Exchange

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RISKING YOUR HEART

How Your Health Records Can Help Predict Your Chance of Heart Attack

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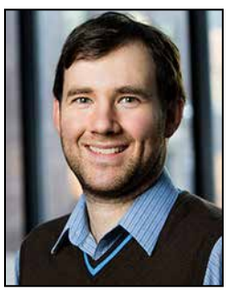

It has been nearly six years since the American College of Cardiology and the American Heart Association released the ACC/AHA cardiovascular risk model (PCE), meant to replace the earlier Framingham model, which uses individual health data in predicting patients' risk of heart attack and stroke over ten-year spans. Health systems and providers have, however, been slow to adopt the new framework: research has identified several flaws in the PCE and suggested that the Framingham Risk Score (FRS) remains more reliable. When it comes to such high-stakes predictive medicine, should clinicians stick with tried and true methods or seek ever-greater customization?

Julian Wolfson, associate professor of biostatistics at the University of Minnesota and lead author on the recent *Journal of the American Heart Association* article "Use and Customization of Risk Scores for Predicting Cardiovascular Events Using Electronic Health Record Data," says, right off the bat, that, "Data scientists, statisticians, and computer scientists still have work to do to develop better algorithms for predicting cardiovascular risk based on patient characteristics. Informaticians also need to develop better pipelines for extracting high-quality data out of messy electronic health data so it can be used to build and evaluate those algorithms." A chance meeting with Carlson School of Management professor emeritus Paul Johnson convinced Wolfson that "there was tremendous potential to apply my statistical expertise to the project." Johnson and Gediminas Adomavicius, chair of the Carlson School of Management's Department of Information and Decision Sciences, had begun on using electronic health records data to build better cardiovascular prediction models.

Wolfson describes his own path to the field as "meandering," though he has been ardently interested in biology since childhood. Books like *Microbe Hunters and The Andromeda Strain* steered him toward microbiology in college, where he discovered that he was better suited to mathematical and computer science applications of his interest. He earned his PhD in biostatistics from the University of Washington, Seattle, and landed a faculty position at the University of Minnesota, where his parents—an epidemiologist and a statistician—had spent a sabbatical many years earlier. Like his involvement in the cardiovascular risk research, the move back to Minnesota felt "serendipitous."

Partnering with Johnson, Adomavicius, and coauthors David M. Vock, Sunayan Bandyopadhyay, Thomas Kottke, Gabriela Vazquez-Benitez, and Patrick J. O'Connor, Wolfson set out to consider several questions in the new *JAHA* piece. First, when used with electronic health data (EHD), do FRS scores, based on data up to 45 years old, yield accurate estimates that are still valid for contemporary patients? Does the PCE model obviate the FRS model? And can refitting risk scores using EHD improve the risk models' accuracy?

> *...established, 'off-the-shelf' cardiovascular risk prediction models" seem to produce relatively accurate, reliable information to guide patients and their care teams.*

To answer these questions, the researchers turned to a virtual data warehouse used by Minnesota's HealthPartners. The dataset was first narrowed to some 84,000 patients who had been enrolled in the health insurance plan for at least 12 consecutive months between the years 2001 and 2011, who had at least two medical clinic visits with blood pressure readings at least 30 days (but no more than 1.5 years) apart, and who had prescription drug coverage. Then the data was split into two halves: the first was used in a "training set" culled to help refit both FRS and PCE scores using the specific population at hand. The second set was used to test the performance of both the original and refitted measures. As the paper reports, "Overall, both the original and refitted FRS and PCE produced relatively accurate risk predictions," and, "in fact, the FRS performs somewhat better than the PCE in our cohort." Further, "Refitting models using EHD did not offer substantive improvements... and is unlikely to be necessary in practice." The authors are also careful to point out that their data did not include modifications to the risk models that might attempt to estimate the effects of post-baseline interventions on patients' risk of heart attack or stroke, as the goal of the study was to evaluate the performance of existing risk models, which do not explicitly account for such interventions.

ABOUT Exchange, a publication from the Medical Industry Leadership Institute, features dialogue on medical industry research and application. The content is a summary of research from both academia and the medical industry, followed by commentary on the importance of the research and its application. Topics highlighted in the Exchange span all sectors of the medical industry and include commentary from leaders in the field, as well as researchers from the University of Minnesota and other academic institutions.

In summary, both the FRS and PCE remain valid predictive tools to guide health policy and individual patient care. For both clinicians who have been reticent to adopt a newer model, let alone customize that model with EHD on their specific patient population, and those eager to adopt the newest, most innovative approaches, all this is good news: even what Wolfson calls "established, 'off-the-shelf' cardiovascular risk prediction models" seem to produce relatively accurate, reliable information to guide patients and their care teams.

Wolfson returns to these folks—patients and medical caregivers—when he thinks about the competing cardiovascular risk measures: "It doesn't make daily headlines, but in the medical community, there is an ongoing debate about how to best manage patients who are at risk of heart attack or stroke." Trusting the measures that identify high-risk patients is a first step toward preventing such often devastating health events. ■

Commentary

***Michael D Miedema, MD, MPH**, Director of Cardiovascular Prevention, Minneapolis Heart Institute*

Cardiovascular Risk Prediction: A Crystal Ball that isn't Crystal Clear

In the 1950s, heart attacks had spiked in the United States, and there were virtually no treatment options. A group of scientists gathered over 5,000 middle-aged men and women in Framingham, Massachusetts, using close observation to help determine what does and doesn't increase risk for cardiovascular disease (CVD). Their main take-home was that CVD is a multifactorial disease. It's not just cholesterol that causes a heart attack, but cholesterol and blood pressure and blood sugar and smoking and diet and exercise and so forth.

So the Framingham investigators built what's known as the Framingham Risk Score (FRS), which factors in multiple different measurable risk factors to determine the absolute risk for a specific patient's cardiovascular event in the next 10 years. Initially published in the 1970s, the FRS had limited clinical utility because the calculations were so complex (there wasn't an app for that) and there were so few prevention options for CVD. Fast-forward to 2013, and suddenly risk prediction models became much more relevant as the American College of Cardiology/American Heart Association (ACC/AHA) issued cholesterol guidelines recommending preventative statin therapy based on absolute risk of CVD.

While the FRS was the landmark CVD risk prediction model, valid concerns had been raised regarding the lack of ethnic diversity in Framingham as well as the validity of applying the FRS to modern populations (rates of CVD have drastically decreased in the US over the last 50 years). Therefore, the ACC/AHA cholesterol guidelines committee created a new model, the pooled cohorts equation (PCE), which has become an integral part of CVD prevention in the U.S., including guidelines for cholesterol, aspirin, and blood pressure.

The advent of the electronic health record has created the opportunity to further analyze the validity of the FRS and PCE in large populations of "real-world" patients, as Julian Wolfson and his colleagues have done in their recent publication. By looking at the performance of the PCE and FRS in a large, modern sample, they confirmed that both risk scores are reasonably well-calibrated. Importantly, while multiple studies have shown that the FRS and PCE can over-predict risk when applied to modern cohorts—possibly because cohort populations are biased toward lower CVD rates since healthier individuals are more likely to volunteer for such studies—Wolfson and colleagues showed that both measures are appropriate when applied, via electronic health record data, to a more representative, "real-world" sample of patients.

This study also found that both models provide only modest discrimination for CVD, with a C-statistic of ~0.75. Essentially, the C-statistic measures a model's predictive capacity, with a 1.0 suggesting a perfect diagnostic took with no false-positives or false-negatives. Models with a c-statistic of ~0.9 are excellent tests, models with a c-statistic of ~0.8 are good tests, and models in the ~0.7 range are only modestly predictive. Because multiple studies have shown that CVD events frequently occur in individuals deemed low-risk by either the PCE or FRS and that they relatively infrequently occur in those individuals deemed high-risk, improving the discrimination of CVD risk models is a difficult, but crucial goal for diagnosticians. In fact, most newly discovered biomarkers and genetic tests have failed to improve on basic risk models. One promising improvement has arisen out of studies showing that coronary artery calcium scoring, a marker underlying plaque build-up, can personalize risk assessment and significantly improve risk prediction models, bringing their c-statistics into the more favorable ~0.8 range. Thus the recently released 2018 ACC/AHA cholesterol guidelines recommend the use of coronary artery calcium scoring for individuals at intermediate risk of CVD to help determine whether statins should be prescribed.

Wolfson and his colleagues have done a nice job of demonstrating the use of electronic health record data to assess the performance of the FRS and PCE in a modern, real-world population. These data are important for clinicians as we engage patients in discussions about their cardiovascular risk and the potential benefits of various preventive interventions. If the goal of cardiovascular prevention is to develop a CVD risk "crystal ball" so that we can know with certainty which patients to treat aggressively and which patients can avoid unnecessary therapies, further research is needed. For now, we need to be clear with our patients that when it comes to predicting their CVD risk, our crystal ball isn't crystal clear. ■