions about technology, such as the Center for Medical Technology Policy.[77] Payers also may have an interest in funding research on practical clinical questions that have direct relevance to reimbursement decisions.[78] Some practical clinical questions have been funded by government agencies such as the Veterans' Administration and the National Institutes of Health, but the proportion of these budgets available for practical clinical trials appears to be limited.[79,80] A special agency to foster studies of comparative effectiveness is also under consideration.[81] The relative paucity of funding for practical clinical questions and comparative effectiveness studies deserves a prominent place in policy discussions.

In addition to the paucity of funding, the marked inefficiency of the current research system—resulting in high costs and extended duration of many clinical studies—reduces the number of questions that can be addressed. The prohibitive costs and time also may discourage researchers from developing and implementing ideas for investigator-initiated research. In this setting, even the availability of increased funding may not guarantee major achievements in research, as suggested by the

fact that despite the doubling of expenditure in research and development by industry, productivity in terms of new US Food and Drug Administration (FDA) approvals has progressively decreased in the last decade.[76] Improving the research system will require active collaboration among all of the interested parties—ie, academic, professional, and government organizations and industry. One such collaboration initiated under the FDA's Critical Path Program is the Clinical Trials Transformation Initiative.[82] The mission of this initiative is to identify practices that, through broad adoption, will increase the quality and efficiency of clinical trials.

Key research stakeholders should collaborate in generating a prioritized list of research topics. The ACC/AHA guideline writing group is now assisting in addressing this need by recommending an agenda of research priorities based on important questions that arise in the writing process about where evidence is needed.

A separate issue is the heavy focus of industry on efficacy studies in restricted patient populations necessary to gain FDA approval. Although initially important to document a drug's efficacy without the confounding of multiple disease states and interacting medications, it is also necessary to study new drugs and devices in the broader population of patients who will receive them in actual practice. These latter studies could be initiated while a drug application is waiting for review by regulatory authorities (phase 3b) or shortly after market approval.[83] These more practical clinical trials would typically address the questions that physicians and third-party payers would have in seeking the proper application of these new treatments in practice.[84]

Study Limitations

Our analysis does not account for potential changes over time in the aims of guidelines writing committees, which may have influenced the number of recommendations and the distribution across classes. Moreover, in 1990, the class II level of recommendation was expanded to classes IIa and IIb. With this definition change, standards and thresholds to determine class of recommendation may have not remained constant. Our analysis was designed to evaluate comprehensive guideline documents; therefore, the data included in this article do not reflect recommendations in focused guideline updates that have been recently released for some documents but not yet incorporated into the comprehensive documents (eg, stable angina, percutaneous coronary intervention, ST-elevation myocardial infarction). These focused updates are driven primarily by results of recent randomized clinical trials but address only a limited number of issues. The change in levels of evidence could be evaluated only in a limited number of guidelines, which are those that are updated more frequently, and may not be representative of the entire cohort of guidelines.

It was beyond the scope of this article to analyze and compare cardiovascular guidelines released by other societies and noncardiovascular guidelines. Finally, this article only addressed ACC/AHA practice guidelines, and the results cannot be directly applied to other types of documents, such as "appropriateness criteria."

CONCLUSION

Our finding that a large proportion of recommendations in ACC/AHA guidelines are based on lower levels of evidence or expert opinion highlights deficiencies in the sources of definitive data available for the generation of cardiovascular guidelines. To remedy this problem, the medical research community needs to streamline clinical trials, focus on areas of deficient evidence, and expand funding for clinical research. In addition, the process of developing guidelines needs to be improved with information about the impact that recommendations based on lower levels of evidence has on clinical practice. Finally, clinicians need to exercise caution when considering recommendations not supported by solid evidence.

Author Contributions: Dr Tricoci had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Tricoci, Allen, Kramer, Califf, Smith.
Acquisition of data: Tricoci, Allen.
Analysis and interpretation of data: Tricoci, Allen, Kramer, Califf, Smith.
Drafting of the manuscript: Tricoci, Allen, Kramer.
Critical revision of the manuscript for important intellectual content: Tricoci, Allen, Kramer, Califf, Smith.
Statistical analysis: Tricoci, Allen.
Obtained funding: Allen, Kramer.
Administrative, technical, or material support: Califf.
Study supervision: Tricoci, Califf, Smith.
Financial Disclosures: Dr Tricoci reports that as a faculty member of the Duke Clinical Research Institute, an academic clinical research organization, his salary is partially supported by research grants from Schering-Plough. Dr Kramer reports that as a faculty member of the Duke Clinical Research Institute, an academic clinical research organization, and as executive director of the Clinical Trials Transformation Initiative (CTTI), her salary is supported in part by CTTI membership fees paid by the following companies: Amgen Inc, Bayer, bioMerieux, Biotronik, Bristol-Myers Squibb, CR Bard Inc, Eli Lilly, Gemin X, Genentech, GlaxoSmithKline, Hoffman-La Roche Inc, Human Genome Sciences Inc, J&J Medical Devices & Diagnostics, J&J Pharmaceutical Research and Development, Novartis, Pfizer, St Jude Medical, The Medicines Company, and Wright Medical. Dr Califf reports that he receives research funding from Novartis Pharmaceutical and Schering-Plough; is a member of the speakers bureaus for Heart.org, Kowa Research Institute, and Novartis Pharmaceutical; and consults for ABC, Amylin, Bayer, Boehringer Ingelheim, Boston Scientific, GSK, Heart.org, Kowa Research Institute, Medtronic, Nitrox LLC, Novartis Pharmaceutical, Roche, Sanofi-Aventis, Schering-Plough, SCIUS, Targacept, University of Florida, and Vivus; and owns equity in Nitrox LLC. No other financial disclosures were reported.
Funding/Support: This project was supported by grant U18HS010548 from the Agency for Healthcare Research and Quality. Dr Smith's efforts in this work were supported by a Distinguished Scholarship from the Rose Azus Cardiac Research Education Fund, Sharp Hospital Foundation, San Diego, California.
Role of the Sponsors: No sponsor of this research participated in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.
Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

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Clinical Practice Guidelines and Scientific Evidence

To the Editor: Dr Tricoci and colleagues[1] published an analysis indicating that American College of Cardiology/American Heart Association (ACC/AHA) guidelines are largely developed from lower levels of evidence or expert opinion. They concluded that there is a "need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived." Their first conclusion could have been better substantiated by a critical appraisal of the ACC/AHA guideline methods.[2]

First, the ACC/AHA does not appear to follow Institute of Medicine recommendations to separate the systematic review process from guideline formulation.[3] Rather, the same writers appear to perform both processes.

Second, the ACC/AHA uses an overly simplistic, outdated hierarchy of study design (randomized controlled trials [RCTs] at the top) to assess level of evidence. Different types of clinical questions are best answered with different study designs. Moreover, in several recent ACC/AHA guidelines I could find no mention of quality assessment of the trials included in the body of evidence.

Third, the ACC/AHA does not document the systematic review underlying each recommendation using standard reporting criteria.[4] It appears that citations supporting each recommendation may be selected by guideline authors.

Fourth, class I recommendations are those where " . . . there is evidence and/or general agreement that [an intervention] is useful and effective." If the expert panel agrees, then supporting evidence is not required to recommend an intervention, inconsistent with an evidence-based process.

Fifth, a class IIa recommendation is based on conflicting evidence or on divergent expert opinions, yet guideline writers can use phrases such as "is reasonable" or "is probably recommended."

Sixth, I find no explicit process for translating evidence into recommendations, other than level of evidence (ie, study design) and the opinion of experts. It is important to understand what other factors are considered and how the usefulness of an intervention is determined.

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Financial Disclosures: Dr Norris reported being a member of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group; she has not received any compensation for this.

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To the Editor: In their study, Dr Tricoci and colleagues[1] pointed out that less than one-fifth of recommendations advocating a particular procedure or treatment in ACC/AHA practice guidelines were based on level A evidence. However, in using the ACC/AHA evidence grading schema to judge the quality of evidence underpinning guideline recommendations, I believe they have overestimated the strength of this evidence base. For example, under the ACC/AHA schema RCTs or meta-analyses are deemed to be level A evidence (or at worst level B if there is only a single RCT or the RCTs are small) irrespective of study conduct, end points evaluated (surrogate outcomes vs patient-centered outcomes), or the applicability of that RCT to the clinical scenario for which the recommendation is being made.

In a study evaluating the evidence cited in support of cardiovascular treatment recommendations in 9 current national guidelines (from the United States, Canada, and Europe),[2] my colleagues and I found that although two-thirds of the hypertension, diabetes, or dyslipidemia therapy recommendations cited RCTs or meta-analyses as supporting evidence, more than half of the cited studies dealt with populations, interventions, or outcomes sufficiently dissimilar to those specified in the guideline recommendation to leave the applicability of that evidence to that recommendation open to debate. As a result, only 45% of the therapy recommendations citing RCTs or meta-analyses in these 9 prominent evidence-based guidelines met a priori definitions for high-quality evidence using a grading scheme (such as that of the Canadian Hypertension Education Program[3] or the Grading of Recommendations Assessment, Development and Evaluation [GRADE] Working Group[4]) that went beyond considerations of internal validity alone to take into account clinical relevance and direct applicability of that

Letters Section Editor: Robert M. Golub, MD, Senior Editor.

evidence to the clinical scenario for which the recommendation was being made.

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Financial Disclosures: None reported.

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To the Editor: The study by Dr Tricoci and colleagues[1] underlined the difference between the reality of clinical work (which is extremely complex and cannot easily be reduced to simple standardized procedures) and clinical practice guidelines. These guidelines are intended to cover clinical reality as far as possible. However, the broader the reality, the less precise the guidelines become. From 1984 to 2008, the number of recommendations increased from 1330 to 1973 (a 48% increase), but only 11% of these recommendations were classified as level of evidence A, with 48% classified as level of evidence C.

Jorge Luis Borges wrote a 1-paragraph story[2] of a fictional empire where the art of cartography had attained great perfection. The map of a single province occupied an entire city. In time these gigantic maps were no longer satisfactory to the cartographers, who then designed a map of the empire with a size equal to that of the same territory: in effect, the map completely coincided with the empire represented. Successive generations found this map useless and abandoned it to the ravages of time. Eventually nothing remained of the map but ruins.

Guidelines seem to be striving to be such a map, with an illusory attempt to embrace the entire clinical reality. It is not clear how many physicians read and adhere to these lengthy and increasingly complicated guidelines or feel capable of choosing between disparate guidelines. Rather than endeavor to design a map with an answer for every question, I believe that it would be preferable to educate clinicians to handle clinical reality directly and without filtered advice. Physicians must be trained in a correct methodological approach to identify problems, identify the pertinent literature, and establish coherent solutions that often may not be sustained by rigorous RCTs.

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To the Editor: The study by Dr Tricoci and colleagues[1] and the accompanying Editorial by Drs Shaneyfelt and Centor[2] both rightly justified a cautious approach to standardizing a field on a national level through the use of clinical practice guidelines. However, there is a difference between standardizing care in a field and standardizing care locally, in a hospital or within a specific unit.

Even if based on lower levels of evidence, unit-based practice guidelines may still be able to recognize that approaches are roughly equivalent, with none standing out as superior. Narrowing the choices for the sake of clarity may provide a level of consistency necessary for smooth workflow and safe practices. Variations in practice on a local level contribute to confusion. Too many choices may lead to errors: hand offs can be inconsistent and nurses and ancillary staff may have difficulty adapting. With larger practices, standardization allows for more consistency, particularly for a single patient's care over a period of days to weeks.

Centralization of guidelines, as Shaneyfelt and Centor proposed, may not be the only beneficial direction. An individualized approach to practice guidelines—accounting for local demographics, resources, and conventions—may be more appropriate and effective.

A critical question, therefore, is whether in a given hospital service, faced with many equivalent therapeutic approaches to a single problem, standardization improves outcomes.

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Financial Disclosures: None reported.

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To the Editor: We strongly disagree with the Editorial by Drs Shaneyfelt and Centor[1] that impugned the clinical practice guidelines process and urged clinicians to reject calls for adherence to guidelines. As past chairs of the ACC/AHA Task Force on Practice Guidelines, we believe that their concerns have already been answered by the current ACC/AHA clinical practice guideline process.[2]

First, although an average of 50% of recommendations in ACC/AHA guidelines are based on evidence level C (expert consensus), the conclusion by Shaneyfelt and Centor that all of these recommendations reflect subjective bias was not justified. Many recommendations are based on sound clinical judgment that will never be tested in a clinical trial (eg, obtaining a 12-lead electrocardiogram in a patient presenting to the emer-

gency department with chest pain). As part of the deliberate ACC/AHA guidelines review process, the work of the writing committee is typically critiqued by an additional 35 to 50 physician leaders.[2] Thus, the final recommendations reflect the input from extensive peer review and are not simply the opinion of the writing committee members.[2,3]

Second, the values and goals of the writing committees are summarized elsewhere and are reiterated in the preamble of every guideline.[2,3] Third, relationships with industry are submitted by every writing committee member and reviewer and are published with each document.[2] It is current policy that the chair of a writing committee must be free of any relevant relationships with industry. Members are recused from voting on any recommendation for which they have a relationship with industry.

Fourth, the majority of current guidelines focus on broad-based disease management.[3] Comorbidities and key subgroups are addressed (older patients, women, diabetes mellitus, renal failure). Guidelines remain fresh by focused updates,[3] which were excluded from the analysis by Dr Tricoci and colleagues.[4]

When clinicians practice in accordance with guidelines, patient outcomes can be improved.[5] There should be a reduction in the variation of health care delivery through use of evidence-based medicine.[3] The data from Tricoci et al did not justify rejection of the use of guidelines to drive practice. Instead, novel funding sources for clinical research are needed to inform future iterations of guidelines regarding critical issues such as comparative effectiveness (among a wide array of options, not just those tested in clinical trials) and shared decision making (for which few high-quality studies are presently available).[3]

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Financial Disclosures: None reported.

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To the Editor: In their Editorial, Drs Shaneyfelt and Centor[1] called for several key changes for developing guidelines, including transparency, centralization, prioritization, and flexibility. The authors concluded that "[u]nless there is evidence of appropriate changes in the guideline process, clinicians and policy makers must reject calls for adherence to guidelines."

However, data from the CRUSADE[2] and OPTIMIZE[3] registries, which studied adherence to therapy based on ACC/AHA guidelines for acute coronary syndromes and acute heart failure, respectively, have demonstrated that increased adherence to clinical practice guidelines is associated with improved in-hospital and follow-up morbidity and mortality. These registries have enrolled more 113 000 patients at more than 600 US hospitals and have had a significant effect on validating the role of clinical practice guidelines in real-world settings. Beyond the US experience, countries such as China have also demonstrated improved outcomes associated with increased adherence to local guidelines.[4] We view these domestic and global experiences as supportive of the overall guideline process.

The authors cited the work of Fonarow et al,[5] who evaluated the effect of adherence to ACC/AHA performance measures on 90-day outcomes following hospitalization for acute heart failure. Prescription of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (1 of the ACC/AHA measures) was associated with improved clinical outcome. The absence of such an effect of the other measures does not refute their value because the purpose of these process of care measures is not to improve short-term outcome directly but to improve the provision of appropriate care processes.

While the development and dissemination of clinical guidelines can and should be improved, there are significant benefits realized from evidence-based guidelines that are currently in place. The next steps to determining how the clinical guidelines should be executed across broad populations are outcome and comparative-effectiveness studies on their application. Such research would serve to improve the evidence base on which the guidelines are based and demonstrate real-world improvements in patient-level care. Strengthening the process and increasing adherence to guidelines is likely to improve patient morbidity and mortality; however, rejecting guidelines unless "appropriate changes" are realized seems ill-advised.

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To the Editor: Without commenting on the review of clinical practice guidelines in cardiovascular disease by Dr Tricoci and colleagues,[1] we take issue with the corresponding Editorial by Drs Shaneyfelt and Centor[2] regarding such guidelines in general. The Editorial endorsed a major assumption—also promoted as a tenet of evidence-based medicine—that data based on the highest level of evidence provide an unequivocal path to improved patient care.

The Editorial considered the substantial proportion of recommendations based on results from nonrandomized studies to represent a failure of the process of developing guidelines. Similarly, the finding that many topics involve conflicting evidence was considered disconcerting. These issues were attributed mainly to the influence of specialty societies and to financial conflicts of interest. Conspicuously absent from the Editorial, however, was any mention of problems with hierarchies of evidence themselves.[3,4]

The structure of RCTs minimizes bias because of differences in participants' susceptibility to the outcome, and the benefits of numerous landmark trials can hardly be overstated. Nevertheless, limitations of RCTs[4] are too often ignored. Trials usually emphasize internal validity in terms of the patients who participated, but typically at the expense of external validity or generalizability that is crucial to the underlying reason to conduct a trial—a goal of improving patient care.

When trials in oncology enroll mostly younger patients without comorbidity, whereas most patients with cancer are older and have comorbid illness, do the results still apply? If an observational study of clinical practice finds that a drug (spironolactone) is associated with increased hospitalization and mortality, should the finding be considered weaker evidence than the original trial suggesting the same drug reduced mortality? Moreover, conflicting evidence for guideline development should be neither surprising nor disconcerting, because RCTS on the same topic often produce discordant results.[4,5]

We agree with the main point of the Editorial that the overall approach to guidelines needs improvement and that such guidelines should be "guides, not rules, and one size certainly does not fit all patients."[2] Yet, the development of guidelines, as well as overall clinical care, will benefit from a more rigorous approach to evaluating evidence. Greater emphasis should be given to the validity of observational study designs[3,4] and to the critical issue of representative results.

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To the Editor: In their Editorial, Drs Shaneyfelt and Centor[1] stated that guideline development should "be centralized, for example under the guidance of . . . a group similar to the US Preventive Services Task Force [USPSTF]." Why search for what already exists? The USPSTF guidelines are comprehensive, neutral, evidence-based, and referenced. They are updated as frequently as necessary. Their only shortcoming is that they seem to receive insufficient attention.

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To the Editor: In addition to the issues regarding clinical practice guidelines raised in the Editorial by Drs Shaneyfelt and Centor,[1] another unintended consequence of the use of guidelines is the potential adverse effect on medical education. It may be standard rhetoric to state that guidelines are just guides, and physicians must use their discretion in clinical decision making. However, bombarding students with guidelines for all scenarios in seminars, textbooks, and journals is like providing them with the printout of the destination without showing the road map. It may seem more efficient in the short-term but does little to enhance discriminatory skills and numbs the facility for critical thinking.

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In Reply: Dr Norris raises concerns about the process of guideline writing and development by the ACC/AHA. Our study focused on understanding the evolution of classes of recommendation to their present state and, more importantly, the extent to which the various levels of evidence were

present within each class of recommendation. In our review, we found nothing to suggest that the ACC/AHA evaluation of evidence results in an inaccurate assessment of the existing evidence base, although this was not a primary objective of our study and was not systematically reviewed. We judged the language used for classes of recommendation and levels of evidence to be appropriate. Given the evolution of changes in the classes of recommendation and levels of evidence ratings of the ACC/AHA, it is our conclusion that the need for recommendations is increasing at a rate much greater than the available evidence base. This situation must be addressed to comply with the request of the Institute of Medicine and others for broad use of evidence-based medicine in patient care.

The study cited by Dr McAlister regarding the importance of clinical outcomes compared with surrogate measures in the assessment of evidence underlying guideline recommendations confirms our conclusion that a broader evidence base is needed.

Dr Enia's intriguing reference to cartography reflects the concern that increasingly complex guidelines may be disregarded by clinicians. This is a legitimate concern, which we addressed in our discussion. Clear recommendations based on a strong evidence base presented in a concise, easily accessible format are an asset to efforts designed to improve physician awareness and patient outcomes. In addition, tools simplifying physicians' direct access to relevant studies are certainly desirable.

Drs Pettker and Funai raise the issue of a locally standardized practice as opposed to a field standardized practice. While standardization of practice, when equivalent choices are available, may offer practical advantages, there is currently no evidence that this will improve outcomes. On the other hand, there are reports that adherence to evidence-based guideline recommendations is associated with improved outcomes.[1]

In response to Drs Antman and Gibbons, we agree that the results of our analysis should not lead to a call for rejecting guidelines, but rather to expanding the evidence-based foundation from which guidelines are derived.

While all approaches to clinical practice guidelines can be critiqued, there is ample evidence that the application of the ACC/AHA guidelines and derivative performance measures has resulted in an important decline in mortality from acute coronary syndromes.[2,3] Thus, we hope that such critiques of the guidelines process will not detract from our main finding: the ability of the clinical research system to generate critical evidence is seriously inadequate. When adequate evidence is not available, there is no guideline process that can make up for the missing knowledge.

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Financial Disclosures: Dr Tricoci reported that as a faculty member of the Duke Clinical Research Institute, an academic clinical research organization, his salary is partially supported by research grants from Schering-Plough. Dr Califf reported that he receives research funding from Novartis Pharmaceutical and Schering-Plough; is a member of the speakers' bureaus for Heart.org, Kowa Research Institute, and Novartis Pharmaceutical; consults for ABC, Amylin, Bayer, Boehringer Ingelheim, Boston Scientific, GSK, Heart.org, Kowa Research Institute, Medtronic, Nitrox LLC, Novartis Pharmaceutical, Roche, Sanofi-Aventis, Schering-Plough, SCIUS, Targacept, University of Florida, and Vivus; and owns equity in Nitrox LLC. No other disclosures were reported.

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In Reply: We recognize that many excellent guidelines exist. We object to calling recommendations guidelines unless they meet rigorous standards. Expert opinions are important but should be labeled expert opinions rather than guidelines. The presence of fewer guidelines might actually have a greater effect on health care than the current explosion of guidelines. If guideline committees wrote 2 parallel reports—one presenting guidelines and another identifying issues that need more data and for which only expert opinion can be given—then practicing physicians would better understand those issues that deserve guidelines.

Drs Antman and Gibbons point out that many expert recommendations made in guidelines are based on sound clinical judgment and will never be tested in a clinical trial. However, what is considered sound clinical judgment changes over time. Not long ago experts recommended against using β-blockers in patients with heart failure and recommended suppressing premature ventricular contractions after myocardial infarction.[1,2] Expert opinion should not be labeled as a *guideline* because of the implied importance that term carries; it should be called a *consensus statement*. We applaud the ACC/AHA for their efforts to reduce bias and to be transparent in their guideline development process. Unfortunately, many other guideline producers have not acted similarly.

Antman and Gibbons and Drs Huffman and Bonow point to studies showing improved patient outcomes with adherence to guidelines. The cited studies retrospectively analyzed adherence to class I recommendations (conditions for which there is evidence for and/or general agreement that a given procedure or treatment is beneficial, useful, and effective) on cardiovascular outcomes. We agree that providing patients with proven therapies, whether recommended in a guideline or not, is desirable. We are concerned that guidelines recommending unproven therapies or diagnostic tests based on opinion alone might not lead to improved outcomes.

Drs Concato and Horwitz highlight the limitations of the overreliance on RCTs in developing guidelines. Randomized controlled trials are designed to maximize internal validity, often sacrificing generalizability. Guidelines may be developed with the same bias of sacrificing generalizability or flexibility. Concato and Horwitz further comment that conflicting evidence on the same topic should not be surprising or disconcerting. If guideline developers choose one study over another based on their values and biases, it seems that the resulting document should be labeled a consensus statement rather than a guideline.

Guidelines produced in one setting may not be applicable to another. Local adaptation of guidelines, as suggested by Drs Pettker and Funai, may improve flexibility, taking into account organizational and cultural context of local practices.[3] Whether local adaptation of guidelines leads to better adherence or outcomes is unclear.[4] What is clear is that physicians will still be accountable to national standards and performance measures.

Dr Bobrow questions why we are calling for further government involvement in guidelines development when the USPSTF already exists. The USPSTF only develops preventive guidelines while our Editorial focused on diagnostic and treatment guidelines.

Finally, Dr Kothari raises an interesting concern about the unintended consequence of guidelines on clinical reasoning skills of trainees. With proper guidance, guidelines could actually enhance clinical reasoning skills by helping trainees consider other factors such as patient preferences, cost, or competing health priorities that render many guideline recommendations nonapplicable to individual patients.

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Treatment for Individuals With HIV/AIDS Following Release From Prison

To the Editor: Dr Baillargeon and colleagues[1] offered compelling evidence of the poor continuity of care for individuals with human immunodeficiency virus (HIV)/AIDS transitioning to community-based health care following release from prison. This study documented discontinuity in antiretroviral therapy, but many other chronic medical conditions are affected by poor transitions of care, including diabetes, asthma, and mental illness. Disenrollment of inmates from Medicaid, Medicare, and veterans' benefits during incarceration means that even those eligible for such benefits face substantial lag time in re-enrollment at release. Former inmates may resort to costly health care utilization to have basic medical needs met,[2] resulting in inappropriate use of scarce public resources for health care. Discharge planning through the AIDS Drug Assistance Program may help reduce discontinuities in prescription drug treatment for individuals with HIV/AIDS, but for most inmates with chronic disease, such programs are unavailable. Interruptions in care can result in increased recidivism, medicolegal consequences, and mortality.[3-5]

Gaps in medical care often result from boundaries between publicly funded health care delivery systems, including jails, prisons, public health systems, universities, and the Veterans Administration. Investment in preventive care in one setting may not be rewarded by cost savings in the same setting. The lack of integration of medical care between different publicly funded delivery systems affects individuals across the spectrum of criminal justice involvement, including parole and probation. Prisons are not mandated to provide health care for individuals under correctional supervision in the community, but these individuals are sometimes denied access to care in the community because of their legal status. A lack of integration among different public systems thwarts efforts to improve transitions in care from prisons to communities, to reduce adverse outcomes, and to lower costs.

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To the Editor: Dr Baillargeon and colleagues[1] tracked the continuity of HIV therapy in a cohort of inmates in Texas following their release from prison, finding that a high percentage had gaps in HIV therapy, predisposing them to viral resistance and disease progression. Serious as these findings are, there is a much greater collective experience with