Estimated versus observed 10-year atherosclerotic cardiovascular event rates in a rural population-based health initiative: The Heart of New Ulm Project

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ABSTRACT

Objective: Assess discrepancy between estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk and observed 10-year event rates in a rural population participating in cardiovascular health initiative.

Methods: The study included a rural sample of individuals participating in the Heart of New Ulm (HONU), a population-based health initiative aimed at reducing ASCVD risk in a rural community. HONU conducted over 100 baseline screening events with 5221 individuals participating in 2009. For this analysis, we included participants who were aged 40–79 years, free of ASCVD at baseline, and had adequate data to calculate 10-year ASCVD risk. Electronic health record data and state death records were used to determine rates of non-fatal myocardial infarction and stroke, and ASCVD death from 2010–2019. ASCVD event rates were compared to estimated 10-year risks calculated using the Pooled Cohort Equations, stratified by sex and clinically relevant risk categories.

Results: The sample (*n* = 2819, mean ± SD age 56.1 ± 9.9 years, 59.6% female) had a low prevalence of tobacco use (8.1% current smokers) and diabetes (6.5%) and a high prevalence of hypertension (44.4%) and hyperlipidemia (56.6%). The median estimated 10-year ASCVD risk for the entire sample was 5.7% (IQR 2.3–13.5%) with an observed 10-year ASCVD event rate of 3.4%. The largest gap between observed and estimated risk was in those at intermediate/high (≥7.5%) ASCVD risk (median 10-year risk 15.8% [IQR 10.4–29.0], observed ASCVD event rate 6.4%).

Conclusio: In a sample of rural participants exposed to a multifaceted ASCVD prevention initiative, observed rates of ASCVD were substantially lower compared to estimated ASCVD risk. The potential for significantly lower than predicted ASCVD event rates in certain populations should be included in the clinician-patient risk discussion.

1. Introduction

Accurate assessment of atherosclerotic cardiovascular disease (ASCVD) risk is essential to the optimal allocation of therapies for the primary prevention of ASCVD. The Pooled Cohort Equations (PCE), developed in conjunction with the 2013 American College of Cardiology/American Heart Association (ACC/AHA) cholesterol guidelines, provides a 10-year estimate of ASCVD risk to help guide treatment decisions for statin therapy in adults without established ASCVD [1]. While the PCE has been validated in the general US population, the calibration of the PCE to certain modern populations has been questioned, underpinned by the demographically heterogeneous nature of the US [2]. There is evidence that the PCE overestimates ASCVD risk in certain populations such as postmenopausal women, and underestimates risk in others, such as those with chronic inflammatory diseases or lower socioeconomic status [3–7].

The Heart of New Ulm (HONU) Project was a 10-year community-based cardiovascular prevention initiative started in 2009 in New

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Ulm, Minnesota with the goal of reducing ASCVD events [8–10]. This rural community is served by a single healthcare system which afforded the unique opportunity of surveillance for ASCVD events utilizing a single electronic health record (EHR). The aim of this study is to compare estimated ASCVD risk, as calculated by the PCE, to observed rates of ASCVD events in this rural population exposed to a multi-tiered approach to cardiovascular prevention. A better understanding of the calibration of the PCE to specific populations can help foster a more open and accurate clinician-patient risk discussion [11].

2. Methods

The Heart of New Ulm (HONU) was a community-based intervention project, initiated in 2009, aimed at reducing the rate of myocardial infarctions and cardiometabolic risk factors in rural New Ulm, Minnesota [8,9]. New Ulm is located in the 56073 zip code and is approximately 100 miles southwest of the Minneapolis-St. Paul metropolitan area. Healthcare in the community is provided by a single facility, New Ulm Medical Center, which is a part of the Allina Health System. Patients needing higher level care are sent to other Allina hospitals, all of which use a single EHR. The HONU Project was developed as a collaborative partnership between Allina Health, the Minneapolis Heart Institute Foundation, and the community of New Ulm. This study was reviewed and approved by the Allina Health Institutional Review Board.

Screenings were available to those age 18 and older who lived or worked in the community of New Ulm. Lasting a total of 8 months starting in 2009, 109 heart health screening events were held at worksites, the medical center and a variety of community locations. A total of 5221 community residents completed a heart health screening which included biometric risk assessment as well as lifestyle behavior questionnaires [9,12].

A community health profile was generated based on data obtained from these baseline community screenings. This health profile was used to identify risk factors to address with evidence-based interventions tailored to the community's most prevalent risk factors, which were identified as overweight/obesity, metabolic syndrome, low fruit and vegetable consumption and low use of preventative medication among those with elevated CVD risk [9]. The project utilized the social ecological framework to drive the community intervention strategy, offering programs that span the individual level through policy level, underscoring the dynamic interrelations among various personal and environmental factors [12]. They were broadly categorized as preventative health care services, life-style behavior change programming at the workplace and community, social marketing, and environmental reengineering based on a social-ecological model of health determinants and health promotion [13,14]. Detailed descriptions of the main HONU interventions are described elsewhere [8,9,12,15,16].

Individuals were included in the current analysis if they resided in the New Ulm zip code, were age 40–79 at the time of screening, had adequate data to calculate 10-year ASCVD risk (sex, age, race, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for high blood pressure, diabetes, and smoking status), and had no ASCVD at baseline. Individuals were excluded if they did not have consent to use of data for research purposes at the time of the 10-year follow up.

ASCVD events were ascertained via the EHR as a single health system serves the entire New Ulm region. PCI and CABG events were ascertained via ICD 9/10 procedure codes. MI, stroke, and CV death were screened via ICD 9/10 diagnosis codes and confirmed via chart review by a physician (MM and TK). Minnesota Department of Health records were also used to monitor for cardiovascular death. A detailed methodology can be found in a prior publication [17]. Heavy alcohol consumption was defined as >14 drinks per week for men and >7 drinks per week for women. Moderate alcohol consumption was defined as 1–14 drinks per week for men and 1–7 drinks per week for women. Sufficient exercise was considered $\geq$ 150 min per week of a moderate intensity exercise equivalent while sufficient fruit/vegetable intake was

considered $\geq$ 5 servings per day. A 16-point scale was used to assess life stress and $\geq$ 8 points was considered high stress. Hypertension was defined as a resting blood pressure $\geq$ 140/90 mmHg or the use of blood pressure lowering therapy. Patients were considered to have hyperlipidemia if they had an LDL $\geq$130 mg/dl or were on lipid-lowering therapy. An elevated glucose was defined as a fasting blood glucose $\geq$ 100 mg/dl. Metabolic syndrome was defined as the presence of at least three of the following: a waist circumference $\geq$40in for men or $\geq$35in for women, triglycerides $\geq$150mg/dL or taking triglyceride lowering therapy, an HDL <40mg/dL for men or <50 mg/dL for women, a resting blood pressure $\geq$130/85 mmHg or the use of blood pressure lowering therapy, and an elevated fasting glucose or the use of diabetic therapy.

Demographics, medical history, and risk factor data were reported as frequencies and percentages for categorical variables or mean and standard deviation for continuous variables. Estimated 10-year ASCVD event rates were calculated on every individual utilizing the PCE calculator [1]. The estimated and observed outcome data from these were stratified both by ASCVD event 10-year risk at baseline (low, <5%; borderline, 5–7.4%; intermediate/high, $\geq$7.5%) as well as sex [18]. Median and interquartile ranges were obtained for the stratified data for estimated 10-year ASCVD risk.

3. Results

A total of 5221 people participated in the initial HONU heart health screenings in 2009 of which 2819 met the final inclusion criteria for this study (Fig. 1). The mean $\pm$ SD age was 56.1 $\pm$ 9.9 years and 59.6% were female (Table 1). Only 32.5% of the cohort had a college level degree or higher (Table 1). Prevalent cardiometabolic risk factors included hyperlipidemia (56.6%), hypertension (44.4%), obesity (40.1%), metabolic syndrome (37.4%), with relatively low prevalence of diabetes (6.5%). Despite this, anti-hypertensive medication and lipid lowering therapy were underutilized (28.8% and 20.7%, respectively).

Utilizing the PCE, most participants had either a low, <5% 10-year ASCVD risk (46.5%) or an intermediate/high, $\geq$7.5% 10-year ASCVD risk (41.8%) whereas only 11.7% had a borderline, 5-7.4% 10-year
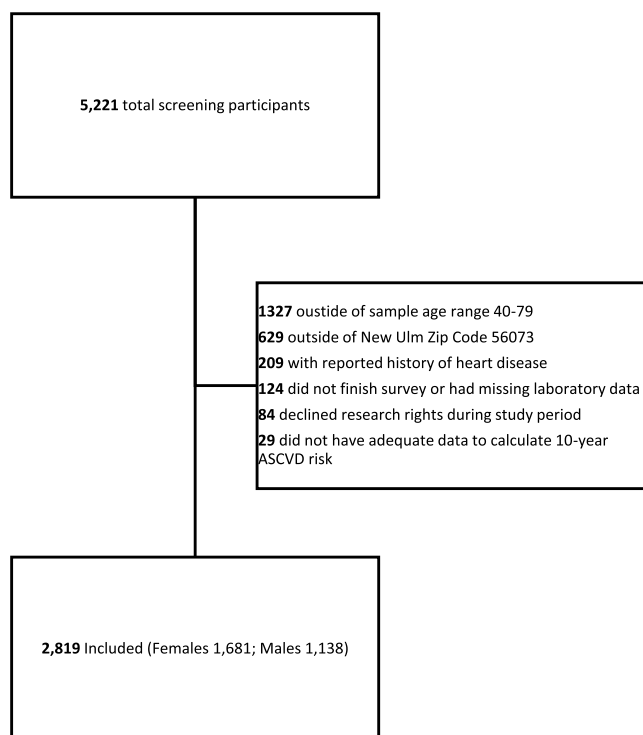

5,221 total screening participants

1327 oustide of sample age range 40-79
629 outside of New Ulm Zip Code 56073
209 with reported history of heart disease
124 did not finish survey or had missing laboratory data
84 declined research rights during study period
29 did not have adequate data to calculate 10-year ASCVD risk

2,819 Included (Females 1,681; Males 1,138)

Fig. 1. Summary of exclusion criteria to reach final studied population.

Table 1
Baseline demographics, risk factors, and medical history collected at 2009 New Ulm Heart Health Screenings for residents aged 40–79 without clinical ASCVD (*n* = 2819).

|	n, % or mean (SD)
Age in years,	56.12 (9.89)
40–49	827, 29.3%
50–59	1029, 36.5%
60–69	629, 22.3%
70–79	334, 11.9%
Sex	
Female	1681, 59.6%
Male	1138, 40.4%
Race	
White	2795, 99.2%
College degree or higher	911, 32.5%
Health care coverage	2754, 98.2%
Diabetes	182, 6.5%
Cigarette smoking	
Current	227, 8.1%
Former	895, 31.8%
Alcohol consumption (drinks/week)	
Heavy	131, 4.7%
Moderate	1506, 53.8%
≥150 min of moderate physical activity/week	1777, 64.4%
≥ 5 servings fruits/vegetables/day	492, 17.6%
High Stress	291, 10.7%
Hypertension (>140/90mmHg)	1251, 44.4%
Hyperlipidemia (LDL≥130 or on lipid lowering therapy)	1595, 56.6%
Total cholesterol (mg/dl)	202.83 (37.03)
LDL (mg/dl)	122.08 (32.78)
HDL (mg/dl)	53.49 (13.88)
Triglycerides (mg/dl)	136.41 (84.32)
BMI (kg/m²)	
Overweight: 25.0–29.9	983, 35.2%
Obese: ≥ 30.0	1119, 40.1%
Metabolic syndrome	1043, 37.4%
Medication Use	
Daily aspirin	837, 31.3%
Medication for diabetes	157, 5.6%
Medication for cholesterol	584, 20.7%
Medication for hypertension	813, 28.8%

ASCVD risk (Table 2). The median 10-year ASCVD risk across the total sample was 5.7% and was higher among males compared to females (7.9% vs 4.1%) (Central Illustration).

The 10-year incidence of ASCVD events in the population (3.4%) was lower than the median 10-year ASCVD risk (ratio of observed to predicted 0.596, absolute difference 2.3%). The largest observed event difference was in the high-risk cohort where the incidence of ASCVD events was much lower (6.4%) than the expected risk of 15.8% (ratio 0.405, absolute difference 9.4%) (Table 2). Across all risk cohorts for both males and females, the incidence of ASCVD events increased as risk increased. However, the incidence of ASCVD events was also consistently lower than the predicted event rate across all risk cohorts individually (Central Illustration).

4. Discussion

In this rural, largely White population, we found that the PCE significantly overestimated the 10-year risk of ASCVD events. This pattern was observed across the spectrum of baseline ASCVD risk and in both men and women. Overall, the PCE overpredicted ASCVD events by about 67% (5.7% v 3.4%). The PCE overpredicted the ASCVD risk in men more than in women with 57% of predicted events occurring in men and 66% in women. In particular, the largest gap in estimated vs observed event rates was in individuals with a predicted ASCVD risk ≥7.5% with an absolute difference in predicted versus observed risk of 10.1% in men and 8.5% in women.

Multiple prior studies have shown that the PCE tends to overestimate ASCVD risk in various populations. Three early external validation studies, the Women's Health Study, the Physicians' Health Study, and the Women's Health Initiative (WHI) showed an overestimation of ASCVD risk across all risk groups, in some instances more than doubling the observed risk [19–22]. The PCE was initially developed from a pooled cohort of multiple national cohorts and data collection in the earliest of these cohorts started in the 1960s and most cohorts had concluded by the early 1990s. Increased awareness of ASCVD risk factors and increased statin use among contemporary cohorts, compared to the earlier cohorts, has been proposed as a possible reason for this phenomenon. However, a subsequent analysis of the Women's Health Study adjusting for statin use as well as the use of modern
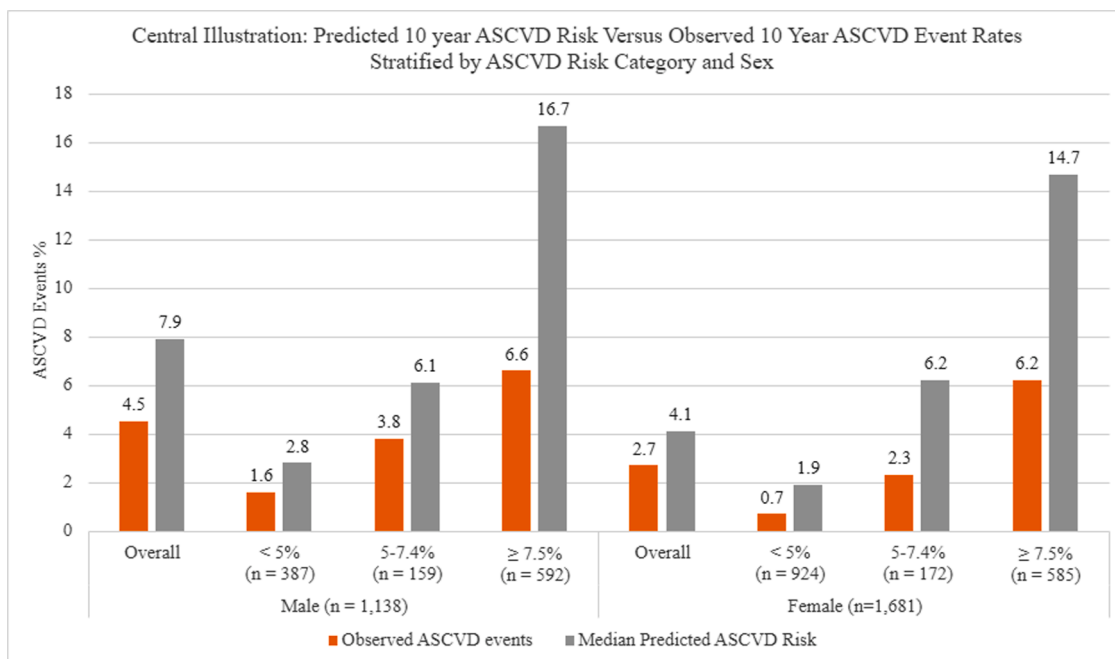
Central Illustration. Predicted 10 year ASCVD Risk Versus Observed 10 Year ASCVD Event Rates Stratified by ASCVD Risk Category and Sex.

revascularization therapies continued to demonstrate overprediction of ASCVD risk utilizing the PCE [5]. The largest study demonstrating over-prediction of ASCVD risk by the PCE was conducted at Kaiser Permanente Northern California, examining 307,591 individuals without diabetes [23]. They also found that the PCE substantially overestimated the observed ASCVD event rate and was poorly calibrated in both men and women, as well as all racial subgroups (non-Hispanic whites, non-Hispanic blacks, Asian/Pacific Islanders, and Hispanics). Notably, they excluded any individuals who had taken statins during the study period or 5-years prior from their analysis.

Other studies have suggested that the under-ascertainment of ASCVD events may be the reason for the apparent overestimation of ASCVD risk by the PCE. The Reasons for Geographic and Racial Differences in Stroke (REASONS) study, examined the ASCVD risk of 10,997 individuals who had an LDL-C of 70–189 mg/dl without diabetes and were not on statin therapy [24]. The PCE calibration was initially poor (Hosmer-Lemeshow χ^2 84.2, p-value < 0.001), overpredicting ASCVD risk by as much as 5%. The analysis was then repeated in 6121 individuals, adding ASCVD events from Medicare claims data, and the calibration of the PCE improved significantly (Hosmer-Lemeshow χ^2 11.4, p-value 0.18). When the analysis was further restricted to the 3333 individuals with Medicare claims data who had an LDL-C of 70–189 mg/dl without diabetes and were not on statin therapy, calibration improved further (Hosmer-Lemeshow χ^2 5.4, p-value 0.71). Considering these findings, the WHI cohort, which initially relied on annual questionnaires, was reanalyzed in the 6071 women who had Medicare claims data [6]. Without utilizing Medicare claims data, PCE calibration was poor (Hosmer-Lemeshow χ^2 91.87, p-value < 0.001) due to an over-prediction of ASCVD risk. The addition of ASCVD events from Medicare claims data improved the calibration substantially overall (Hosmer-Lemeshow χ^2 3.316, p-value 0.19) and across all ethnicities and age groups. Unlike the REASONS and WHI studies, our study did not rely on self-reporting to ascertain ASCVD events, hence this phenomenon is less likely to explain our findings.

Interestingly, the PCE appears to underestimate the ASCVD risk in certain populations as well. An analysis of 1272 appropriately treated HIV-positive men (94.6% of the cohort was on anti-retroviral therapy and 77.1% had achieved viral suppression) found that the PCE underestimated ASCVD risk across all risk groups. While part of this discrepancy can be explained by HIV specific chronic inflammation and immune dysregulation, the study does highlight that the PCE may fail to identify certain high-risk groups [25]. The PCE may also underestimate risk in individuals from socioeconomically disadvantaged areas. A study conducted by the Cleveland Clinic examined 109,793 individuals, implementing a Neighborhood Disadvantage Index (NDI) as a measure of socioeconomic status [26]. The performance of the PCE in predicting ASCVD events was then analyzed by NDI percentiles. For individuals in the highest 10th percentile by NDI, the PCE underpredicted ASCVD risk across all risk groups. Calibration improved as the NDI decreased, with the PCE being well calibrated for individuals in the lowest 10th percentile by NDI. In fact, the NDI accounted for 32% of geographic variability in observed ASCVD event rates, while PCE only accounted for 10% of the observed geographic variability, demonstrating the substantial impact of socioeconomic status on ASCVD risk.

Despite its limitations, the PCE remains an excellent clinical tool, utilizing routinely available clinical information to estimate future ASCVD risk and enabling the clinician and patient to determine the potential benefit of early preventative interventions. However, the calibration of the PCE can vary significantly based on an individual's background and comorbid conditions. Hence, the PCE is best utilized as a starting point for discussing ASCVD prevention with the patient. The PCE does not appear to adequately risk-stratify individuals from resource poor areas who may benefit from statin therapy if lifestyle interventions are difficult to implement. Those with high-risk conditions that are not included in the PCE, such as HIV infection or chronic autoimmune disease, may benefit from statin therapy even if the predicted ASCVD risk is low. On the other hand, the disutility of statin

therapy may outweigh the benefit in patients with an intermediate predicted ASCVD risk who do not have high-risk conditions. In these scenarios, novel biomarkers and diagnostic techniques, such as coronary artery calcium scoring and the risk enhancing factors detailed in the most recent 2018 cholesterol guidelines can help further risk-stratify to guide the timing of preventive interventions [18,27].

5. Limitations

This study has several limitations. The cohort was almost entirely White and thus may not be generalizable to individuals of other races and/or ethnicities. Additionally, our cohort is comprised of those who volunteered at health screening events which may lead to selection bias. Our event rate was relatively low, limiting sub-group analysis. Furthermore, while a single health system serves the city of New Ulm, individuals who may have had events outside of the city may have been missed. Part of the discrepancy between the predicted and observed ASCVD event rates may be secondary to the preventive interventions of the HONU initiative with prior research showing a modest reduction in total ASCVD events compared to a matched comparison community with similar demographics [17]. Under-ascertainment of events from the EHR is also a possibility, although cases were manually reviewed to ensure accuracy. Approximately 11% of the cohort had non-ASCVD death during the study period, which is not accounted for in our endpoints (Table 2).

6. Conclusion

Our study shows that the estimated 10-year ASCVD risk in a rural population exposed to a multifactorial prevention initiative was substantially higher than the observed event rates. While there are likely a myriad of factors contributing to this overestimation of risk, this finding highlights the importance of conveying the uncertainties of risk assessment to patients as well as the potential for substantially lower observed event rates with aggressive preventive interventions as part of the clinician/patient risk discussion.

CRediT authorship contribution statement

Christopher Van Hove: Formal analysis, Conceptualization, Writing – original draft, Writing – review & editing. **Ayman Haq:** Formal analysis, Conceptualization, Writing – original draft, Writing – review & editing. **Angela Phillips:** Formal analysis, Conceptualization, Writing – original draft, Writing – review & editing. **Abbey Sidebottom:** Visualization, Data curation, Formal analysis, Conceptualization, Writing – review & editing. **Marc Vacquier:** Visualization, Data curation, Formal analysis, Conceptualization. **Gretchen Benson:** Visualization, Data curation, Formal analysis, Conceptualization, Writing – review & editing. **Thomas Knickelbine:** Visualization, Writing – review

Table 2
Predicted 10-year ASCVD risk by the Pooled Cohort Equations vs Observed 10-year ASCVD events stratified by ASCVD risk category.

	Total (n = 2819)			
10-year ASCVD risk score category	Total	< 5%	5–7.4%	≥ 7.5%
	n = 2819	n = 1311	n = 311	n = 1177
Median [IQR] Predicted 10-year ASCVD risk	5.7 [2.3–13.5]	2.2 [1.3–3.4]	6.2 [5.6–6.6]	15.8 [10.4–29.0]
10-year ASCVD event rate	97 (3.4%)	12 (0.9%)	10 (3%)	75 (6.4%)
Ratio of Observed vs Predicted Risk	0.596	0.401	0.484	0.405
Absolute Difference in Observed and Predicted Risk	2.3%	1.3%	3.2%	9.4%

& editing. **Michael D Miedema:** Visualization, Formal analysis, Conceptualization, Writing – original draft, Writing – review & editing.

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