

# The New Cholesterol and Blood Pressure Guidelines Perspective on the Path Forward

Harlan M. Krumholz, MD, SM

**After much delay**, deliberation, and drama, the long-awaited updates of the cholesterol and blood pressure guidelines were released during the last 6 months.<sup>1,2</sup> These guidelines were intended to distill the wisdom that emerged since the last versions of these authoritative documents were released more than a decade ago. In 2008, the National Institutes of Health (NIH) appointed some of the nation's top experts to these respective committees and provided guidance throughout almost the entirety of their 5-year development. These documents were designed to provide instructions to the nation and the world about how to manage these common risk factors for cardiovascular disease. The decision by the NIH not to oversee the final release of the documents only intensified the interest in them.

## Related articles

For those who sought fresh ideas and new directions, the guidelines met expectations. The authors did what few writing groups with established experts do—they took a step back and questioned the assumptions of the past and, likely, the way

Emerging from these documents and others is a sense that guidelines should inform but not dictate, guide but not enforce, and support but not restrict.

that they had been teaching and practicing for decades. The cholesterol group dismantled the imperative to treat to lipid target levels, emphasized the importance of making decisions with an appreciation of absolute risk, and highlighted the difference between drugs that have been shown to reduce risk and those that have not among those that reduce low-density lipoprotein cholesterol (LDL-C) levels. The blood pressure group redefined treatment thresholds for hypertension and highlighted that the evidence was not established for many patients targeted for intervention by performance measures and public health campaigns.

The release of the guidelines was supposed to be a celebration, but the reception was not uniformly welcoming. From the outset, critics identified areas of concern. Some concerns were technical, such as the accuracy of the method to calculate risk of cardiovascular disease in the cholesterol guidelines, a critical element in its primary prevention recommendations.<sup>3</sup> Other criticisms were concep-

tual, such as whether the absence of strong evidence should lead to a change in blood pressure treatment thresholds.<sup>4</sup> The controversy left patients and physicians in limbo, not knowing whether to embrace the guidelines or withhold judgment.

Remarkably, the most radical aspect of the cholesterol guidelines—the decision to abandon targets for treatment—has drawn relatively little reaction. The guideline is mainly embroiled in a controversy about the calculator it endorses to assess patient risk. The guideline indicates that in the 40- to 75-year age group, patients without cardiovascular disease and without markedly elevated LDL-C levels or diabetes should have their risk calculated, and if they have a 10-year risk of cardiovascular disease of 7.5% or more they are classified as a group in which benefit far exceeds risk. The exactness of the risk threshold naturally led to a focus on the method of calculating that risk. To address risk calculation, the NIH commissioned another guideline group to produce tools for the assessment of cardiovascular risk.<sup>5</sup> However, different experts provided evidence that this risk calculator substantially overestimates risk, while the authors of the risk score have defended it.<sup>3,6</sup>

The 2 studies of the risk equations in this issue of *JAMA* illustrate the predicament of proving that the risk equations are good enough. The study by Muntner and colleagues,<sup>7</sup> which includes 2 authors of the cardiovascular risk guideline, investigates the performance of the risk equations in the NIH-sponsored Reasons for Geographic and Racial Differences in Stroke (REGARDS), a cohort study designed to investigate high stroke mortality in black patients in the southeastern United States. In their analysis of 10 997 study participants (aged 45-79 years) for whom atherosclerotic cardiovascular disease (ASCVD) risk may trigger a discussion of statin initiation (those without clinical ASCVD or diabetes, LDL-C between 70-189 mg/dL, not taking statins), and 338 adjudicated events (192 coronary heart disease events and 146 strokes), the authors found that the observed and predicted 5-year ASCVD risks were similar, indicating that these risk equations were reasonably well calibrated in the population for which they were designed to be used, but demonstrated moderate to good discrimination. The authors also particularly sought to determine if the undercounting of events by observational studies might account for the apparent overestimation of risk. They found that the outcomes surveillance methods in REGARDS missed about a quarter of the events that were identified when they used Medicare claims data, which presumably would be more comprehensive. The study has the disquieting conclusions that the

lack of active surveillance in observational studies may lead to many missing end points, which may explain the appearance of overestimation of risk in some cohorts.

The study by Kavousi and colleagues<sup>8</sup> evaluates the risk equations in the Rotterdam study, which enrolled a healthy European cohort of 4854 study participants with a mean age of 65 years.<sup>1</sup> Based on 344 “hard” ASCVD events (192 in men and 151 in women) during 10 years of follow-up, the authors found that the risk equations markedly overestimated risk and had, in their view, poor calibration and moderate to good discrimination. In addition, based on the risk equations and the new cholesterol guidelines, statins would have been recommended for 96% of men and 66% of women. This study raises substantial concerns about the generalizability of the risk equations and also raises the question of whether a threshold for treatment, which is admittedly arbitrary and is imbued with values about what level of risk is worth treating, is relevant to all countries. The authors could similarly ask whether these metrics are uniformly relevant to all patients even within a country.

The blood pressure guidelines also have been embroiled in controversy. In this case, it is more about whether to translate a lack of evidence into a change in the treatment threshold. The contentiousness of this issue was demonstrated by a recent article by a dissenting group of 5 of the 17 authors of the high blood pressure guidelines<sup>4</sup> who maintain that the blood pressure treatment threshold should not change and signal that the guideline was published with less than unanimous consensus. The difference of opinion is important, as shown by the article by Navar-Boggan and colleagues<sup>9</sup> in this issue of *JAMA*, who estimate that compared with the JNC-7 blood pressure guideline, the 2014 blood pressure guideline would be associated with a reduction in the proportion of US adults considered to have treatment-eligible hypertension from 20.3% to 19.5% among adults aged 18 to 59 years and from 68.9% to 61.2% among those aged 60 years or older. Extrapolating these findings to the US population would suggest that almost 6 million adults would no longer be classified as needing a hypertension medication and almost 14 million who previously were considered to not have met the guideline goal would now be considered to have their blood pressure in a reasonable range.

What is the path forward? In an era of online publications and rapid responses, fueled by the press and social media, consensus in medicine may become more elusive than in the past. However, past consensus may have been based on assumptions about evidence and patients that were never true. Perhaps this rift with these 2 new guidelines reveals the problem with the expectation that guidelines should express certainty and not emphasize the limits of evidence and role of the patient. If this is so, then the path forward may reside within these revolutionary guidelines. For within them is an even more disruptive and previously less noticed idea that could have a longer-lasting influence on medical practice. A feature of both guidelines is a focus on how guideline recommendations should be used and what constitutes good decision making.<sup>10</sup> If this idea, increasingly expressed in some guidelines, takes hold, then it may be what many will remember about them decades from now.

Both guidelines make clear that they are providing evidence-based recommendations, not ironclad rules. The blood pressure guidelines state that “these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”<sup>11</sup> In the cholesterol guidelines, for primary prevention, where the issue of the risk threshold is relevant, the authors put a step before the treatment decisions that states that patients and their physicians should engage in a discussion of patient preferences in addition to risks, benefits, and drug-drug interactions.<sup>2</sup>

Many guidelines have a paternalistic tone. The embedded assumption is that it is possible to tell physicians what should be done based on some limited clinical characteristics of the patients—and that the patients’ role in the decision is absent. Then, these documents can get translated into quality metrics that judge quality based on specific actions and into board questions that test competence based on answering how a patient—with whom a physician has never spoken—should be treated. However, not all guidelines, quality measures, and board questions adopted this perspective. For example, the cardiovascular core measures of the Centers for Medicare & Medicaid Services always allowed physicians to document if there was a reason that guideline-recommended therapy was not provided, such that it was not judged to be poor care if, for example, the patient’s preference was not to pursue that strategy.

Emerging from these documents and others is a sense that guidelines should inform but not dictate, guide but not enforce, and support but not restrict. Guidelines can provide options and recommendations for those seeking to improve the quality and quantity of their lives.<sup>11–13</sup> They can indicate strategies that are, in the opinion of the experts, outside of evidence and unworthy of pursuit. They can highlight points of uncertainty. But they should not reduce physicians to automatons and patients to passive recipients of guideline dictums. The idea of there being a “right answer” is what has entangled these guidelines in controversy, and the evolution away from this approach will have marked implications for quality measurement and board examinations. If the guidelines focus on providing recommendations and promoting choice, then the debate changes. There will still be opinions about how to interpret the evidence, such as whether to recommend therapy based on risk, but it may feel different if the guideline is not assumed to impose practice.

Future work in this area should include the following.

**Strengthen the Evidence** | Informed choice is best accomplished with strong evidence that can be personalized for an individual facing a decision.<sup>14</sup> Funding is needed for comparative effectiveness studies that reflect the challenges of everyday practice, such as whether adding a third blood pressure medication will produce a meaningful reduction in risk. It is necessary to learn from clinical experience, utilizing big data analytics to harvest knowledge from the collective experience in a way that can be useful at the bedside or clinic visit or at home. Clinicians need to know what works for whom, the size of the likely benefits, and the trade-offs in risk.<sup>15</sup>

Research into how best to assess risk needs to continue, and no single approach should be enshrined such that others cannot supersede it. Also, public dialogue about the science should be encouraged and disagreements embraced as essential elements for progress.

**Strengthen the Implementation** | The implementation of guidelines that have nuance and rely on the communication of what is known and what is uncertain requires approaches that are beyond those available to the current generation of clinicians. Physicians and other health care professionals need to abandon ideas of simple algorithms and move guideline implementation into the era of truly personalized medicine. One-size-fits-all algorithms need to give way to tools that enhance the combining of medical information, customized for the particular decision, with patient preference to produce the opportunity for each patient to make the best choice. Development and testing of tools that improve the ability to communicate information to decision makers are needed, along with investigation into better ways of assessing the quality of decisions, rather than just assessing whether specific actions were taken.<sup>16,17</sup>

**Strengthen the Patient's Voice** | Finding ways to ensure that patients have agency over their decisions in ways that are genuine will be increasingly important.<sup>17</sup> Patients and physicians

need to work together, with the clinicians in a position to assist decisions but not impose choices. Physicians need to invite discussion, support informed choice, and instill patients with the courage to participate. Patients need to know that the medical facts alone are insufficient to determine what is right for them. Their context, preferences, values, and goals must be part of the decision if the final choice is to be in alignment with their best interests.

These guidelines, with their innovations and controversy, have established a new course. Navigating it may be uncomfortable and will perhaps force clinicians to grapple with issues that have been ignored for too long. **While it is important to advocate for health and promote healthy environments and behaviors on the broader scale, for medical decision making, it is even more important to ensure informed choice with the full participation of the person who will incur the risks and benefits of the decision.**<sup>16</sup> When viewed through this lens, the controversies about the guidelines become less contentious and the focus shifts to refining the evidence and producing better ways to communicate what is known for decision-making purposes. By directing attention to that message, already firmly embedded in these guidelines with their bold recommendations and deference to patient preference, they may have accomplished more than they ever envisioned.

#### ARTICLE INFORMATION

**Author Affiliation:** Robert Wood Johnson Foundation Clinical Scholars Program, Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, Department of Health Policy and Management, Yale School of Public Health, and Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut.

**Corresponding Author:** Harlan M. Krumholz, MD, SM, Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, 1 Church St, Ste 200, New Haven, CT 06510 (harlan.krumholz@yale.edu).

**Published Online:** March 29, 2014.  
doi:10.1001/jama.2014.2634.

**Conflict of Interest Disclosures:** The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Krumholz reports that he is the recipient of research grants from Medtronic and from Johnson & Johnson, through Yale University, to develop methods of clinical trial data sharing and is chair of a cardiac scientific advisory board for UnitedHealth.

**Funding/Support:** Dr Krumholz is supported by grant U01 HL105270-04 (Center for Cardiovascular Outcomes Research at Yale University) from the National Heart, Lung, and Blood Institute.

**Role of the Sponsor:** The National Heart, Lung, and Blood Institute had no role in the preparation, review, or approval of the manuscript or decision to submit the manuscript for publication.

#### REFERENCES

1. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of

high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520.

2. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published online November 7, 2013]. *J Am Coll Cardiol*. doi:10.1016/j.jacc.2013.11.002.

3. Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. *Lancet*. 2013;382(9907):1762-1765.

4. Wright JT Jr, Fine LJ, Lackland DT, Ogedegbe G, Dennison Himmelfarb CR. Evidence supporting a systolic blood pressure goal of less than 150 mm Hg in patients aged 60 years or older: the minority view [published online January 14, 2014]. *Ann Intern Med*. doi:10.7326/M13-2981.

5. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published online November 12, 2013]. *J Am Coll Cardiol*. doi:10.1016/j.jacc.2013.11.005.

6. Lloyd-Jones DM, Goff D, Stone NJ. Statins, risk assessment, and the new American prevention guidelines. *Lancet*. 2014;383(9917):600-602.

7. Muntner P, Colantonio LD, Cushman M, et al. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. *JAMA*. doi:10.1001/jama.2014.2630

8. Kavousi M, Leening MJG, Nanchen D, et al. Comparison of application of the ACC/AHA

guidelines, Adult Treatment Panel III guidelines, and European Society of Cardiology guidelines for cardiovascular disease prevention in a European cohort. *JAMA*. doi:10.1001/jama.2014.2632.

9. Navar-Boggan AM, Pencina MJ, Williams K, Sniderman AD, Peterson ED. Proportion of US adults potentially affected by the 2014 hypertension guideline. *JAMA*. doi:10.1001/jama.2014.2531.

10. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. *JAMA*. 2013;309(2):139-140.

11. Montori VM, Brito JP, Ting HH. Patient-centered and practical application of new high cholesterol guidelines to prevent cardiovascular disease. *JAMA*. 2014;311(5):465-466.

12. Ting HH, Brito JP, Montori VM. Shared decision making: science and action [published online February 4, 2014]. *Circ Cardiovasc Qual Outcomes*. doi:10.1161/CIRCOUTCOMES.113.000288.

13. Krumholz HM. Target cardiovascular risk rather than cholesterol concentration. *BMJ*. 2013;347:f7110.

14. Krumholz HM. Real-world imperative of outcomes research. *JAMA*. 2011;306(7):754-755.

15. Krumholz HM. Patient-centered medicine: the next phase in health care. *Circ Cardiovasc Qual Outcomes*. 2011;4(4):374-375.

16. Krumholz HM. Informed consent to promote patient-centered care. *JAMA*. 2010;303(12):1190-1191.

17. Krumholz HM. Variations in health care, patient preferences, and high-quality decision making. *JAMA*. 2013;310(2):151-152.