A recent individual participant meta-analysis of statin trials has established beyond reasonable doubt that a patient’s pretreatment vascular risk is the most important, easily measurable determinant of the effectiveness of statins. In this meta-analysis, the calculated baseline vascular risk was a much better predictor of absolute treatment benefit than the degree of low-density lipoprotein cholesterol (LDL-C) lowering (Figure), and the relative benefits of lipid lowering were largely independent of baseline low-density lipoprotein levels. Numerous studies have already demonstrated that a calculated risk is a much better predictor of future vascular events than LDL-C levels alone, or indeed any other single cardiovascular risk factor. Therefore, many patients with average LDL-C levels but high calculated vascular risk will benefit significantly more from statins than patients at low vascular risk but with higher LDL-C levels. A similar individual participant meta-analysis of trials of blood pressure–lowering drugs is currently underway, and the preliminary findings are consistent with the statin results (Johan Sundstrom, MD, PhD, unpublished data, 2013).

When these findings are considered alongside the evidence that clinicians perform poorly when attempting to calculate patients’ vascular risk in their heads, it is not surprising that national and international guidelines now recommend that clinicians use a risk calculator before making new treatment decisions. Most of these risk calculators are now available as electronic tools that mathematically combine multiple individual risk factors to predict a patient’s probability of having a vascular event over the next 5 or 10 years.9 It is therefore of considerable concern that this issue of Circulation reports on a comparison of 25 CVD risk calculators using 128 hypothetical patients that found up to a 5-fold difference in predicted CVD risk for the same patient. The authors rightly conclude that the choice of calculator will have “an important impact on both risk categorization and absolute risk estimates.”

There are 2 factors likely to account for most of the variation between these calculators. First, different risk equations calculate the probabilities of different CVD outcomes. For example, a calculator that estimates total CVD (ie, both hard CVD [myocardial infarction, stroke, and coronary heart disease death] and soft CVD [new angina, transient ischemic attacks, congestive heart failure, and peripheral vascular disease]) would predict more than twice as many outcomes as a calculator that only predicts hard CVD events.2

Second, a calculator needs to be calibrated to the population to which it is to be applied, either by developing a calculator derived from a cohort study in the target population or by recalibrating an existing calculator to the target population. The former is ideal but is a major undertaking, whereas recalibration of existing equations is relatively straightforward and has been demonstrated to significantly improve the accuracy of risk prediction in both high- and low-income populations. For example, a Framingham Heart Study coronary heart disease calculator recalibrated in a Chinese population reduced an almost 7-fold overestimation of risk (eg, predicted 10-year coronary heart disease risk of 20% compared with a 3% observed 10-year risk) to a modestly underestimated risk (predicted 10-year risk, 1.5%).11

Although it is reassuring that the major differences between vascular risk calculators can be explained, the report by Allan et al highlights several important issues that need addressing now. First, what set of outcomes should be used in vascular risk calculators? The evidence-based medicine literature recommends that we should focus on “outcomes that matter to patients.” As patients, we are concerned with outcomes that impact our ability to “adapt and self manage,” whereas researchers developing risk calculators prioritize well-defined and easily measurable outcomes, such as mortality or hard CVD. More patient-focused calculators would therefore predict a broader range of outcomes than researchers would usually select. The other necessary characteristics of a meaningful set of outcomes for risk calculators are that they share similar predictors and similar treatments.

We therefore recommend using a broad outcome definition that encompasses a wide range of symptomatic “atherosclerotic” events that affect the heart and brain, as well as the peripheral circulation, and we would also include the vascular complications of diabetes and renal disease. To be included, the usual management of selected outcomes should involve lowering of blood pressure, lowering of lipid levels, or the management of dysglycemia and overweight, for example. Furthermore, to reduce the complexity of measuring multiple outcomes, perhaps the threshold for inclusion should be a hospital admission or death. This latter criterion would certainly make the recalibration of existing calculators much
Another major issue raised in the study by Allan et al is the currency of risk calculators. The authors only selected calculators they believed were commonly used, and the majority identified were derived from data collected last century. However, CVD mortality has been declining steadily at 2% to 3% per year for >30 years in many Western countries, and there have been major changes in CVD risk factor distributions during the same period. Yet few of these calculators have ever been recalibrated, and if CVD event rates continue to fall, recalibration will need to be performed on a regular basis.

In the United Kingdom, the QRISK research group has addressed the calibration issue by developing new, regularly updated CVD risk prediction equations using data prospectively extracted from the general practice records of millions of patients. Most British general practitioners now have access to QRISK electronic risk calculators, with each iteration based on more complete data. A New Zealand research collaboration has prospectively provided several thousand primary care practitioners with PREDICT, a Web-based decision support system that generates individualized CVD risk prediction scores based on a modified Framingham prediction equation and that also generates personalized treatment recommendations. The PREDICT system simultaneously stores a risk profile on each patient (currently ≈300,000 individual records) on a secure Web server that is subsequently linked by use of an encrypted national health identifier to drug-dispensing, laboratory test result, hospitalization, and death records. These data were initially used to validate existing calculators, and new risk-prediction calculators are now under development. The SCORE (Systematic Coronary Risk Evaluation) research group in Europe has taken an alternative approach using data from regional research cohorts to develop population-specific risk-prediction calculators calibrated to high- and low-risk countries.

A well-calibrated equation is, however, only 1 component of accurate risk prediction. The other significant challenge for risk calculator developers is to further improve the ability of prediction equations to discriminate between low- and high-risk patients. The ideal calculator will identify a relatively small proportion of a population who are responsible for a relatively large proportion of subsequent events. A range of novel risk markers are currently being investigated, but new, cheap, noninvasive measures that substantially improve prediction remain elusive and should be a research priority. Although current calculators have only modest predictive accuracy, it is important to appreciate that they are a major improvement on the traditional approach that in effect used semiarbitrary thresholds of blood pressure or blood lipid levels as proxies for high CVD risk. Following this traditional approach, patients with identical raised blood pressure or lipid levels could be recommended for identical treatments, despite >10-fold differences in their absolute CVD risks.

However, the major challenge today is to reduce barriers to the routine use of vascular risk calculators. In our experience, there are 2 main barriers to the regular use of calculators: they can be time consuming to apply, and their output is often difficult to understand and communicate. The traditional approach to CVD risk prediction and risk communication simply involved measuring blood pressure or blood lipids, then informing patients that their levels were too high and required treatment. The modern approach requires taking multiple measurements, inputting these into a calculator, and then facing the challenge of communicating unfamiliar risk probabilities to patients. Although the latter approach will always be more time consuming than measuring and managing single risk factors, a systematic review has identified several features that facilitate its use, including "automatic provision of decision support as part of clinician workflow, provision of recommendations rather than just assessments and provision of decision support at the time and location of decision making."

With regard to communicating the output of risk calculators, both clinicians and patients have problems understanding probabilities. A recent approach that has been demonstrated to significantly improve patients’ understanding of their vascular
risk is to translate absolute risks into a metric commonly known as “heart age.”20 Informing a 55-year-old male that his predicted 9% risk of a CVD event over the next 5 years means that he has the heart age of a 68-year-old man is more understandable than just being told his 5-year CVD risk.21,22

In conclusion, vascular risk calculators are essential clinical tools, although as demonstrated by Allan et al9 in this issue of Circulation, many of those in current use are flawed. Fortunately, the main deficiencies these researchers identified can be remedied. Nonetheless, there remains substantial room for improving vascular risk calculators, in their consistency, predictive power, and usability.

Disclosures

None.

References


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