Published in final edited form as:

Prev Med. 2021 July ; 148: 106555. doi:10.1016/j.ypmed.2021.106555.

Fewer patients receive recommendations for pharmacotherapy in primary prevention using the 2018 atherosclerotic cardiovascular disease risk estimator

Alessandra M. Campos-Staffico^a, David Cordwin^a, Yuting Ding^a, Corey A. Lester^a, Robert D. Brook^b, Jasmine A. Luzum^a, Michael P. Dorsch^{a,*}

^aDepartment of Clinical Pharmacy, College of Pharmacy, University of Michigan, Ann Arbor, MI 48109, USA

^bDivision of Cardiovascular Medicine, Department of Internal Medicine, Medical School, University of Michigan, Ann Arbor, MI 48109, USA

Abstract

Shortly after the introduction of the 2013 original Pooled Cohort Equation (PCE), an overestimation of risk was suggested. As such, the updated 2018 PCE was developed to more accurately assess atherosclerotic cardiovascular disease (ASCVD) risk in the population. Hence, this study aims to compare drug prescribing recommendations in a large, real-world patient population, depending on which PCE is used to estimate 10-year ASCVD risk. This retrospective cohort study identified 20,843 patients aged between 40 and 75 years with no previous ASCVD. The 10-year ASCVD risk score was assessed by using both PCE. Patients were assigned to the four risk categories according to the 2018 ACC/AHA guideline. The percentage of patients qualifying for guideline-recommended primary prevention with statins and/or anti-hypertensives were compared between both PCE. Risk reclassification occurred in 26.7% of patients overall ($n = 5571$), of which 98.1% ($n = 5466$) were assigned to lower risk categories with the updated PCE. Non-diabetic (14.0%) patients no longer met the threshold for recommending statins as primary prevention with the updated PCE. Likewise, 13.8% of patients with stage I hypertension no longer met the threshold for recommending antihypertensive drugs with the updated PCE. In conclusion, risk reclassification occurred among 26.7% of patients overall, mostly due to lower risk categories assigned by the updated PCE. Up to 14.0% of patients no longer met the threshold for recommending statin therapy and/or antihypertensive drugs by using the updated PCE. These findings suggest that using the updated PCE could translate into fewer patients receiving pharmacotherapy for ASCVD primary prevention.

Keywords

Risk assessment; Atherosclerotic disease; Primary prevention

*Corresponding author. mdorsch@med.umich.edu (M.P. Dorsch).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ypmed.2021.106555>.

1. Introduction

In 2013, the American College of Cardiology/American Heart Association (ACC/AHA) guideline on the treatment of blood cholesterol introduced the Pooled Cohort Equations (PCE) to aid in estimating atherosclerotic cardiovascular disease (ASCVD) risk in a 10-year period (Stone et al., 2014). The guideline recommended using the PCE to identify patients that would most benefit from initiating statin therapy for primary prevention. This original PCE was developed and validated based on data from five different studies dating back to 1960 (Goff et al., 2014). Subsequently, the original PCE was shown to overpredict the risk in more contemporary populations, as they are exposed to a lower burden of ASCVD risk factors than the original cohorts (DeFilippis et al., 2015; Rana et al., 2016).

The updated PCE was developed in 2018 to improve model discrimination and calibration of 10-year ASCVD risk for patients in contemporary lower-risk populations in the US. This was accomplished by both updating the data with modern cohorts and by adjusting the statistical methods to reduce the risk of overfitting. Thereby, the probability of overestimation was reduced, along with the risk of extreme estimates with black individuals (Yadlowsky et al., 2018).

The 2013 and 2018 cholesterol clinical practice guidelines utilize the original PCE to recommend statin therapy and dosage (Grundy et al., 2019; Stone et al., 2014). Additionally, the most recent hypertension clinical practice guideline also uses the original PCE to stratify patients with stage 1 hypertension that would benefit from pharmacotherapy (Whelton et al., 2018). Due to the need to assign categorical thresholds for treatment decisions in the real world, individuals could receive different clinical recommendations depending on which PCE is used to assign risk. This could have a large impact on the overall number of patients treated or not treated, given the large number of Americans at risk for ASCVD. However, the prevalence of changes in drug prescribing recommendations according to the original and the updated PCE has not been previously quantified. Therefore, the objective of this study was to compare drug prescribing recommendations in a large, real-world patient population, depending on whether the original or the updated PCE is used to estimate patients' ASCVD risk.

2. Methods

2.1. Study design and cohort identifications

This retrospective cohort study was conducted to investigate differences in primary prevention recommendations based on 10-year ASCVD risk scores. The primary focus was to compare prescribing recommendations between two different ASCVD risk scores (i.e., original and updated). The secondary focus was to compare prescribing recommendations to actual prescriptions. The initial participant cohort was active patients at Michigan Medicine – a large academic healthcare system in the United States – who had at least one result for a cholesterol panel between June 2017 and June 2018. To match the methods and guideline-based recommendations for the use of the PCE, adults aged 40–75 years with no clinical ASCVD and/or index dates after December 1st, 2013 were included in the analysis. All data were obtained from the University of Michigan Electronic Health Record (EHR)

data warehouse, as described elsewhere (Dorsch et al., 2019), and more detailed information is shown in Supplementary Methods. The complete CONSORT Diagram is found in Fig. 1.

The study was carried out in accordance with The Declaration of Helsinki and was approved by the University of Michigan Institutional Review Board with a waiver of informed consent.

2.2. ASCVD risk score assessments

First, the 10-year ASCVD risk scores were assessed twice for each patient using the original PCE proposed by the 2018 ACC/AHA Guidelines (Grundy et al., 2019; Stone et al., 2014) and the updated PCE (Goff et al., 2014; Yadlowsky et al., 2018). The risk scores obtained with each PCE were used to assign patients into four risk categories defined by the 2018 AHA/ACC Guideline, as such: low (<5%), borderline (5- < 7.5%), intermediate (7.5–20%) and high risk (20%) (Grundy et al., 2019).

The risk categories assigned with risk scores obtained with the original PCE were defined as the reference and, subsequently, were compared to the risk categories assigned with risk scores obtained with the updated PCE. In case of risk categories agreement, patients were stratified into concordant risk categories. In case of risk categories disagreement, patients were stratified into discordant risk categories if they were assigned to higher or lower estimated risk categories in relation to the reference.

2.3. Identification of pharmacological treatment

All medication histories in the EHR were used to determine whether patients were prescribed statin around the index date. A list of statin medications was used, which included combination therapy. The prescription start and stop dates had to meet one of the following criteria to be considered as on statin treatment during the index date: (i) Index date minus 30 days was less than or equal to the start date and less than or equal to the index date. (ii) The start date was less than or equal to the index date and the stop date was greater than or equal to the index date. (iii) If the stop date is absent in the prescription, the stop date was estimated based on the formula: Stop Date = (Quantity/Frequency) × (Refills+1).

2.4. Statistical analyses

Categorical variables were defined as counts and percentages, and differences between groups were assessed by the χ^2 test. Continuous variables were characterized by either mean $\pm$ standard deviation (SD), if normally distributed, or median (interquartile range (IQR)), if not normally distributed. Patients were stratified into four concordant categories (low, borderline, intermediate, and high risk) and two discordant risk categories (higher or lower estimated risk category in relation to the reference) according to the abovementioned criteria. Cohen's kappa coefficient, which accounts for chance of agreement (Cohen, 1960), and corrected kappa, which accounts for the maximum possible kappa (Umesh et al., 1989), were calculated to estimate the degree of agreement of the risk categories, along with their respective 95% confidence intervals (95%CI). Kappa values 0 indicate no agreement, 0.01–0.20 none to slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1.00 nearly perfect agreement (McHugh, 2012). Wilcoxon matched-pairs signed rank

test was used to compare risk scores calculated by using the original and updated PCE. A two-sided p -value of <0.05 was considered statistically significant. STATA software version 15.0 for Mac were used for all analyses and Violin plots.

3. Results

3.1. Study population

A total of 20,843 patients aged between 40 and 75 years with no previous history of ASCVD were identified. They were assigned to 4 concordant risk categories [low ($n = 11,624$), borderline ($n = 499$), intermediate ($n = 2538$) and high risk ($n = 611$)] and 2 discordant risk categories (patients who had lower estimated risk ($n = 5466$) and higher estimated risk ($n = 105$) by using the updated PCE compared to the original PCE). The median age, systolic blood pressure, total and HDL cholesterol were, respectively, 54(14) years, 124(24) mmHg, 210(57) mg/dL and 55(22) mg/dL. Most patients were female (57.1%), white (78.9%), nondiabetic (85.2%), nonsmokers (91.0%), and did not undergo hypertensive treatment (69.6%). The baseline characteristics of all patients are shown in Table 1.

3.2. Comparison of ASCVD risk score assessments

The median 10-year ASCVD risk scores assessed using the original PCE vs. updated PCE with respective p -values for each risk category were [low: 1.84(2.14) vs. 1.34(1.49), $p < 0.001$]; [borderline: 6.86(0.95) vs. 5.51(0.86), $p < 0.001$]; [intermediate: 14.40(4.71) vs. 9.86(3.29), $p < 0.001$]; [high: 34.67(12.07) vs. 25.73(8.79), $p < 0.001$] and [overall: 4.09(7.81) vs. 2.82(4.92), $p < 0.001$]. As patients in primary prevention may have had a higher risk without treatment and may be above the cut-off points of the updated PCE, we performed a sensitivity analysis with statin- and antihypertensive-naïve patients. However, the risk scores assessed using the original remained significantly different from the risk scores assessed using the updated PCE (Table 2 – Supplementary Materials). Violin plots comparing the 10-year ASCVD risk scores in each risk category are shown in Fig. 2.

3.3. Degree of agreement between risk categories

A total of 5571 patients (26.7%) were assigned to discordant risk categories, of which 5466 (26.2%) represented a lower risk category and 105 (0.5%) represented a higher risk category using the updated PCE compared to the original PCE. Overall, 73.27% of patients ($n = 15,272$) were assigned to concordant risk categories, which was significantly greater than the number of agreements expected by chance alone ($n = 9220.2$, 44.24%, $p < 0.001$). Cohen's kappa coefficient was 0.521 (95% CI: 0.512–0.530), which is interpreted as a moderate level of agreement between risk categories assessed by the original and updated PCE. The corrected kappa was 0.689, when correcting for linear weights.

3.4. Statin prescribing for non-diabetic patients

A total of 15,251 non-diabetic patients (73.2%) aged between 40 and 75 years, LDL-C 70–189 mg/dL and with no previous history of ASCVD were identified (Table 2). Among them, 11,331 patients (74.3%) were assigned to concordant risk categories, of which 1439 patients met the guideline recommendations for primary prevention with statins. However, 300 patients only (20.8%) had statin on their medication history. In contrast, of the 9614 patients

assigned in concordant risk categories with no recommendation for primary prevention pharmacotherapy, 331 of them (3.4%) were prescribed a statin.

In terms of discordant risk categories, 3920 patients (25.7%) were identified, of which 3895 (25.5%) had a lower intensity statin recommended with the updated PCE and 13 (0.09%) had a higher intensity statin recommended with the updated PCE. Among those who were assigned to a lower risk category with the updated PCE, 2139 patients (14.0%) no longer met the threshold for recommending primary prevention drug therapy. Alternatively, all 13 patients (0.09%) who had higher estimated risk with the updated PCE would qualify for a primary prevention recommendation.

3.5. Antihypertensive drugs prescribing for stage I hypertension patients

A total of 4153 patients (19.9%) were identified according to the guideline criteria, and the frequency distribution is shown in Table 3. In the concordant categories, 702 patients (16.9%) met criteria to be prescribed antihypertensive drugs, of which 432 of them (61.5%) had prescription records for these drugs. In the discordant categories, 572 patients (13.8%) had a lower risk score with the updated PCE and would no longer met the threshold for recommending antihypertensive drugs. Alternatively, 6 patients (0.1%) had a higher risk score and would qualify for antihypertensive treatment with the updated PCE.

4. Discussion

This is the first study in a large, real-world patient population to compare guideline recommendations for primary prevention between the original 2013 PCE and the updated 2018 PCE risk assessment models. Although the updated PCE was derived mainly using the same data as the original PCE, the small fraction of new data used to derive the updated PCE still led to the reclassification of 26.7% of patients overall (Table 1 – Supplementary Material). Hence, statin prescribing recommendations changed for a substantial number of patients. The vast majority of the patients assigned to discordant risk categories were reclassified to a lower risk category (26.2%) with the updated PCE. As a consequence, this substantial disagreement between PCEs could affect prescribing of statins and/or antihypertensive drugs for primary prevention in a large number of patients.

There are a variety of different tools that clinicians can use to estimate ASCVD risk, but it is not always obvious which PCE is implemented in those tools. Some institutions directly implement the PCE into the EHR automatically calculating the ASCVD risk in patients' charts or in clinicians' notes (Lloyd-Jones et al., 2019). At our own institution, the original PCE is implemented in the EHR in both of these ways. Also, clinicians commonly use the "ASCVD Risk Estimator Plus" app created by the American College of Cardiology, which uses the original PCE to estimate risk ("ASCVD Risk Estimator Plus," 2021). In contrast, other websites have calculators using the updated PCE instead ("Cardiovascular Risk Assessment (10-year, Revised Pooled Cohort Equations 2018)," 2021). Therefore, our findings show that the various tools available to providers could result in discordant prescribing recommendations for approximately one in every four patients.

In terms of representativeness, our patient sample has demographic and clinical characteristics similar to the whole American population, except for the higher frequency of Asians and lower of African Americans compared to the average of the US population. Therefore, if we extrapolate the findings from our patient sample to the entire US, then the total numbers of Americans that no longer met the threshold for recommending statin and anti-hypertensive therapies or receive recommendation of lower intensity statin with the updated PCE are very large. In data reported by the AHA, more than 24 million Americans with ASCVD risk score $\geq 7.5\%$ were recommended for prescribing statin as primary prevention using the original PCE (“Prevalence and Number of US Adults Eligible for and Currently Using Statin Therapy (NHANES 2011–2014),” 2021). In our findings, the use of the updated PCE reclassified 14.0% of non-diabetics with ASCVD risk score $\geq 7.5\%$ to risk categories in which statins are not recommended for primary prevention. Therefore, if we extrapolate this percentage to the entire U.S., more than 3.7 million non-diabetic Americans would no longer meet the threshold for recommending statins prescription as primary prevention, if the updated PCE was used. In our patient sample, 0.1% of non-diabetic patients who had no recommendation for primary prevention with statins were reclassified to risk categories in which statins are recommended. Extrapolating these percentages, approximately 23,000 non-diabetic Americans would be recommended statins for primary prevention if the updated PCE is used.

According to hypertension estimates reported by the ACC/AHA (Bress et al., 2019), up to 6.5 million Americans have stage I hypertension and ASCVD risk score $\geq 10\%$, and therefore would meet indications for antihypertensive drugs. In our findings, 13.8% of patients were reclassified to risk categories in which anti-hypertensive drugs would not be recommended with the updated PCE. If we extrapolate that percentage to the entire U.S., then up to 910,800 Americans would no longer meet the threshold for recommending antihypertensive treatment. Alternatively, 0.1% of patients with stage I hypertension in our sample were reclassified to recommendations for treatment with anti-hypertensive drugs. If extrapolated again to the entire U.S., then up to 9500 Americans with stage I hypertension would be recommended antihypertensive drugs if using the updated PCE.

It is important to acknowledge that some believe that the risk cut-offs (i.e., at 5%, 7.5%, and 20%) are arbitrary (Lopez-Jimenez et al., 2014). Indeed, ASCVD risk is multifactorial, and thus it does not realistically exist as convenient, discrete risk categories (e.g., low, borderline, intermediate, and high risk). ASCVD risk exists as a continuous distribution in a population, but clinical application requires stratifying that continuous risk into discrete categories. In determining the specific risk cut-offs, the guideline authors weighed an individual’s absolute risk of ASCVD and potential treatment benefits against the potential absolute risks for harm from therapy. Those decisions were evidence-based, by reviewing, summarizing, and citing hundreds of studies (Grundy et al., 2019). The 7.5% cut-off in the 2013 guidelines was based on RCT evidence that showed a clear net absolute benefit of statin therapy when ASCVD risk was $\geq 7.5\%$ (Stone et al., 2014). The addition of the 20% cut-off in the 2018 guidelines stems from epidemiologic and trial data showing the recurrent event rate for patients with ASCVD is at minimum 20% over 10 years, which has also been used in previous cholesterol guidelines (National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood

Cholesterol in Adults (Adult Treatment Panel III), 2002). This led to the recommendation to use high-intensity statins in the primary prevention group with an ASCVD risk of >20%, since they theoretically have similar risk to those with previous ASCVD. Thus, we do not agree that the specific risk cut-offs for treatment recommendations are arbitrary. Moreover, data shows that the PCE are well-calibrated near the decision thresholds (Muntner et al., 2014); further supporting the relevance of the specific risk cut-offs for determining treatment recommendations.

Despite the clinical relevance and strong evidence base supporting the risk categories and their corresponding treatment recommendations, it is important to note that it is not the final arbiter in the treatment decision. In fact, the risk categories and their corresponding treatment recommendations are only intended to be the *starting* point in the treatment discussion with the patient (Lloyd-Jones et al., 2019). Moreover, the calculated risk is often mistaken to be the patient's individual absolute risk, but it should be interpreted as the probability of an event occurring in a group of patients with a number of characteristics in common with the patient (Stern and Brook, 2019). Several risk-enhancing factors are not taken into account in the PCEs (e.g., family history of ASCVD, chronic kidney disease, chronic inflammatory conditions) and the Coronary Artery Calcium (CAC) score plays a pivotal role in improving the specificity of medical decision regarding the recommendation of primary prevention in those where the risk of ASCVD remains uncertain. However, clinicians can use their judgment to reclassify patients into a different risk category based on those factors alone (Lloyd-Jones et al., 2019). Regardless, the decision of which PCE to use to estimate risk and start the treatment discussion with the patient is still important because providing risk estimation has been associated with changes in prescribing behaviors (Lloyd-Jones et al., 2019).

As shown in Table 1 of Supplementary Material, the updated PCE was derived using 74.2% of the data used to derive the original PCE. The main difference lies in the substitution of patients from the Framingham Heart Study – a true cohort of natural history – by patients of the Jackson Heart Study and the Multi-Ethnic Study of Atherosclerosis (MESA) – two observational studies that measure the CAC score (Osawa et al., 2016; Sung et al., 2016). Knowledge of the CAC score can lead physicians to intervene in the disease's natural progression through prescription of primary prevention drugs, reducing the atherosclerotic risk. Thus, this could explain differences in risk estimation of the original and the updated PCE.

The public health implications of fewer individuals recommended for drug prescribing by utilizing the updated PCE are still unclear. Regarding our results, fewer low-risk patients recommended for primary drug prevention would be considered a “non-evidence-based” practice, according to the updated PCE. Roughly a quarter of patients would not receive “inappropriate” drug treatment. On the other hand, if the cut-off points for treatment are not believed to be real thresholds whereby individuals will (or will not) benefit from treatment, then fewer individuals in the population would be candidates for potentially beneficial treatments, which could lead to worse outcomes. At this point, the scenario closest to reality still remains undefined.

Despite all the proven benefits, the frequency of patients recommended for primary prevention who were actually prescribed a statin is still low in our sample. In our findings, among all patients with recommendation for primary prevention assigned to concordant categories, non-diabetic patients with a risk score 5% had the lowest frequency of statin prescription of 19.9%. Patients at high risk (ASCVD 20%) also had a low frequency of statin prescription of 16.5%. These numbers are considerably lower than the national average of 30.3% (“Prevalence and Number of US Adults Eligible for and Currently Using Statin Therapy (NHANES 2011–2014),”, 2021). Although these findings are alarming, our study group has been showing how concerning the low frequency of statin prescription is among patients recommended for primary prevention (Dorsch et al., 2019). The frequency of prescribing antihypertensive drugs is also not ideal, but it seems to be better than statins, as more than 60% of patients with stage I hypertension and risk score 10% had records of prescription of antihypertensive drugs.

Although our study was developed in an academic setting, there are still significant gaps in the implementation of proven and effective evidence-based ASCVD prevention strategies. According to our findings, the priority goal set by the CDC/CMS Million Hearts Initiative to optimize care of over 80% of those who need blood pressure or cholesterol control was far from being achieved (CDC and CMS, 2021). Therefore, we must focus on improving strategies to enhance guideline-directed pharmacotherapy in order to effectively reduce the high burden of ASCVD.

Some limitations must be taken in consideration when reading this study. This is a low-risk cohort overall and the population-based risk assessment may have been impacted by social determinants of health not measured in our study, such as nutrition, lifestyle and advancing age. Although atherosclerotic disease has a temporal progression, the ASCVD risk was assessed only at a cross-sectional time point, resulting in a limitation of this study. The knowledge of the CAC score in modern cohorts, used to derive the updated PCE, must be interpreted as a potential confounding factor, which could account for some of the overestimation of the atherosclerotic risk. Also, our findings are limited to a single health system that primarily serves southeastern Michigan. All data were obtained from the EHR, which limits the research to certain variables and may increase the amount of missing data. Although our data collection has followed standardized protocols, there is no standardization for the clinical care routine and, as a limitation of observational studies, unmeasured residual confounding may have been incorporated. However, the frequency of missing data in our data set was considered low (2.4%) and all participants were excluded in order to reduce bias. The statin and antihypertensive prescribing were defined from EHR data, and conditions that would contraindicate both classes of drugs were not investigated. Clinician reasoning could not be obtained to determine the thought process of prescribing these drugs. We did not have access to pharmacy prescription fill records, so adherence could not be assessed. Future studies should pool data from EHRs and pharmacy claims data.

5. Conclusion

In conclusion, the 10-year ASCVD risk score equations have only moderate level of agreement, resulting in a risk reclassification of 26.7% of patients overall in a sample from a single, large academic medical center, mostly due to decrements in risk estimation using an updated model. Most importantly, 14.0% of non-diabetic patients and 13.8% of patients with stage I hypertension no longer met guideline recommendations for statin therapy and antihypertensive drug therapy, respectively, when using the updated PCE. These findings suggest that using the updated PCE could translate into fewer patients receiving statin and antihypertensive therapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

JAL is funded by the National Heart, Lung and Blood Institute (NHLB) of the National Institute of Health (NIH), USA (grant IDs: K08 HL146990 and L30 HL110279).

Declaration of Competing Interest

Dr. Dorsch has received honoraria from Jansen and research funding from BMS/Pfizer, Amgen, Agency for Healthcare Research and Quality, NIH/National Institute of Aging, and the American Heart Association in the past 2 years. All other authors declare that there is no conflict of interest.

References

- ASCVD Risk Estimator Plus [WWW Document], 2021. American College of Cardiology. <http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/> (Accessed 6.15.20).
- Bress Adam P., Colantonio Lisandro D., Cooper Richard S., Holly Kramer, Booth John N., Odden Michelle C., Kirsten Bibbins-Domingo, Daichi Shimbo, Whelton Paul K., Levitan Emily B., George Howard, Bellows Brandon K., Dawn Kleindorfer, Safford Monika M., Paul Muntner, Moran Andrew E., 2019. Potential cardiovascular disease events prevented with adoption of the 2017 American College of Cardiology/American Heart Association blood pressure guideline. *Circulation* 139, 24–36. 10.1161/CIRCULATIONAHA.118.035640. [PubMed: 30586736]
- Cardiovascular Risk Assessment (10-year, Revised Pooled Cohort Equations 2018) [WWW Document], 2021. MSD Manual Professional Version. https://www.msdmanuals.com/en-sg/professional/multimedia/clinical-calculator/clinicalcalculator_en_v45392360 (Accessed 6.15.20).
- CDC and CMS, 2021. Million Hearts [WWW Document]. <https://millionhearts.hhs.gov/about-million-hearts/index.html#ref> (Accessed 9.25.20).
- Cohen J, 1960. A coefficient of agreement for nominal scales. *Educ. Psychol. Meas* 20, 37–46. 10.1177/001316446002000104.
- DeFilippis AP, Young R, Carrubba CJ, McEvoy JW, Budoff MJ, Blumenthal RS, Kronmal RA, McClelland RL, Nasir K, Blaha MJ, 2015. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. *Ann. Intern. Med* 162, 266–275. 10.7326/M14-1281. [PubMed: 25686167]
- Dorsch MP, Lester CA, Ding Y, Joseph M, Brook RD, 2019. Effects of race on statin prescribing for primary prevention with high atherosclerotic cardiovascular disease risk in a large healthcare system. *J. Am. Heart Assoc* 8, e014709 10.1161/JAHA.119.014709. [PubMed: 31707943]
- Goff DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, Greenland P, Lackland DT, Levy D, O'Donnell CJ, Robinson JG, Schwartz JS, Shero ST, Smith SC, Sorlie P, Stone NJ, Wilson PWF, 2014. 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. *Circulation*. 10.1161/01.cir.0000437741.48606.98.

- Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith SC, Sperling L, Virani SS, Yeboah J, 2019. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J. Am. Coll. Cardiol* 73, 3168–3209. 10.1016/j.jacc.2018.11.002. [PubMed: 30423391]
- Lloyd-Jones DM, Braun LT, Ndumele CE, Smith SC, Sperling LS, Virani SS, Blumenthal RS, 2019. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American Heart Association and American College of Cardiology. *J. Am. Coll. Cardiol* 73, 3153–3167. 10.1016/j.jacc.2018.11.005. [PubMed: 30423392]
- Lopez-Jimenez F, Simha V, Thomas RJ, Allison TG, Basu A, Fernandes R, Hurst RT, Kopecky SL, Kullo IJ, Mulvagh SL, Thompson WG, Trejo-Gutierrez JF, Wright RS, 2014. A summary and critical assessment of the 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: filling the gaps. *Mayo Clin. Proc* 89, 1257–1278. 10.1016/j.mayocp.2014.06.016. [PubMed: 25131697]
- McHugh ML, 2012. Interrater reliability: the kappa statistic. *Biochem. Med. (Zagreb)* 22, 276–282. [PubMed: 23092060]
- Muntner P, Colantonio LD, Cushman M, Goff DC, Howard G, Howard VJ, Kissela B, Levitan EB, Lloyd-Jones DM, Safford MM, 2014. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. *JAMA* 311, 1406–1415. 10.1001/jama.2014.2630. [PubMed: 24682252]
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), 2002. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation* 106, 3143–3421. [PubMed: 12485966]
- Osawa K, Nakanishi R, Budoff M, 2016. Coronary artery calcification; report from the multi-ethnic study of atherosclerosis. *Glob. Heart* 11, 287–293. 10.1016/j.heart.2016.08.001. [PubMed: 27741976]
- Prevalence and Number of US Adults Eligible for and Currently Using Statin Therapy (NHANES 2011–2014) [WWW Document], 2021. American Heart Association. <https://healthmetrics.heart.org/prevalence-and-number-of-us-adults-eligible-for-and-currently-using-statin-therapy-nhanes-2011-2014/> (Accessed 4.30.20).
- Rana JS, Tabada GH, Solomon MD, Lo JC, Jaffe MG, Sung SH, Ballantyne CM, Go AS, 2016. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. *J. Am. Coll. Cardiol* 67, 2118–2130. 10.1016/j.jacc.2016.02.055. [PubMed: 27151343]
- Stern RH, Brook RD, 2019. Do risk-enhancing factors enhance risk estimation? *Circ. Cardiovasc. Qual. Outcomes* 12, e006078. 10.1161/CIRCOUTCOMES.119.006078. [PubMed: 31718296]
- Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC, Watson K, Wilson PWF, 2014. 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. *Circulation*. 10.1161/01.cir.0000437738.63853.7a.
- Sung JH, Yeboah J, Lee JE, Smith CL, Terry JG, Sims M, Samdarshi T, Musani S, Fox E, Ge Y, Wilson JG, Taylor HA, Carr JJ, 2016. Diagnostic value of coronary artery calcium score for cardiovascular disease in African Americans: The Jackson Heart Study. *Br. J. Med. Med. Res* 11. 10.9734/BJMMR/2016/21449.
- Umesh UN, Peterson RA, Sauber MH, 1989. Interjudge agreement and the maximum value of kappa. *Educ. Psychol. Meas* 49, 835–850. 10.1177/001316448904900407.

- Whelton Paul K., Carey Robert M., Aronow Wilbert S., Casey Donald E., Collins Karen J., Cheryl Dennison Himmelfarb, DePalma Sondra, M., Samuel Gidding, Jamerson Kenneth A., Jones Daniel W., MacLaughlin Eric J., Paul Muntner, Bruce Ovbiagele, Smith Sidney C., Spencer Crystal C., Stafford Randall S., Taler Sandra J., Thomas Randal J., Williams Kim A., Williamson Jeff D., Wright Jackson T., 2018. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension* 71, e13–e115. 10.1161/HYP.0000000000000065. [PubMed: 29133356]
- Yadlowsky S, Hayward RA, Sussman JB, McClelland RL, Min YI, Basu S, 2018. Clinical implications of revised pooled Cohort equations for estimating atherosclerotic cardiovascular disease risk. *Ann. Intern. Med* 169, 20–29. 10.7326/M17-3011. [PubMed: 29868850]

Fig. 1.

CONSORT diagram.

PAD: Peripheral Arterial Disease. CHD: Coronary Heart Disease. CVD: Cerebrovascular Disease. SBP: Systolic Blood Pressure. HDL: High-Density Lipoprotein.

Fig. 2.

Violin plots of 10-year ASCVD risk scores calculated by original PCE and updated PCE and assigned to risk categories.

Bold line represents the median and dashed lines represent the interquartile range of 10-year ASCVD risk scores. A p -value <0.001 were obtained for each of the following subgroups:

A. Overall patients; B. Low risk; C. Borderline risk; D. Intermediate risk and E. High risk.

Table 1

Baseline characteristics of all patients.

Characteristics	Overall	Original and Updated PCE Risk Category Concordant				Original and Updated PCE Risk Category Discordant	
		Low (<5%)	Borderline (5 – 7.5%)	Intermediate (7.5 – 20%)	High (20%)	Lower estimated risk with Updated PCE	Higher estimated risk with Updated PCE
Patients, n (%)	20843 (100)	11624 (55.8)	499 (2.4)	2538 (12.2)	611 (2.9)	5466 (26.2)	105 (0.5)
Age, years	54 (14)	49 (10)	54 (9)	62 (11)	68 (8)	63 (11)	49 (8)
Gender, n (%)							
Female	11899 (57.1)	8151 (70.1)	169 (33.9)	733 (28.9)	145 (23.7)	2682 (49.1)	19 (18.1)
Male	8944 (42.9)	3473 (29.9)	330 (66.1)	1805 (71.1)	466 (76.3)	2784 (50.9)	86 (81.9)
Race, n (%)							
African American	1687 (8.1)	650 (5.6)	41 (8.2)	316 (12.5)	83 (13.6)	591 (10.8)	6 (5.7)
American Indian or Alaska Native	41 (0.2)	24 (0.2)	5 (1.0)	4 (0.2)	3 (0.5)	5 (0.1)	0 (0.0)
Asian	2101 (10.1)	1501 (12.9)	47 (9.4)	127 (5.0)	35 (5.7)	379 (6.9)	12 (11.4)
Caucasian	16451 (78.9)	9089 (78.2)	394 (79.0)	2025 (79.8)	472 (77.3)	4387 (80.3)	84 (80.0)
Native Hawaiian and other Pacific Island	16 (0.1)	6 (0.1)	1 (0.2)	1 (0.0)	2 (0.3)	6 (0.1)	0 (0.0)
Other	547 (2.6)	354 (3.0)	11 (2.2)	65 (2.6)	16 (2.6)	98 (1.8)	3 (2.9)
Total cholesterol, (mg/dL)	210 (57)	209 (54)	203 (57)	206 (60)	195 (68)	217 (58)	184 (55)
LDL-C, (mg/dL)	132 (54)	126 (49)	132 (52)	138 (60)	140 (68)	142 (57)	111 (78)
HDL-C, (mg/dL)	55 (22)	58 (23)	48 (19)	48 (17)	44 (16)	54 (21)	47 (24)
Triglycerides, (mg/dL)	115 (84)	106 (74)	132 (95)	136 (103)	158 (112)	124 (84)	119 (97)
HbA1c, (%)	5.6 (0.6)	5.5 (0.4)	5.7 (0.8)	5.8 (0.9)	6.7 (1.9)	5.7 (0.5)	6.4 (2.7)
Glomerular Filtration Rate, (mL/min)	81 (22)	83 (21)	82 (23)	80 (23)	73 (27)	78 (21)	89 (24)
Systolic Blood Pressure, (mmHg)	124 (24)	119 (19)	134 (19)	135 (21)	146 (30)	128 (20)	138 (38)
Lipid lowering therapy, n (%)	3880 (18.6)	1014 (8.7)	151 (30.3)	910 (35.9)	293 (48.0)	1474 (27.0)	38 (36.2)
Statins, n (%)	3170 (15.2)	758 (6.5)	124 (24.8)	808 (31.8)	269 (44.0)	1178 (21.6)	33 (31.4)
Antihypertensive drugs, n (%)	6332 (30.4)	1878 (16.2)	231 (46.3)	1369 (53.9)	444 (72.7)	2348 (43.0)	62 (59.0)
Body Mass Index, (Kg/m²)	28.4 (8.1)	27.6 (8.4)	30.8 (8.4)	29.9 (8.0)	30.0 (7.7)	28.8 (7.4)	28.4 (14.6)

Characteristics	Overall	Original and Updated PCE Risk Category Concordant				Original and Updated PCE Risk Category Discordant	
		Low (<5%)	Borderline (5 – 7.5%)	Intermediate (7.5 – 20%)	High (20%)	Lower estimated risk with Updated PCE	Higher estimated risk with Updated PCE
Diabetes mellitus, n (%)	3078 (14.8)	740 (6.4)	175 (35.1)	874 (34.4)	480 (78.6)	739 (13.5)	70 (66.7)
Smoking status, n (%)							
Never	13353 (64.1)	8280 (71.3)	272 (54.6)	1255 (49.5)	269 (44.0)	3225 (59.0)	52 (50.0)
Current	1883 (9.0)	527 (4.5)	98 (19.7)	551 (21.7)	170 (27.8)	507 (9.3)	30 (28.8)
Former	5599 (26.9)	2812 (24.2)	128 (25.7)	731 (28.8)	172 (28.2)	1734 (31.7)	22 (21.2)
Original PCE risk score, (%)	4.09 (7.81)	1.84 (2.14)	6.86 (0.95)	14.40 (4.71)	34.67 (12.07)	8.52 (5.39)	6.23 (2.69)
Updated PCE risk score, (%)	2.82 (4.92)	1.34 (1.49)	5.51 (0.86)	9.86 (3.29)	25.73 (8.79)	5.04 (2.88)	7.65 (3.63)
Difference in risk scores, (%)	1.11 (2.65)	0.44 (0.83)	1.28 (1.47)	3.76 (3.84)	8.37 (9.64)	3.34 (3.09)	– 1.39 (1.48)

LDL-C: Low Density Lipoprotein Cholesterol; HDL-C: High Density Lipoprotein Cholesterol; HbA1c: Glycosylated Hemoglobin; PCE: Pooled Cohort Equations.

Table 2

Frequency distribution of risk categories according to scores assessed by the original and updated PCE of non-diabetic patients aged between 40 and 75 years, LDL-C 70–189 mg/dL and with no previous history of ASCVD. Patients with discordant risk categories are italicized.

Characteristics & statin recommendation	Original PCE risk categories				Participants, n(%)
	No DM + risk <5% No statin*	No DM + risk 5–7.5% Possible moderate-intensity statin*	No DM + risk 7.5–20% Moderate-intensity statin*	No DM + risk 20% High-intensity statin*	
Updated PCE risk categories & statin recommendation	No DM + risk <5%				
	No statin*				
	With statin prescription, n(%)	134 (8.5)	69 (12.4)	0 (0.0)	534 (4.5)
	Without statin prescription, n(%)	1448 (91.5)	487 (87.6)	1 (100.0)	11219 (95.5)
	Total, n(%)	1582 (10.4)	556 (3.6)	1 (0.0)	11753 (77.0)
	No DM + risk 5 – 7.5% Possible moderate-intensity statin*				
	With statin prescription, n(%)	42 (15.1)	227 (17.0)	0 (0.0)	269 (16.6)
	Without statin prescription, n(%)	236 (84.9)	1107 (83.0)	1 (100.0)	1356 (83.4)
	Total, n(%)	278 (1.8)	1334 (8.7)	1 (0.0)	1625 (10.7)
	No DM + risk 7.5 – 20% Moderate-intensity statin*				
	With statin prescription, n(%)	0 (0.0)	284 (21.2)	116 (27.6)	400 (22.6)
	Without statin prescription, n(%)	1 (100.0)	1058 (78.8)	305 (72.4)	1370 (77.4)
	Total, n(%)	1 (0.0)	1342 (8.8)	421 (2.8)	1770 (11.6)
	No DM + risk 20% High-intensity statin*				
	With statin prescription, n(%)	0 (0.0)	0 (0.0)	16 (16.5)	18 (17.5)
	Without statin prescription, n(%)	0 (0.0)	0 (0.0)	81 (83.5)	85 (82.5)
	Total, n(%)	0 (0.0)	6 (0.1)	97 (0.6)	103 (0.7)
Participants, n(%)	With statin prescription, n(%)	331 (3.4)	176 (9.4)	582 (18.0)	1221 (8.0)
	Without statin prescription, n(%)	9296 (96.6)	1690 (90.6)	2656 (82.0)	14030 (92.0)
	Total, n(%)	9627 (63.2)	1866 (12.2)	3238 (21.2)	15251 (100)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

PCE: Pooled Cohort Equations; LDL-C: Low Density Lipoprotein Cholesterol; DM: Diabetes Mellitus.

^aAccording to the 2018 ACC/AHA guideline, non-diabetic patients aged between 40 and 75 years, LDL-C between 70 and 189 mg/dL with no previous history, a 10-year ASCVD risk score of 5 to <7.5% and if risk enhancers are present, a moderate-intensity statin should be discussed. If 10-year ASCVD risk score of 7.5–20% and risk enhancers present, a moderate-intensity statin is recommended with aim of lowering LDL-C by 30–49%. If 10-year ASCVD risk score of 20% and multiple ASCVD risk factors, a high-intensity statin is recommended with aim of lowering LDL-C by 50% or more.

Table 3

Frequency distribution of risk categories according to scores of 10% assessed by the original and updated PCE of patients with stage I hypertension (BP 130–139 mmHg) aged between 40 and 75 years and with no previous history of ASCVD. Patients with discordant risk categories are italicized.

Characteristics & antihypertensive drugs recommendation	Original PCE score risk categories		Participants, n (%)
	Risk <10% HTN drug*	Risk 10% HTN recommended*	
Updated PCE risk categories & antihypertensive drugs recommendation	Risk <10%		
	No HTN drug*		
	In use of antihypertensive, n(%)	284 (49.7)	1123 (32.6)
	Not in use of antihypertensive, n(%)	288 (50.3)	2322 (67.4)
Updated PCE risk categories & antihypertensive drugs recommendation	Total, n(%)	572 (13.8)	3445 (83.0)
	Risk 10% HTN recommended*		
	In use of antihypertensive, n(%)	432 (61.5)	434 (61.3)
	Not in use of antihypertensive, n(%)	270 (38.5)	274 (38.7)
Participants, n(%)	Total, n(%)	702 (16.9)	708 (17.0)
	In use of antihypertensive, n(%)	841 (29.2)	1557 (37.5)
	Not in use of antihypertensive, n(%)	2038 (70.8)	2596 (62.5)
	Total, n(%)	2879 (69.3)	4153 (100)

^a According to the 2017 ACC/AHA guideline, patients with stage I hypertension and 10-year ASCVD risk score 10% are recommended to be prescribed antihypertensive drugs aiming blood pressure <130/80 mmHg.