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Brief Communication

A population approach using cholesterol imputation to identify adults with high cardiovascular risk: a report from AHRQ's EvidenceNow initiative

Samuel Cykert,[1] Darren A DeWalt,[1] Bryan J Weiner,[2] Michael Pignone,[3] Jason Fine,[4] and Jung In Kim[4]

[1]The Division of General Medicine and Clinical Epidemiology and the Cecil G. Sheps Center for Health Services Research, the University of North Carolina, Chapel Hill, North Carolina, USA, [2]Department of Global Public Health, School of Public Health, University of Washington, Seattle, Washington, USA, [3]The Department of Medicine, The Dell Medical School, University of Texas, Austin, Texas, USA, and [4]The Department of Biostatistics, The Gillings School of Global Public Health, the University of North Carolina, Chapel Hill, North Carolina, USA

Corresponding Author: Samuel Cykert, MD, The Division of General Medicine and Clinical Epidemiology and the Cecil G. Sheps Center for Health Services Research, the University of North Carolina, 145 N. Medical Drive, CB# 7165, Chapel Hill, NC 27599 USA (samuel_cykert@med.unc.edu)

ABSTRACT

Objective: Large practice networks have access to EHR data that can be used to drive important improvements in population health. However, missing data often limit improvement efforts. Our goal was to determine the proportion of patients in a cohort of small primary care practices who lacked cholesterol data to calculate ASCVD risk scores and then gauge the extent that imputation can accurately identify individuals already at high risk. 219 practices enrolled. Patients between the ages of 40 and 79 years qualified for risk calculation. For patients who lacked cholesterol data, we measured the effect of employing a conservative estimation strategy using a total cholesterol of 170 mg/dl and HDL-cholesterol of 50 mg/dl in the ASCVD risk equation to identify patients with $\geq$ 10%, 10-year ASCVD risk who were eligible for risk reduction interventions then compared this to a rigorous formal imputation methodology. 345 440 patients, average age 58 years, qualified for risk scores. 108 515 patients were missing cholesterol information. Using the "good value" estimation methodology, 40 565 had risk scores $\geq$ 10% compared to 43 205 using formal imputation. However, the latter strategy yielded a lower specificity and higher false positive rate. Estimates using either strategy achieved ASCVD risk stratification quickly and accurately identified high risk patients who could benefit from intervention.

Key words: informatics, cardiovascular disease, risk scores, registry

Cardiovascular disease (CVD) remains the leading cause of death across the United States and is particularly devastating in the North Carolina counties associated with the "Stroke Belt" where as many as half of these deaths may be preventable.[1,2] Despite this outlook, adoption of new evidence and recommendations in the practice community to potentially reduce this risk remains slow. An example

of this phenomenon is the implementation of the new American College of Cardiology-American Heart Association (ACC-AHA) guidelines for cholesterol management published in 2013.[3] Four years have passed, but the Centers for Medicare and Medicaid Services and most primary care practices have not adopted these recommendations as a standard. A major component of the ACC-AHA

approach is risk-based statin prescribing, but many barriers inhibit implementation of these guidelines, such as poor capability of many certified electronic health records (EHRs) to automate atherosclerotic cardiovascular disease (ASCVD) risk calculation and to measure and create reports on guideline adherence. These barriers are particularly onerous for small primary care practices that lack information technology personnel and financial resources to pay vendors to do de novo programming involving new evidence and new quality measures.

In response to the slow diffusion of new patient-centered evidence in primary care, the Agency for Healthcare Research and Quality (AHRQ) launched the EvidenceNOW (EN) grant initiative. EN funded 7 cooperatives across the United States to rapidly implement strategies to reduce CVD risk in small primary practices. When possible, AHRQ wanted EN cooperatives to add newer evidence-based approaches that could affect whole practice populations. Heart Health Now (HHN) is the North Carolina Cooperative for EN and is incorporating on-site practice facilitation services and novel risk stratification tools to achieve CVD risk reduction for North Carolina adults in participating practices. Targets for practice improvement include better hypertension control, aspirin use for patients at appropriate risk, smoking cessation counseling, and the new ACC-AHA recommendations for statin treatment including patients with known ASCVD, diabetics with LDL cholesterol between 70 and 189, all patients with LDL cholesterol > 189, and those identified with high, 10-year ASCVD risk scores. In this report, we describe the implementation of risk stratification and a population health strategy that used formal imputation to identify important CVD risk reduction opportunities for high-risk patients and compared this to an approach that more conservatively employs consistent estimation of good cholesterol values to address the population with missing lab data and identify individuals with a high certainty of ≥ 10% ASCVD risk.

METHODS

HHN is a step-wedged, stratified, cluster randomized trial. Study procedures and methods were published previously.[4] Since cardiovascular risk reduction through quality improvement techniques was the focus of HHN, the UNC Institutional Review Board deemed the study as exempt.

Clinical data for our analysis including all components of the ASCVD risk score (age, smoking status, blood pressure, diabetes status, gender, race, HDL cholesterol, and total cholesterol) were collected from the HHN registry, which was constructed using daily uploads of EHR data from participating practices. Briefly, primary care practices were recruited in North Carolina to implement both new and standard clinical measures that reduce cardiovascular risk for adult patients. The intervention for participating practices began in January 2016 and ended in November 2017. It consisted of provision of "1 to 1" practice coaching to implement quality improvement strategies including rapid cycle techniques.[5,6] Practices also received access to a CVD population management dashboard designed specifically for their practice from the HHN registry. To be eligible, practices had to have 10 or fewer clinicians at a single clinic location and an EHR. All adult patients between the ages of 40 and 79 years were assigned an ASCVD 10-year risk percentage based on published algorithms.[3] 31.4% of patients receiving care at participating sites lacked the cholesterol laboratory data needed for the automated risk calculation. We therefore decided to measure the potential population effect using formal imputation models to

identify patients with a greater than 10%, 10-year ASCVD risk, regardless of known cholesterol value, who would be eligible for risk reduction interventions without delay and compare this approach to consistently inserting estimated "good" values for total cholesterol (170 mg/dl) and HDL cholesterol (50 mg/dl) as a more conservative technique to ensure a high certainty of high risk in the absence of lab results. Mean imputation for HDL and total cholesterol was implemented by separately fitting linear regression models to HDL cholesterol measurements and total cholesterol measurements for subjects with valid cholesterol measurements. The independent variables in the regression models were those variables needed for the calculation of the risk scores: gender, race, age, hypertension, diabetes, smoking, and systolic blood pressure. Outlying cholesterol values exceeding 1000 and subjects with unknown gender were excluded from the model fitting, yielding a total of 236 684 and 236 655 observations for total and HDL cholesterol, respectively. The mean cholesterol values based on the fitted models were imputed for subjects with missing cholesterol values—the group not used in the model fitting. These imputed values were combined with the independent variables described above to calculate risk scores for these subjects.

The more conservative, estimated values were used in the risk scores actually presented to the practices. Although these estimated scores were displayed for potential clinical use, the dashboard still delineated patients whose scores were just estimates and indicated the need for lab data to determine actual risk scores. We also advised practices through personal contact, webinars, web-based modules, and their practice facilitators that individuals with a calculated risk of ASCVD 10-year risk of 10% or higher should receive a strong recommendation for statin therapy and those with 7.5% to 10% risk should be engaged in shared decision making as per the most recent United States Preventive Task Force recommendations.[7]

In addition to showing the effect of rigorous, formal imputation and inserting estimated "good values" to identify patients who are likely high risk even without cholesterol data, we also included bivariate comparisons of patient characteristics to demonstrate the relative comparability of the groups with and without available labs at baseline. We also compared the 2 methodologies using estimated good values and formal imputation for risk scores (dichotomized to ≥ 10% as high risk as indicating treatment vs. all individuals

Table 1. Practice characteristics of primary care sites participating in the Heart Health Now project

Variable	Percentage of practices N = 219
Location rural or micropolitan	52
Clinician owned	59
Federally qualified or rural health center	29
Hospital owned	13
PCMH recognized	61
Number of providers per practice (N)	7

Average practice payer mix	Percentage of patients (standard deviation)
Medicare insured	28 (17)
Medicaid insured	16 (11)
Dual Medicaid and Medicare	10 (10)
Commercially insured	30 (18)
Other insurance	4 (20)
No insurance	12 (14)

Table 2. Patient characteristics of those assigned a 10-year ASCVD risk score in Heart Health Now[a]

Variable	Total populationaged 40–79 yrs. (N = 345 440) percent	Population with lipid labs available (N = 236 925) percent	Population with lipid labs missing (N = 108 515) percent
Female gender	58	58.2	55.1
Black race	20	20.1	20.4
White race	78	78.1	77.9
Hypertension Diagnosis	55	57.1	51.3
Diabetes Diagnosis	17.9	18.6	16.2
Mean age in years (standard deviation)	58 (10)	58.2 (10.5)	57.1 (10.5)

[a]Between group differences shown in Table 2, though small, are all statistically significant ($P < .001$) because of the large numbers contained in each group.

< 10%) to actual results for the subgroup of patients who had labs performed later.

RESULTS

Two-hundred and forty-five primary care practices that manage adult patients enrolled in the study. Twenty-six withdrew before initiating the intervention. For the 219 remaining practice sites, 345 440 patients aged 40 to 79 years were entered into the HHN registry. See Table 1 for practice characteristics and payer mix. Patient characteristics derived from EHR data for the 40 to 79 age group receiving risk scores are shown in Table 2 for the total population, the group with cholesterol labs available at baseline, and the group with missing values needing imputation. Note that all between group differences shown in Table 2, though small, are statistically significant ($P < .001$) because of the large numbers contained in each group. 108 515 patients were missing cholesterol laboratory values needed for the risk score and had values imputed as described above. Over one-third of the patients with the consistent "good value" estimated cholesterol values (40 565) qualified for initiation of statin therapy with an ASCVD risk score ≥ 10% despite this conservative approach. This number increased to 43 205 using the formal imputation model techniques. 22 909 patients did not have cholesterol labs available at baseline but had them performed later. When considering the estimated good value and, separately, the formal imputation ASCVD risk score as a "test," and the actual risk score ≥ 10% as the gold standard, the "test" utilizing the consistent good values estimates of total cholesterol of 170 mg/dl and HDL-C of 50 mg/dl demonstrated a positive predictive value of 97%, a sensitivity of 93.1%, and a specificity of 96.8%. In comparison, the formal mean imputation that was fitted using linear regression modeling for cholesterol values yielded a positive predictive value of 82%, a sensitivity of 86.8%, and a specificity of 81.9%. Note that the new statin prescription rate for risk scores derived from actual lab values was 16.2% compared to 13.5% for the group with estimated scores ($P < .001$).

DISCUSSION

Diffusion of new evidence remains slow and both QI and informatics support in small primary care practices remains lacking.[8] This confluence of factors contributes to suboptimal cardiovascular risk reduction, particularly in rural and underserved areas.[9,10] The ASCVD risk score has been recommended[3] as a tool to identify

high-risk patients for rapid, effective risk reduction.[11] However, our results show that many small practices lack access to cholesterol laboratory values needed to calculate the score for a third of their patients. While we recommend that actual cholesterol values be obtained in a timely manner, the strategy described here suggests 1 of 2 approaches: (1) target high-risk patients for quicker visit outreach and draw the appropriate labs prior to initiating therapy or (2) initiate therapy (and draw baseline labs or not) by reengaging patients at the earliest possible visit. Given that the specificity and positive predictive value of the estimated "good value" risk scores were quite high among those who eventually had available labs and that absolute LDL-C targets are no longer used to titrate treatment in new guidelines,[3] the argument could be made that preventive treatment alone would be more cost effective. The latter approach would avoid treatment delays and result in lower CVD morbidity and mortality for some at highest risk with very few false positive results. By utilizing "good" value estimates for missing cholesterol data on a population basis, we identified thousands of patients in this group who qualified for immediate preventive opportunities while shrinking the group slated for delays to a lower-risk population. The fact that inserting "good" values for cholesterol results performed better than the formal mean imputation technique suggests that formal imputation of cholesterol based on other ASCVD risk factors has limited value; even though 43 205 patients were identified as high risk compared to 40 565 in the "good value" estimated group, the low specificity and positive predictive value suggests that most of this difference represents false positives. Also, the small overall difference in new statin prescribing in practices using estimates compared to practices using actual risk score values suggests that clinicians understand and accept this approach.

In conclusion, a population health strategy using either conservative cholesterol estimation or formal imputation techniques for missing values for ASCVD risk stratification can rapidly identify large numbers of high-risk patients and help avoid delays in implementing risk reduction strategies. Also, in a generic sense, this approach also points out the opportunity to use large aggregates of clinical data, even given the inevitability of missing or imperfect data elements, to systematically benefit large groups of individuals at risk.

interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

CONTRIBUTORS

All authors made substantial contributions to the conception or design of the work (SC, BW, DD, MP); or the acquisition, analysis, or interpretation of data for the work (JF, JK, SC BW, DD, MP); drafting the work or revising it critically for important intellectual content (all authors); final approval of the version to be published (all authors); and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (all authors).

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