Development and External Validation of the SCORE2 Models in Latin America and the Caribbean (SCORE2-LAC) to Estimate 10-Year Cardiovascular Disease Risk

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Abstract

Background and Aims: Despite the high burden of cardiovascular disease (CVD) in Latin America and the Caribbean (LAC), risk prediction models adapted for use in LAC populations remain limited. The aim of this study was to recalibrate the Systematic COronary Risk Evaluation 2 (SCORE2) risk models for estimating 10-year CVD risk in individuals without prior CVD or diabetes mellitus in LAC, resulting in the SCORE2 Latin America and the Caribbean (SCORE2-LAC) models.

Methods: Sex-specific, competing risk-adjusted SCORE2 models were recalibrated to contemporary CVD incidence across four risk regions, defined by country-level age- and sex-standardized CVD mortality rates, using region-specific risk factor distributions. Cardiovascular disease incidence was estimated from CVD mortality data and ratios of the total first-to-fatal CVD events, derived from 40 237 152 individuals (1 261 329 CVD events). External validation included 132 512 individuals without prior CVD or diabetes from 11 cohorts across seven countries (3938 CVD events). Discrimination was assessed using Harrell's C-index.

Results: In the external validation datasets, the pooled C-index of SCORE2-LAC was .740 [95% confidence interval (CI) .716–.763], with cohort-specific C-indices ranging from .674 (95% CI .588–.761) to .789 (95% CI .747–.831). Estimated CVD risk varied several-fold across the four LAC risk regions. For a 50-year-old non-smoker with a systolic blood pressure of 140 mmHg, total cholesterol of 213 mg/dL (5.5 mmol/L), and HDL cholesterol of 50 mg/dL (1.3 mmol/L), the predicted risk ranged from 3% in low-risk countries to 10% in very-high-risk countries for women, and from 4% to 10% for men.

Conclusions: The SCORE2-LAC models provide region-specific contemporary estimates of 10-year CVD risk in apparently healthy individuals, enabling identification of individuals at high CVD risk across LAC. Structured Graphical Abstract.

Keywords: Risk estimation; Cardiovascular disease; Risk factors; Prospective studies.; Latin America and the Caribbean.

Introduction

Cardiovascular diseases (CVDs), particularly ischaemic heart disease and stroke, are the leading causes of death worldwide, accounting for an estimated 8.9 million and 6.8 million deaths in 2023, respectively.[1] Guidelines recommend the use of CVD risk prediction models to identify individuals at elevated CVD risk and to guide preventive treatment decisions.[2–4] These models integrate information on clinical risk factors to typically estimate an individual's 10-year risk of fatal and non-fatal cardiovascular events, thereby identifying those at elevated risk who are most likely to derive absolute benefit from lifestyle modifications and early risk factor treatment.[5,6] For apparently healthy individuals, the Systematic COronary Risk Evaluation 2 (SCORE2) models were implemented in the 2021 European Society of Cardiology (ESC) CVD prevention guidelines.[2,5] Key strengths of SCORE2 are its competing-risk adjustment and systematic recalibration using population-level aggregate data. In this recalibration approach, the original SCORE2 coefficients are retained, while predicted risks are adapted to reflect local CVD event rates and risk factor distributions. This approach was initially applied across European risk regions and was more recently used to develop the SCORE2 Asia-Pacific models.[5,7] The broader validity of this modelling framework is supported by a recent large multinational external validation, in which SCORE2 showed generally good performance across diverse geographical regions and clinical settings.[8]

In Latin America and the Caribbean (LAC), the burden of CVD remains high, with premature mortality from ischaemic heart disease continuing to rise over the past two decades.[1] Despite this high burden of CVD, most existing risk prediction models have been developed and validated primarily in European or North American populations, with relatively few data from LAC populations.[9–11] Since CVD event rates, case fatality, and average risk factor levels vary over time and across populations, models developed in one setting may over- or underestimate risk when applied elsewhere.[12,13] These differences are not fully captured by risk predictors, as they also reflect broader variation in regional and population characteristics, such as socioeconomic context, genetic background, and healthcare systems.[14] Recalibration using representative data is therefore required to ensure that predicted risks accurately reflect contemporary CVD risk in the target population.

The two regionally adapted CVD risk prediction models currently available for use in LAC are the World Health Organization (WHO) CVD risk charts and Globorisk-LAC.[10,15] SCORE2 Latin America and the Caribbean (SCORE2-LAC) extends these existing approaches by applying the SCORE2 recalibration framework to contemporary CVD incidence rates derived from large-scale data sources across LAC. Rather than deriving a new prediction model, the original SCORE2 coefficients were retained, while CVD risk estimates were adapted to reflect differences in the underlying CVD burden and risk factor distributions across LAC populations. The framework also accounts for the competing risk of non-CVD death, thereby limiting the potential overestimation of CVD risk, particularly among older individuals and in populations with high non-CVD mortality. In addition, the availability of data from multiple LAC cohorts allowed extensive external validation of the resulting models in local populations.

The aim of this study was to recalibrate the SCORE2 models using age- and sex-specific CVD incidence and risk factor distributions in LAC and to externally validate the resulting SCORE2-LAC models for 10-year CVD risk estimation in individuals without prior CVD or diabetes mellitus.

Methods

Study design

The SCORE2-LAC project involved several stages (*Figure 1*). First, four risk regions within LAC were defined based on 2019 WHO age- and sex-standardized CVD mortality rates, serving as the basis for subsequent recalibration of the SCORE2 models. Second, the original SCORE2 models were recalibrated within each risk region to reflect contemporary circumstances in LAC using age- and sex-specific CVD incidence and risk factor distributions. Third, external performance of the recalibrated models was assessed using individual participant data from cohort studies. Performance was also compared with two existing risk prediction models: the WHO CVD risk charts and Globorisk-LAC.[10,15] Fourth, risk charts were constructed by estimating the CVD risk for specified risk factor profiles, illustrating variation across risk regions. Finally, to illustrate variation in CVD risk across LAC countries, the models were applied to contemporary, country-specific risk factor levels to estimate 10-year risk distributions and the proportion of individuals in each risk category.

The original SCORE2 models were derived using individual-participant data from 44 cohorts in the Emerging Risk Factor Collaboration and the UK Biobank.[5] For SCORE2-LAC, the original SCORE2 model coefficients were recalibrated to LAC, and no new model derivation was performed. The original SCORE2 models are sex specific and estimate the 10-year risk of a first non-fatal or fatal CVD event in individuals without

Central Illustration: Development and External Validation of the SCORE2 Models in Latin America and the Caribbean (SCORE2-LAC) to Estimate 10-Year Cardiovascular Disease Risk

Structured Graphical Abstract

Key Question

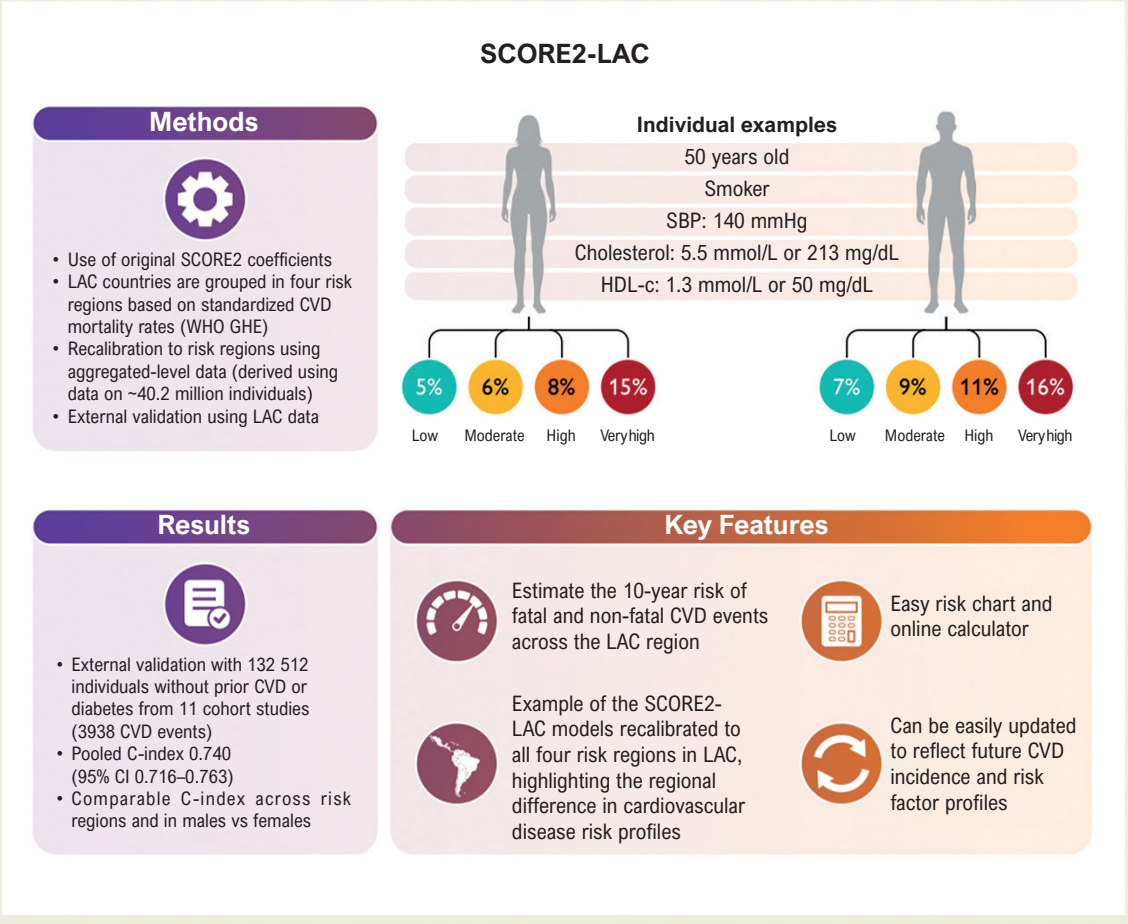
How can the 10-year cardiovascular disease (CVD) risk estimation for individuals without prior CVD or diabetes mellitus be improved in Latin America and the Caribbean (LAC)?

Key Finding

The SCORE2 Latin America and the Caribbean (SCORE2-LAC) models were recalibrated to reflect sex-specific and competing risk-adjusted CVD incidence in four LAC regions, resulting in a pooled C-index of 0.740. Risk varied significantly across LAC risk regions, highlighting regional differences in CVD risk.

Take Home Message

The recalibrated SCORE2-LAC models provide region-specific and contemporary estimates of 10-year CVD risk in apparently healthy individuals, thereby enabling the identification of individuals at higher CVD risk to guide cardiovascular prevention.



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Example of the SCORE2-LAC models recalibrated to all four risk regions in LAC, highlighting the regional difference in cardiovascular disease risk profiles. CI: confidence interval; CVD: cardiovascular diseases; HDL-c: high-density lipoprotein cholesterol; LAC: Latin America and the Caribbean; SBP: systolic blood pressure; WHO GHE: World Health Organization Global Health Estimates. Font: Bijker S, et al. European Heart Journal.

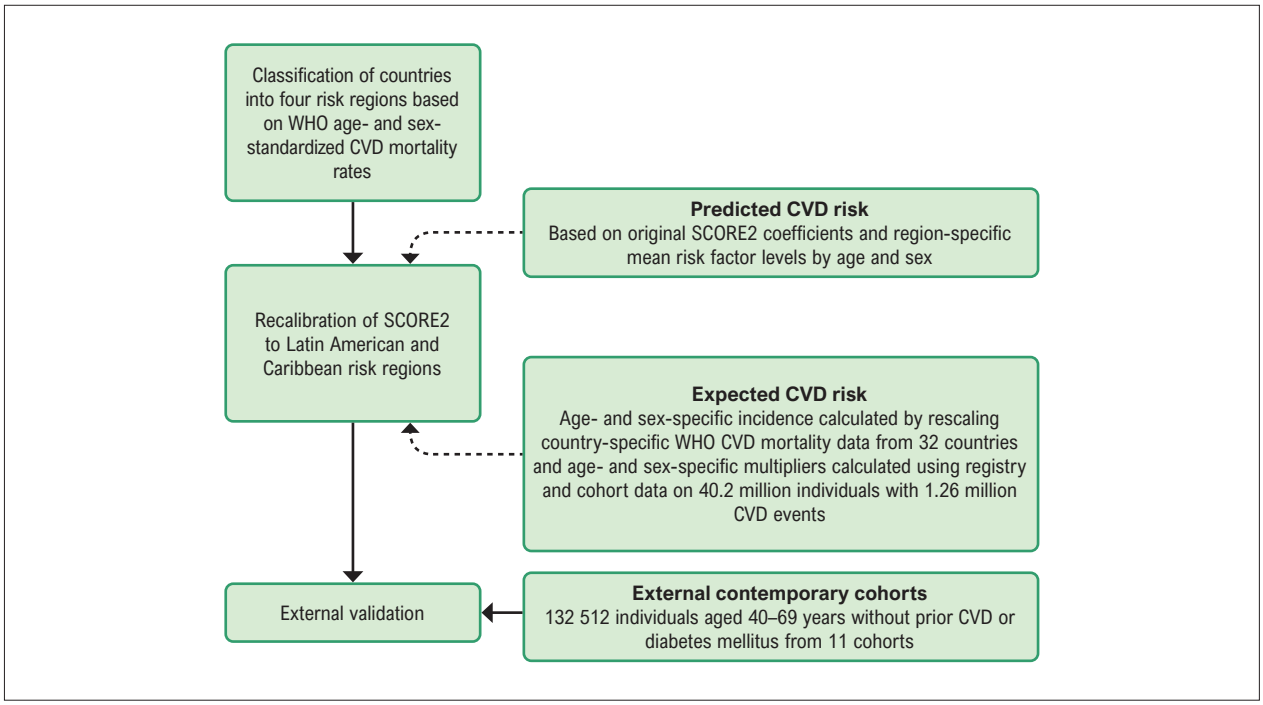


Figure 1 – *Study design. Created with BioRender.com.*

prior CVD, accounting for non-CVD death as a competing risk using Fine and Gray models. Predictors include age, current smoking status, systolic blood pressure (SBP), and total and HDL cholesterol. Throughout this study, sex was used as recorded in the original data sources and was categorized as female or male. Interactions with age were included for all predictors to account for declining relative risk associations with CVD occurrence at older ages[15] (see Supplementary Methods, *Table S1*, for original SCORE2 coefficients). Although SCORE2 is not intended for use in individuals with diabetes mellitus, participants with diabetes were included during model derivation, with adjustment for diabetes status. This was necessary because the population-level mortality rates and risk factor distributions used for recalibration were available only at the aggregate level and could therefore not be restricted to individuals without diabetes. Coefficients of predictors have been shown to be stable over time and across geographic regions.[7,15]

Data sources and procedures

Latin America and the Caribbean countries were grouped into four risk regions according to age- and sex-standardized CVD mortality rates per 100 000 population using the 2019 WHO Global Health Estimates (GHE) (International Classification of Diseases, 10th revision, Chapter IX, I00-I99).[16] The same cut-off values as in the European and Asia-Pacific SCORE2 models were applied to define risk regions: low risk (<100 CVD deaths per 100 000), moderate risk (100 to <150), high risk (150 to <300), and very high risk (≥300) (*Figure 2*; Supplementary data online, *Table S1*). Mortality data were unavailable for French Guiana and several small islands shown in grey in *Figure 2* and Supplementary data online, *Table S1*.

The original SCORE2 models were derived using individual-participant data from 44 cohorts in the Emerging Risk Factor Collaboration and the UK Biobank.[5] For SCORE2-LAC, the original SCORE2 model coefficients were recalibrated to LAC, and no new model derivation was performed. The original SCORE2 models are sex specific and estimate the 10-year risk of a first non-fatal or fatal CVD event in individuals without prior CVD, accounting for non-CVD death as a competing risk using Fine and Gray models. Predictors include age, current smoking status, systolic blood pressure (SBP), and total and HDL cholesterol. Throughout this study, sex was used as recorded in the original data sources and was categorized as female or male. Interactions with age were included for all predictors to account for declining relative risk associations with CVD occurrence at older ages[15] (see Supplementary Methods, *Table S1*, for original SCORE2 coefficients). Although SCORE2 is not intended for use in individuals with diabetes mellitus, participants with diabetes were included during model derivation, with adjustment for diabetes status. This was necessary because the population-level mortality rates and risk factor distributions used for recalibration were available only at the aggregate level and could therefore not be restricted to individuals without diabetes. Coefficients of predictors have been shown to be stable over time and across geographic regions.[7,15]

Data sources and procedures

Latin America and the Caribbean countries were grouped into four risk regions according to age- and sex-standardized



Figure 2 – *Risk regions based on age- and sex-standardized cardiovascular disease mortality rates. Countries were grouped based on age- and sex-standardized cardiovascular disease mortality rates from the World Health Organization Global Health Estimates: low risk (<100 cardiovascular disease deaths per 100 000), moderate risk (100 to <150), high risk (150 to <300), and very high risk (≥300). Countries and territories without sufficient data for risk region assignment, or outside the region of interest, are shown in grey.*

CVD mortality rates per 100 000 population using the 2019 WHO Global Health Estimates (GHE) (International Classification of Diseases, 10th revision, Chapter IX, I00-I99).[16] The same cut-off values as in the European and Asia-Pacific SCORE2 models were applied to define risk regions: low risk (<100 CVD deaths per 100 000), moderate risk (100 to <150), high risk (150 to <300), and very high risk (≥300) (*Figure 2*; Supplementary data online, *Table S1*). Mortality data were unavailable for French Guiana and several small islands shown in grey in *Figure 2* and Supplementary data online, *Table S1*.

For recalibration to LAC, predicted 10-year CVD risks from the original SCORE2 models were aligned with expected 10-year CVD incidence across risk regions, stratified by age and sex (see Supplementary Methods for details). Predicted 10-year risks were obtained by applying the original SCORE2 coefficients to age- and sex-specific mean risk factor levels (smoking and diabetes prevalence, SBP, and total and HDL cholesterol), derived from LAC representation in the Non-Communicable Disease Risk Factor Collaboration (NCD-RisC).[17–20] Expected 10-year CVD incidence was estimated by converting country-specific CVD mortality rates from the WHO GHE 2019, available for 32 LAC countries as detailed in Supplementary data online, *Table S1*, into total CVD incidence (fatal and non-fatal) using age- and sex-specific multipliers within each risk region.[16] These multipliers were derived from total first-to-fatal CVD event ratios calculated using data from the Chilean Ministry of Health dataset, the Barbados National Registry for Chronic Noncommunicable Diseases (BNR-Stroke and BNR-Heart),[21] and the 100 Million Brazilian Cohort study[22] (see Supplementary data online, *Table S2* and *Appendix S1*). Together, these data sources included 40 237 152 LAC individuals and 1 261 329 CVD events, providing region-specific information on fatal and non-fatal CVD events among individuals without prior CVD. Multipliers from the European and Asia-Pacific SCORE2

recalibrations were incorporated into the modelling process to improve the stability of the estimated relationships across age groups. Further details of the data sources and methods are provided in Supplementary Methods, *Figures S1* and *S2*, and *Table S2*.

External validation of the SCORE2-LAC models was performed using data from 132 512 individuals and 3938 CVD events from 11 cohorts that did not contribute to model derivation and recalibration. The following individual studies were included for external validation: the Maule cohort (MAUCO, Chile),[23] the Center of Excellence in Chronic Diseases cohort (CRONICAS, Peru),[24] the National Health Survey (Chile),[25] the CESCAS study (Chile, Uruguay, and Argentina),[26] the Fundación Santa Fe de Bogotá cohort (FSFB, Colombia),[27] the Eventos Cardiovasculares cohort (Argentina),[28] the Mexico City Prospective Study (MCPS),[29] the Rauch city cohort (RAUCH, Argentina),[30] ELSA-Brasil (Brazil),[31] the Mendoza cohort (Argentina),[32] and the Grupo de Análisis de Riesgo cardiovascular y Datos Epidemiológicos Longitudinales—Uruguay (GARDEL-UY, Uruguay). Details and geographical distribution of the cohorts across LAC are provided in Supplementary data online, *Appendix S1.2*, and *Figure S1*.[23–32] In alignment with the original SCORE2 model, individuals aged 40–69 years without prior CVD or diabetes mellitus were included for external validation (ICD codes used to define prior CVD are provided in Supplementary data online, *Table S3*). Cohorts were included if they had baseline measurements of risk factors (predictor information and medical history) and provided at least 1 year of follow-up for CVD events. Cardiovascular disease was defined as a composite of cardiovascular mortality, non-fatal myocardial infarction, and non-fatal stroke. Cardiovascular mortality was defined as death due to coronary heart disease, heart failure, stroke, or sudden death.[33] Follow-up was until the first occurrence of CVD or the end of the registration period. Deaths from non-CVD causes were treated as competing events. Details of ICD-10 codes included in the fatal and non-fatal components of the endpoint are provided in Supplementary data online, *Table S4*.

Statistical analysis

Details of the statistical analysis and recalibration process are provided in the Supplementary Methods. Risk models were recalibrated to risk regions using age- and sex-specific mean risk factor levels and CVD incidence.[12] Cardiovascular disease incidence was estimated from country-specific mortality rates by applying age-, sex-, and region-specific multipliers. The competing risk of non-CVD death was accounted for using a life-table approach. Subsequent calibration of the SCORE2-LAC models was assessed by comparing predicted and estimated 10-year risks across 5-year age groups within each risk region. In addition, calibration was evaluated among individuals without prior CVD in the Chilean Ministry of Health dataset with predicted risks derived using Chilean age- and sex-specific mean risk factor levels from NCD-RisC.[17–20] Calibration was assessed by comparing mean predicted risks with observed 10-year risks based on cumulative incidence across 5-year age groups, as this best reflects the method of recalibration. Calibration of the SCORE2-LAC models was also visually compared with that of the WHO CVD risk charts and Globorisk-LAC using the same approach in this dataset.[10,15] This comparison was performed using the appropriate recalibrated region- or country-specific version of each model, with observed risks defined according to the SCORE2 endpoint. No formal statistical testing was performed on the calibration because the modified Nam–D'Agostino test has no extension to the competing-risk setting and because these tests are inherently power dependent.

Discriminative performance, reflecting the ability of the model to distinguish between individuals who did and did not develop the CVD event of interest, was assessed in the external validation cohorts using Harrell's C-index with adjustment for competing risks, using all observed follow-up within each cohort.[34] C-indices were estimated separately for each cohort overall and by sex. Cohort-specific C-indices were pooled using inverse-variance-weighted random-effects meta-analysis. Pooled estimates were calculated overall and separately by risk region and sex. Sensitivity analyses were performed by restricting the calculation of pooled estimates to cohorts with a median follow-up of at least 8 years and separately by pooling cohorts assessing the full composite CVD endpoint vs those assessing fatal CVD events only. Discriminative performance of SCORE2-LAC in the external validation cohorts was compared with that of the WHO CVD risk charts and Globorisk-LAC. These analyses were restricted to individuals for whom risk could be estimated by all models, thereby ensuring that model performance was compared in the same individuals. For example, although the WHO CVD risk charts can be applied across a broader age range than SCORE2-LAC, analyses were restricted to the age range covered by all models. No direct comparison of discrimination with the original European SCORE2 models was made, as recalibration does not alter the model coefficients and therefore has little impact on discrimination. C-indices were compared within each cohort as the difference between SCORE2-LAC and each comparator model with 95% confidence intervals (CIs) obtained by bootstrap resampling of individuals repeated 1000 times. Calibration was assessed only within the recalibration data sources and not in the external validation cohorts, because cohort-specific event rates were unlikely to be representative for various reasons, including selected participant groups, non-contemporary baseline recruitment, or incomplete alignment between observed outcomes and those predicted by the models.[12,35]

To construct the CVD risk charts for each risk region, predicted risks were estimated using the recalibrated models for specified risk factor profiles. Although the underlying model includes total cholesterol and HDL cholesterol, charts are displayed according to non-HDL cholesterol for practical and presentational purposes. To compare the proportion of the population across CVD risk categories according to the SCORE2-LAC models, predicted risk distributions were estimated for each LAC country using country-specific population structures and age- and sex-specific risk factor

means and prevalences from NCD-RisC. Correlations between risk factors were assumed to be similar to those observed in the MCPS (see Supplementary Methods *S1.3*).[29] In a sensitivity analysis, these estimates were recalculated using the risk factor correlation structure observed in the CESCAS study.[26]

Approaches used to handle missing data are described in the Supplementary Methods. For analytical approaches and reporting standards, the PROBAST guidelines and TRIPOD were used.[36,37] Analyses were performed with R statistical software (version 4.3.2, R Foundation for Statistical Computing, Vienna, Austria) and Stata (version 15.1, StataCorp, College Station, TX, USA).

Results

Model recalibration

Characteristics of the data sources used to derive regional age- and sex-specific multipliers for converting CVD mortality rates into total CVD incidence rates, including non-fatal CVD events among individuals without prior CVD, are presented in Supplementary data online, *Table S2*. The resulting multipliers for each LAC risk region were generally higher in women than in men and decreased with increasing age (see Supplementary data online, *Figure S2*, and *Table S5*). In addition, multipliers tended to be lower in higher-risk regions than in low- or moderate-risk regions, consistent with patterns previously observed in Europe and Asia-Pacific.[5,7] Ten-year cumulative incidence of CVD mortality and the resulting total CVD incidence across risk regions are presented in Supplementary data online, *Figure S3*. Age- and sex-specific mean risk factor levels used for recalibration are presented by risk region in Supplementary data online, *Figure S4*. Across ages, higher-risk regions generally had higher mean SBP, total, and HDL cholesterol levels than lower-risk regions, whereas patterns for smoking and diabetes were less consistent. Despite these differences, application of the original SCORE2 models to these mean risk factor levels resulted in relatively similar predicted risks across risk regions, which did not reflect the differences in expected CVD incidence (see Supplementary data online, *Figure S5*). After recalibration, predicted 10-year CVD risks were well aligned with the estimated total CVD incidence across risk regions (see Supplementary data online, *Figure S5*). Compared with SCORE2-LAC, the corresponding European SCORE2 models generally underestimated expected CVD incidence, particularly among men. Conversely, among older women in the high- and very-high-risk regions, the European SCORE2 models tended to overestimate expected CVD incidence (see Supplementary data online, *Figure S6*).

In the Chilean Ministry of Health dataset, predicted 10-year risks showed good agreement with observed CVD risk among women (observed-to-expected ratio 1.03), whereas predicted risks were lower than observed risks among men (observed-to-expected ratio 1.26; Supplementary data online, *Figure S7*). The WHO CVD risk charts and Globorisk-LAC underestimated observed CVD incidence to a larger extent than SCORE2-LAC, although calibration of the WHO CVD risk charts was similar to that of SCORE2-LAC among women (see Supplementary data online, *Figure S8*). Compared with SCORE2-LAC, the corresponding European SCORE2 models showed greater underestimation of observed CVD risk among men, particularly at older ages, whereas calibration among women was more comparable (see Supplementary data online, *Figure S9*).

SCORE2-LAC models across risk regions

The SCORE2-LAC risk charts for CVD risk estimation across the four risk regions are presented in *Figure 3*. The estimated absolute risk for a given age and combination of risk factor levels differed substantially across risk regions as a result of recalibration. For example, the estimated 10-year CVD risk for a 50-year-old smoker with a SBP of 140 mmHg, total cholesterol of 213 mg/dL (5.5 mmol/L), and HDL cholesterol of 50 mg/dL (1.3 mmol/L) ranged from 7% in the low-risk region to 16% in the very-high-risk region for men and from 5% in the low-risk region to 15% in the very-high-risk region for women (see Supplementary data online, *Figure S10*).

External validation of the SCORE2-LAC models

External validation of the SCORE2-LAC models was performed using data from 11 cohorts from seven LAC countries, including only individuals without previous CVD or diabetes mellitus at baseline. Geographical distribution, baseline characteristics, and a summary of missingness of the external validation cohorts are presented in Supplementary data online, *Figure S1*, *Table S6*, and *Table S7*, respectively. The overall pooled C-index was .740 (95% CI .716–.763) and cohort-specific C-indices ranged from .674 (95% CI .588–.761) to .789 (95% CI .747–.831), indicating moderate-to-good discrimination (*Figure 4*). Moderate between-cohort heterogeneity was observed ($I^2 = 52\%$; $\tau^2 = .0184$ on the logit scale; Cochran's Q = 21.4, df = 12, $P = .044$). The C-indices for the SCORE2-LAC models were broadly similar for women and men and across the risk regions (see Supplementary data online, *Figures S11* and *S12*). Among the six cohorts with a median follow-up of at least 8 years, the pooled C-index of .740 (95% CI .695–.780) was similar to the overall estimate, with substantial between-study heterogeneity ($I^2 = 66\%$; $tau^2 = 0.0263$ on the logit scale; Cochran's Q = 12.4, df = 5, $P = .028$). In a sensitivity analysis in which pooled C-index estimates were calculated separately according to endpoint definition, the pooled C-index was .741 (95% CI .710–.770) among the 11 cohorts assessing the full composite endpoint of fatal and non-fatal CVD events and .727 (95% CI .647–.794) among the two cohorts assessing fatal CVD events only. Discriminative performance was comparable between the SCORE2-LAC models, Globorisk-LAC laboratory and non-laboratory models, and the WHO CVD risk charts laboratory and non-laboratory models across cohorts (see Supplementary data online, *Figures S13* and *S14*). The SCORE2-LAC models showed a slightly higher C-index than the WHO CVD risk charts laboratory models, with a difference in C-index of .006 (95% CI .002–.010).

Original Article

Risk distribution across Latin America and the Caribbean populations

When the recalibrated SCORE2-LAC models were applied to age- and sex-specific risk factor profiles, the proportion of individuals aged 40–69 years with an estimated 10-year CVD risk of >10% varied across risk regions, from 14% in countries in the low-risk region to 60% in countries in the very-high-risk region among men and from .3% to 54% among women (*Figure 5* and Supplementary data online, *Table S8* for used rescaling factors). The proportion of individuals classified

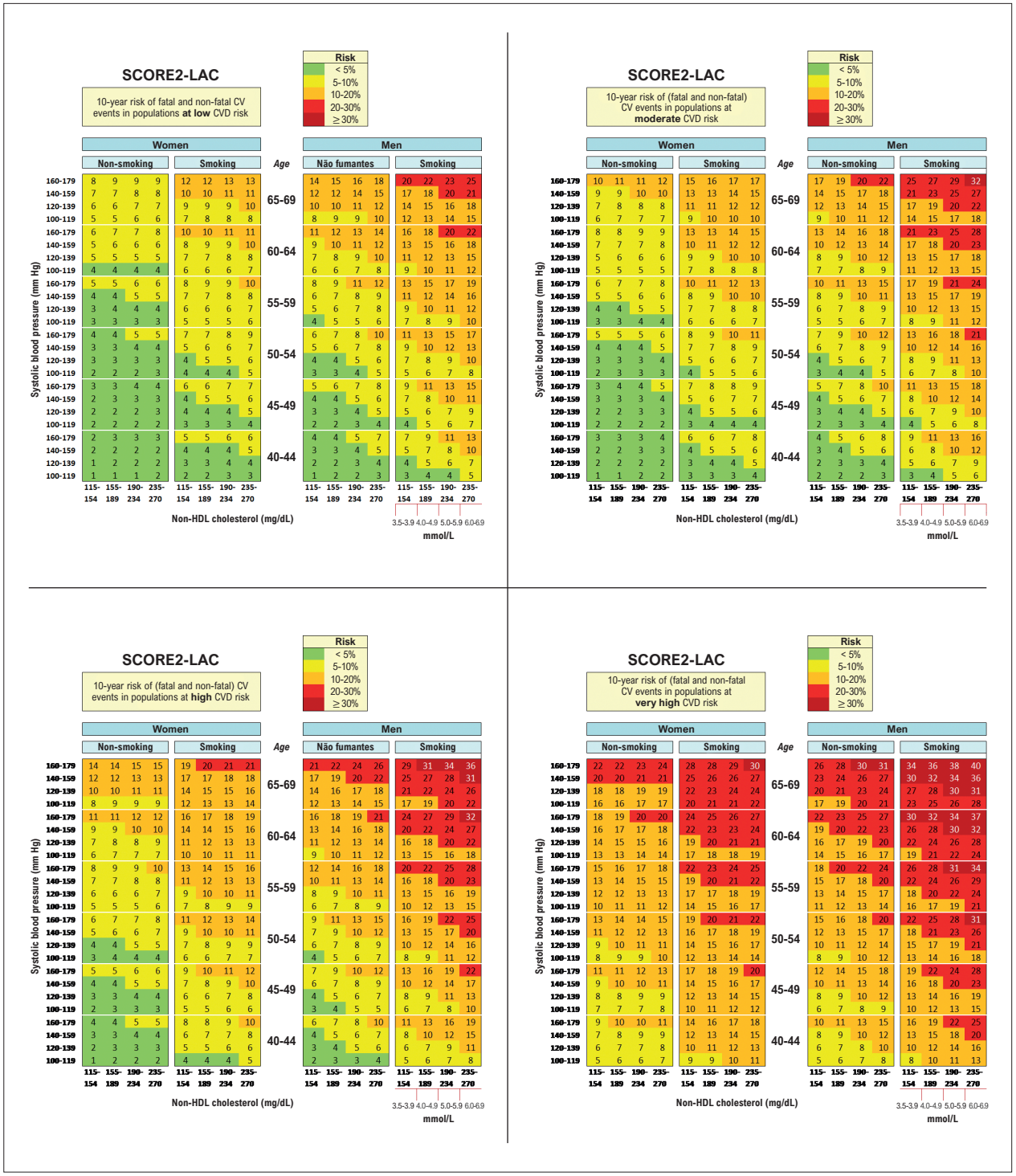


Figure 3 – *Systematic COronary Risk Evaluation 2 Latin America and the Caribbean risk charts for the prediction of 10-year risk in four Latin American and Caribbean risk.*

into higher 10-year CVD risk categories increased with age and was greater in higher-risk regions (see Supplementary data online, *Figure S15*). No notable differences in these risk distributions were observed when the alternative risk factor correlation structure from the CESCAS study was used (see Supplementary data online, *Figure S16*).

Discussion

In the current study, the SCORE2 models were recalibrated and externally validated for 10-year CVD risk prediction in LAC. Using the original SCORE2 coefficients, CVD risk estimates were recalibrated to reflect contemporary CVD incidence rates and risk factor distributions across LAC. The resulting SCORE2-LAC models provide region-specific and contemporary risk estimates for individuals without prior CVD or diabetes mellitus and enable the identification of individuals at higher CVD risk to guide cardiovascular prevention (*Structured Graphical Abstract*).

Cardiovascular disease risk prediction in LAC has largely been based on models developed for use in European or North American populations.[9,11] The main existing regionally adapted approaches include the WHO CVD risk charts and Globorisk-LAC.[10,15] Although the WHO CVD risk charts were originally derived using data that partly overlapped with those used for SCORE2 and included broadly similar predictors, they differ in their recalibration approach. The WHO CVD risk charts were recalibrated for geographically defined regions, which may not fully reflect between-country heterogeneity in CVD incidence. For example, Chile and Argentina were assigned to the same Southern Latin America region in the WHO CVD risk charts, while SCORE2-LAC classified Chile in the low-risk region and Argentina in the high-risk region based on their underlying CVD mortality rates. Accordingly, SCORE2-LAC resulted in substantially different CVD risk estimates for Chile and Argentina, despite these countries being grouped within the same WHO region, as illustrated by the country-specific risk distributions in *Figure 5*. Globorisk-LAC was developed using LAC cohort data and performed country-level recalibration.[10,38] However, total CVD incidence was estimated by converting country-specific CVD mortality rates using previously derived total-to-fatal CVD incidence ratios from geographically proximate countries. The current findings suggest that geographical proximity alone may not fully capture between-country differences in total CVD incidence, as the relationship between CVD mortality and total first CVD incidence varied across SCORE2-LAC risk regions.

SCORE2-LAC extends these existing approaches through risk-region-specific recalibration of absolute CVD risk

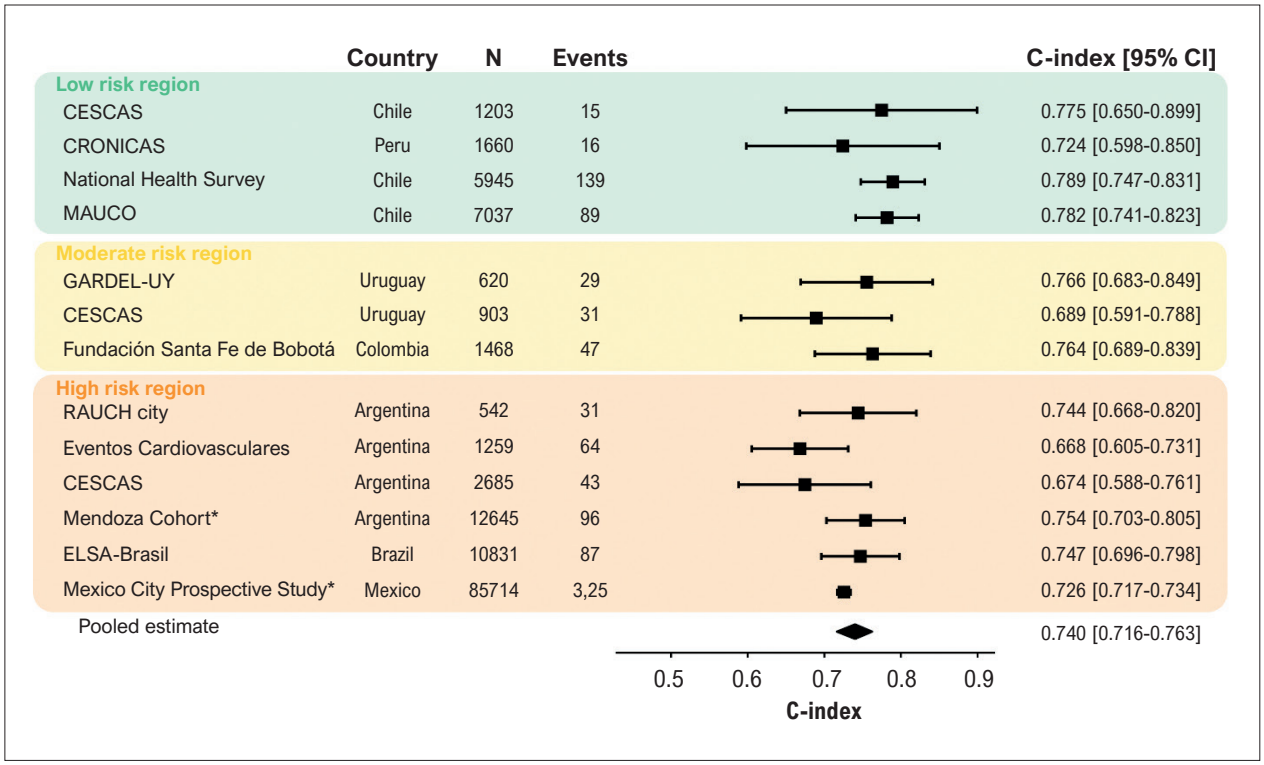


Figure 4 – *Discriminative performance of Systematic Coronary Risk Evaluation 2 Latin America and the Caribbean in external validation cohorts. C-index upon assessing the ability of the Systematic COronary Risk Evaluation 2 Latin America and the Caribbean models to discriminate cardiovascular disease in external validation cohorts. Analyses included individuals aged 40–69 years without a history of cardiovascular disease or diabetes mellitus at baseline. Pooled estimate is the result of pooling all cohort-specific C-index using random-effects meta-analysis. *Only fatal events were assessed. Abbreviation: CI: confidence interval.*

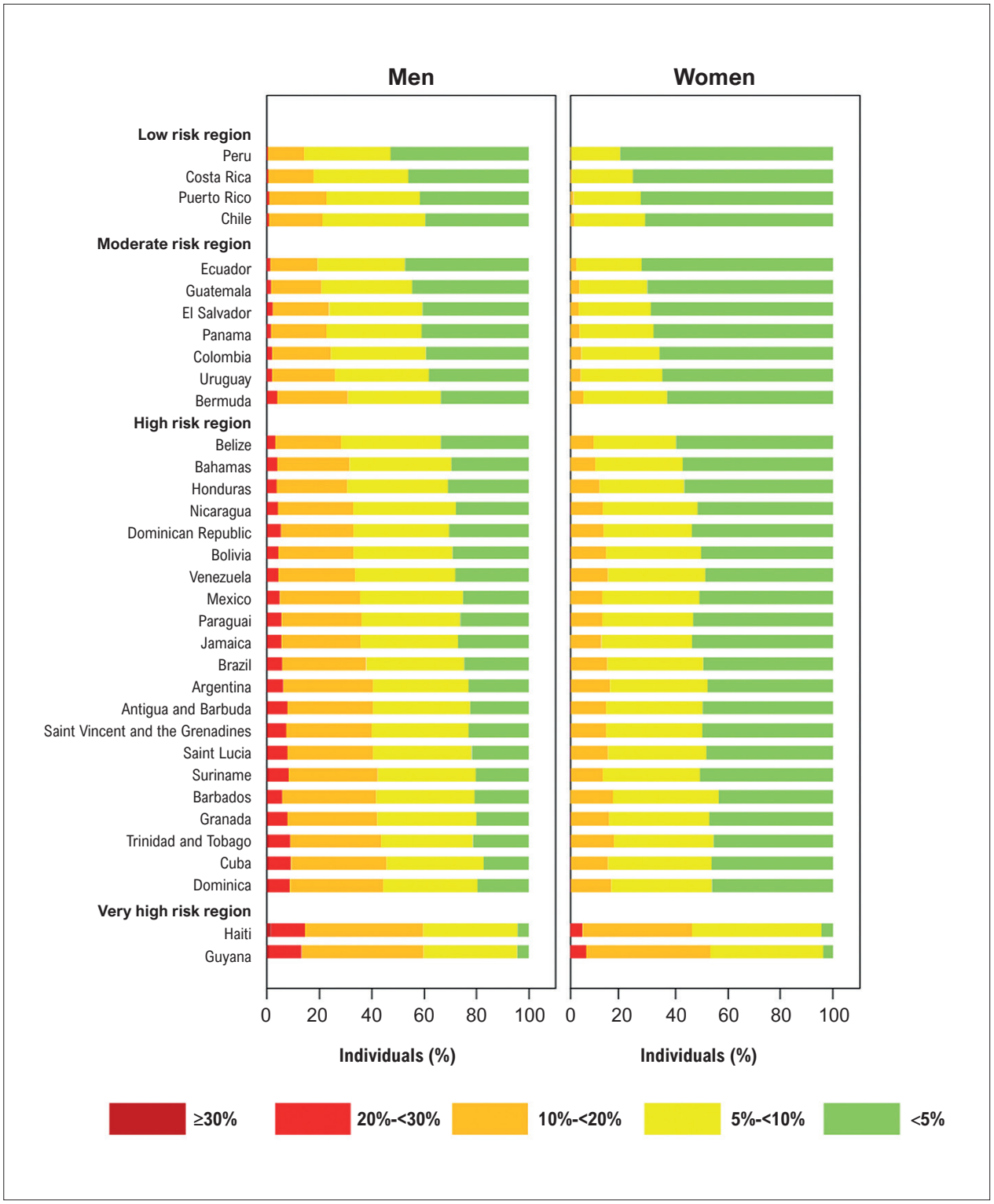


Figure 5 – *Distribution of 10-year cardiovascular disease risk according to Systematic COronary Risk Evaluation 2 Latin America and the Caribbean models across Latin American and Caribbean countries. The proportion of individuals expected in each risk category was estimated to reflect the age- and sex-specific risk factor values and population structure of each country (see Supplementary Methods S1.3). Estimates were derived from country-specific Non-Communicable Disease Risk Factor Collaboration risk factor means and prevalences and an assumed risk factor correlation structure derived from the Mexico City Prospective Study cohort. Risks were estimated for individuals aged 40–69 years without prior cardiovascular disease or diabetes mellitus. Abbreviations: MCPS: Mexico City Prospective Study; NCD-RisC: NCD Risk Factor Collaboration.*

estimates using contemporary data from LAC populations while having discrimination at least as good as local models. The recalibration was informed by large-scale data sources from LAC, including more than 40 million individuals, in which fatal and non-fatal CVD events were directly observed. These data were used to estimate risk-region-specific relationships between CVD mortality and total CVD incidence, allowing mortality rates to be converted to total CVD incidence according to underlying CVD burden rather than geographical location alone. This approach also enabled incidence estimates to be specified for first CVD events among individuals without prior CVD, thereby aligning predicted risks more closely with the target population for primary prevention.

In addition, SCORE2-LAC accounts for the impact of competing risks of non-CVD mortality. This statistical adjustment may prevent the overestimation of absolute CVD risk, particularly in older individuals and in populations with higher risks of non-CVD mortality.[34,39] By accounting for the competing risks, the SCORE2-LAC models may therefore provide more accurate estimates of 10-year CVD risk and the potential benefit of preventive treatment in these populations.[39]

Similar recalibration methods have previously been applied in Europe and Asia-Pacific, and recent multinational external validation findings have provided further support for the robustness of the SCORE2 framework across diverse settings.[8] Although the same age- and sex-standardized CVD mortality cut-offs were used to define risk regions as in previous SCORE2 recalibration efforts, predicted risks differed across the same risk regions. Applying the European SCORE2 models in LAC populations generally resulted in predicted risks below the expected CVD incidence, whereas predicted risks tended to exceed expected incidence among older women in the higher-risk regions. These findings illustrate the potential importance of adapting CVD risk prediction models to the populations in which they are intended to be used, even when broad risk-region categories appear comparable across world regions. At the population level, the regional CVD incidence rates and risk factor distributions used for recalibration may reflect not only conventional risk factor patterns but also the influence of wider social and healthcare determinants. Therefore, SCORE2-LAC may indirectly account for differences in socioeconomic circumstances, healthcare access, and the availability of preventive treatment, although these factors are not explicitly included as individual-level predictors.

The SCORE2-LAC recalibration approach is also designed to be updated as more detailed or contemporary data become available. WHO GHE mortality rates are updated every 3–4 years, while NCD-RisC risk factor estimates are updated regularly as new survey data and analyses are conducted.[16,40] In addition, the individual-level data used to estimate total first-to-fatal CVD incidence ratios have ongoing follow-up, allowing these estimates to be updated to reflect contemporary incidence patterns. Periodic incorporation of these data would allow SCORE2-LAC to remain aligned with changes in CVD incidence and risk factor patterns across LAC. Beyond such temporal updates, more detailed age- and sex-specific data on CVD incidence, mortality, and risk factor distributions could support further refinement for individual countries or subnational regions. This may be particularly relevant for large countries with substantial within-country variation, where a country-level approach may still not fully capture the heterogeneity in CVD burden.[41] Such extensions would, however, require high-quality data on both CVD risk factors and incidence for the intended populations to ensure adequate calibration of risk models.

Similar to SCORE2 Europe and Asia-Pacific, SCORE2-LAC can be used in a simplified form via the 2D risk charts as provided in *Figure 3*. In clinical practice across LAC, the appropriate SCORE2-LAC risk chart can be selected by using the map in *Figure 3* to identify the risk region to which an individual's country is assigned. However, because risk charts require risk factors to be grouped into categories, greater precision may be achieved through online calculators.[42] Therefore, the SCORE2-LAC models will be integrated into online calculators, such as the ESC CVD risk prediction app and the CE-marked U-Prevent medical device, available at www.U-Prevent.com. These digital implementations would also allow future SCORE2-LAC model updates to be incorporated efficiently and made available for use in clinical practice. Because integration into these clinical platforms requires implementation time, the SCORE2-LAC models are currently available through an R Shiny application (https://bijkerks.shinyapps.io/SCORE2-LAC/) and through an extension of the U-Prevent platform (https://feasibility.u-logiq.com/calculators/score2Lac).

The SCORE2-LAC risk charts are presented with colours corresponding to categories of predicted 10-year CVD risk. These categories should not be interpreted as fixed treatment thresholds, as treatment decisions depend on local CVD burden, clinical practice guidelines, healthcare resources, socioeconomic circumstances, and regional risk enhancers. Risk thresholds and corresponding clinical decisions need to be defined at a national or regional level and may be age specific, as in the 2021 ESC prevention guidelines, or independent of age.[2,43] Beyond predicted CVD risk, decisions about preventive treatment should also consider patient and physician preferences, expected treatment benefit and potential harms, comorbidities, other individual clinical factors, and the local availability, coverage, and affordability of preventive treatment. To support national and regional guideline development, estimated proportions of individuals in specific risk categories across countries are presented in *Figure 5*. The estimates for the very-high-risk region should, however, be interpreted cautiously, as no contemporary individual-level data from countries in this region were available.

Discriminative performance reflects the ability of a model to distinguish between individuals who do and do not develop CVD and may therefore provide insight into whether the relative associations between predictors and CVD risk are transportable across populations.[12,13] Because the SCORE2 coefficients were retained without re-estimation and no LAC data were included in the original model derivation, external validation provided an assessment of their transportability to LAC populations. Adequate discriminative performance was

observed for SCORE2-LAC across risk regions and in both sexes. In direct comparisons, the discriminative performance of the SCORE2-LAC models was similar to that of Globorisk-LAC, which was developed using LAC cohort data. Together with the broadly consistent discrimination estimates, these findings provide some confirmatory evidence that the SCORE2 model coefficients are broadly applicable to LAC populations, which is consistent with previous evidence that CVD risk model coefficients are relatively stable across geographical regions.[15]

Accurate calibration is a key requirement for CVD risk prediction models intended to guide clinical decision-making, as treatment recommendations are typically based on estimated absolute risk rather than relative ranking of individuals.[44] Ideally, calibration would be assessed in nationally representative external validation data sources, such that observed event rates reflect contemporary population-level CVD incidence. However, cohorts generally have some form of selection due to their recruitment strategies or have incomplete risk factor data and/or follow-up of both fatal and non-fatal outcomes. These challenges are not unique to the current study and reflect the scarcity of these data sources worldwide, especially in lower- and middle-income countries. External calibration assessment against independent observed CVD incidence was available only in the Chilean Ministry of Health data, representing the low-risk region. In these data, predicted risks were compared on a population level rather than a cohort level, using national risk factor and CVD incidence data. SCORE2-LAC-predicted risks were generally well aligned with observed national CVD incidence, particularly among women, although some underestimation remained among men. This may partly reflect the hospital-based registry population, which may have had a higher baseline CVD risk than the general population. As comparable contemporary CVD incidence data become available in the moderate-, high-, and very-high-risk regions, further external validation will be important to evaluate calibration across the full range of populations for which SCORE2-LAC is intended and to further strengthen confidence in its applicability throughout the region.

The SCORE2-LAC models are not intended for use in individuals with diabetes mellitus, similar to the original European SCORE2 models. For this population subgroup, dedicated models, such as SCORE2-Diabetes, have previously been developed to estimate CVD risk.[45] Future validation studies should verify whether the SCORE2-LAC recalibration scales enable accurate risk prediction in individuals with diabetes mellitus in the LAC region, or whether additional recalibration efforts are required.

Several potential limitations of the SCORE2-LAC models need to be considered. First, although contemporary individual-level data used to inform recalibration and external validation were available for the low-, moderate-, and high-risk region countries, only a subset of countries within each region was represented. Findings on model performance are, therefore, extrapolated to some extent to other countries within the same risk region for which no individual-level data were available. This limitation is greatest for the very-high-risk region, comprising Haiti and Guyana, for which no individual-level data were available to inform recalibration or external validation. Although population-level data on cause-specific CVD mortality and risk factor distributions were available for both countries, the underlying mortality data were of lower quality, particularly for Haiti. In addition, total first-to-fatal CVD incidence ratios had to be extrapolated from populations with similar age-standardized CVD mortality rates. Absolute risk estimates for the very-high-risk region should therefore be interpreted cautiously. Further validation and refinement of these estimates in these and other underrepresented settings remain important as additional longitudinal data become available.[46]

Data on medication use, family history, socioeconomic position, nutrition, physical activity, renal function, and ethnic background were not included in the original SCORE2 models, as these variables were not consistently available across the cohorts and registries used for model derivation.[5] Interpretation of risk estimates therefore requires clinical judgement, especially for individuals in whom these factors may be relevant (e.g. those receiving lipid- or blood pressure-lowering therapy; those with previous tobacco exposure, a family history of CVD,[47] chronic kidney disease[48]; or those from socioeconomically disadvantaged or higher-risk ethnic groups[14]). For individuals with several of these risk modifiers, approaches have been developed to incorporate such factors alongside existing CVD risk prediction models.[48,49]

For risk estimation using SCORE2-LAC, laboratory measurements, including cholesterol levels, are required. This could limit applicability in some resource-limited settings, particularly compared with non-laboratory models, such as the WHO CVD risk charts and Globorisk-LAC, for which versions without laboratory measurements are available.[10,15] However, previous studies have shown that imputation strategies using individual-level data can provide risk estimates with good predictive performance when laboratory measurements are unavailable.[50] As access to electronic health records and routinely collected healthcare data continues to increase across the region, such approaches may help facilitate implementation of laboratory-based risk prediction models in settings where complete risk factor information is not consistently available.

In conclusion, the SCORE2-LAC models provide region-specific and contemporary estimates of 10-year CVD risk in individuals without prior CVD or diabetes mellitus across LAC. As part of the SCORE2 family of risk prediction models, SCORE2-LAC uses contemporary methodology and regionally relevant data to support cardiovascular risk assessment and primary prevention in the region.

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Disclosure of Interest

Nothing to declare.

Data Availability

Data used for the current study are available upon reasonable request and approval of the individual cohorts or collaborative groups.

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Ethical Approval

Relevant ethical approval and participant consent were already obtained in all studies that contributed data to this work.

Pre-registered Clinical Trial Number

None supplied.

Appendix

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References

1. GBD 2023 Causes of Death Collaborators. Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990–2023: a systematic analysis for the global burden of disease study 2023. Lancet 2025;406:1811–72. https://doi.org/10.1016/S0140-6736(25)01917-8
2. Visseren F, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2021;42:3227–337. https://doi.org/10.1093/eurheartj/ehab484
3. Khan SS, Coresh J, Pencina MJ, Ndumele CE, Rangaswami J, Chow SL, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. Circulation 2023;148:1982–2004. https://doi.org/10.1161/CIR.0000000000001191
4. National Institute for Health and Care Excellence (NICE). Cardiovascular disease: risk assessment and reduction, including lipid modification (NG238), 2023.

5. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. Eur Heart J 2021;42:2439–54. https://doi.org/10.1093/eurheartj/ehab309

6. Khan SS, Matsushita K, Sang Y, Ballew SH, Grams ME, Surapaneni A, et al. Development and validation of the American Heart Association's PREVENT equations. Circulation 2024;149:430–49. https://doi.org/10.1161/CIRCULATIONAHA.123.067626

7. Hageman S, Huang Z, Lee H, Kaptoge S, Dorresteijn JA, Pennells L, et al. Risk prediction of cardiovascular disease in the Asia-Pacific region: the SCORE2 Asia-Pacific model. Eur Heart J 2025;46:702–15. https://doi.org/10.1093/eurheartj/ehae609

8. Neuen BL, Major RW, Grams ME, Sang Y, Coresh J, Ballew SH, et al. Multinational validation of the PREVENT and SCORE2 cardiovascular risk equations across 6.4 million individuals. Nat Med 2026;32:2629–38. https://doi.org/10.1038/s41591-026-04437-z

9. Damen JAAG, Hooft L, Schuit E, Debray TPA, Collins GS, Tzoulaki I, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. BMJ 2016;353:i2416. https://doi.org/10.1136/bmj.i2416

10. Consortium of Latin America and the Caribbean (CC-LAC). Derivation, internal validation, and recalibration of a cardiovascular risk score for Latin America and the Caribbean (Globorisk-LAC): a pooled analysis of cohort studies. Lancet Reg Health Am 2022;9:100258. https://doi.org/10.1016/j.lana.2022.100258

11. Carrillo-Larco RM, Altez-Fernandez C, Pacheco-Barrios N, Bambs C, Irazola V, Miranda JJ, et al. Cardiovascular disease prognostic models in Latin America and the Caribbean: a systematic review. Glob Heart 2019;14:81–93. https://doi.org/10.1016/j.gheart.2019.03.001

12. Pennells L, Kaptoge S, Wood A, Sweeting M, Zhao X, White I, et al. Equalization of four cardiovascular risk algorithms after systematic recalibration: individual-participant meta-analysis of 86 prospective studies. Eur Heart J 2019;40:621–31. https://doi.org/10.1093/eurheartj/ehy653

13. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk. A Review for Clinicians. J Am Coll Cardiol 2009;54:1209–27. https://doi.org/10.1016/j.jacc.2009.07.020

14. Kist JM, Vos RC, Mairuhu ATA, Struijs JN, van Peet PG, Vos HMM, et al. SCORE2 cardiovascular risk prediction models in an ethnic and socioeconomic diverse population in the Netherlands: an external validation study. EClinicalMedicine 2023;57:1–10. https://doi.org/10.1016/j.eclinm.2023.101862

15. WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health 2019;7:e1332–45. https://doi.org/10.1016/S2214-109X(19)30318-3

16. World Health Organization. Global Health Estimates [Internet]. 2024. https://www.who.int/data/global-health-estimates (9 December 2024, date last accessed).

17. World Health Organization. WHO report on the global tobacco epidemic, 2025: warning about the dangers of tobacco. Health and Medicine through History: From Ancient Practices to 21st-Century Innovations: Volume 1: Antiquity through the 18th Century: Volume 2: 19th through 21st Centuries: Volume 3: Data and Documents. Geneva: Bloomsbury Publishing Plc., 2025. https://doi.org/10.2471/B09466

18. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. Lancet 2024;404:2077–93. https://doi.org/10.1016/S0140-6736(24)02317-1

19. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021;398:957–80. doi:https://doi.org/10.1016/S0140-6736(21)01330-1

20. NCD Risk Factor Collaboration (NCD-RisC). Repositioning of the global epicentre of non-optimal cholesterol. Nature 2020;582:73–7. https://doi.org/10.1038/s41586-020-2338-1

21. Harvey A, Howitt C, Campbell JM, Forde SAA, Hambleton I, Bascombe I, et al. Gender differences in trends in incidence and mortality of acute myocardial infarction in the small island developing state of Barbados. Cureus 2024;16:e56729. https://doi.org/10.7759/cureus.56729

22. Barreto ML, Ichihara MY, Pescarini JM, Ali MS, Borges GL, Fiaccone RL, et al. Cohort profile: the 100 million Brazilian cohort. Int J Epidemiol 2022;51:E27–38. https://doi.org/10.1093/ije/dyab213

23. Ferreccio C, Huidobro A, Cortés S, Bambs C, Toro P, Van de Wyngard V, et al. Cohort profile: the Maule cohort (MAUCO). Int J Epidemiol 2020;49:760–1i. https://doi.org/10.1093/IJE/DYAA003

24. Miranda JJ, Bernabe-Ortiz A, Smeeth L, Gilman RH, Checkley W, Casas JP, et al. Addressing geographical variation in the progression of non-communicable diseases in Peru: the CRONICAS cohort study protocol. BMJ Open 2012;2:e000610. https://doi.org/10.1136/bmjopen-2011-000610

25. Margozzini P, Passi-Solar A, Scholes S, Valdivia G, Ferreccio C, Bedregal P, et al. Rpubs [Internet]. 2021. Cohort profile: The Chilean National Health Examination Survey (Encuesta Nacional de Salud, Chile ENS). https://rpubs.com/DataCovid/ens_cohort (12 December 2025, date last accessed).

26. Rubinstein AL, Irazola VE, Poggio R, Bazzano L, Calandrelli M, Lanas Zanetti FT, et al. Detection and follow-up of cardiovascular disease and risk factors in the Southern Cone of Latin America: the CESCAS I study. BMJ Open 2011;1:e000126. https://doi.org/10.1136/bmjopen-2011-000126

27. Rodríguez-Ariza CD, Cabrera-Villamizar A, Rodríguez-Pulido AL, Callegari S, Ossa Rodríguez NA, Pinilla-Roncancio M, et al. External validation of the ACC/AHA ASCVD risk score in a Colombian population cohort. Sci Rep 2023;13:6139. https://doi.org/10.1038/s41598-023-32668-4

28. Tartaglione J, Grazioli GC, Sarmiento M, Goldstraj LM. Eventos cardiovasculares en una población cerrada. Seguimiento a 10 años. Rev Argent Cardiol 2008;76:347–51. https://doi.org/10.7775/wef00j91

29. Tapia-Conyer R, Kuri-Morales P, Alegre-Díaz J, Whitlock G, Emberson J, Clark S, et al. Cohort profile: the Mexico City prospective study. Int J Epidemiol 2006;35:243–9. https://doi.org/10.1093/ije/dyl042

30. Salazar MR, Espeche WG, Aizpurúa M, Leiva Sisnieguez BC, Leiva Sisnieguez CD, Dulbecco CA, et al. Risk of cardiovascular disease according to blood pressure categories in an Argentinian cohort. Rev Fac Cien Méd Univ Nac Cordoba 2016;73:181–7. https://doi.org/10.31053/1853.0605.v73.n3.14812

31. Schmidt MI, Duncan BB, Mill JG, Lotufo PA, Chor D, Barreto SM, et al. Cohort profile: longitudinal study of adult health (ELSA-Brasil). Int J Epidemiol 2015;44:68–75. https://doi.org/10.1093/ije/dyu027

32. Obra Social de Empleados Públicos de Mendoza (OSEP). Open Data - OSEP Mendoza [Internet]. 2026. https://osepmendoza.com.ar/web/datos-abiertos-3/ (18 July 2026, date last accessed).

33. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987–1003. https://doi.org/10.1016/S0195-668X(03)00114-3

34. Wolbers M, Koller MT, Witteman JCM, Steyerberg EW. Prognostic models with competing risks methods and application to coronary risk prediction. Epidemiology 2009;20:555–61. https://doi.org/10.1097/EDE.0b013e3181a39056

35. Huang JY. Representativeness is not representative: addressing major inferential threats in the UK Biobank and other big data repositories. Epidemiology 2021;32:189–93. https://doi.org/10.1097/EDE.0000000000001317

36. Moons KGM, Wolff RF, Riley RD, Whiting PF, Westwood M, Collins GS, et al. PROBAST: a tool to assess risk of bias and applicability of prediction model studies: explanation and elaboration. Ann Intern Med 2019;170:W1–33. https://doi.org/10.7326/M18-1377

37. Moons KGM, Altman DG, Reitsma JB, Ioannidis JPA, Macaskill P, Steyerberg EW, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): explanation and elaboration. Ann Intern Med 2015;162:W1–73. https://doi.org/10.7326/M14-0698

38. Hajifathalian K, Ueda P, Lu Y, Woodward M, Ahmadvand A, Aguilar-Salinas CA, et al. Globorisk - A novel risk score for predicting cardiovascular disease risk in national populations: a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol 2015;3:339–55. https://doi.org/10.1016/S2213-8587(15)00081-9

39. Hageman SHJ, Dorresteijn JAN, Pennells L, van Smeden M, Bots ML, Di Angelantonio E, et al. The relevance of competing risk adjustment in cardiovascular risk prediction models for clinical practice. Eur J Prev Cardiol 2023;30:1741–7. https://doi.org/10.1093/eurjpc/zwad202

40. NCD Risk Factor Collaboration (NCD-RisC). NCD-RisC methodology [Internet]. 2026. https://www.ncdrisc.org/methods.html (16 July 2026, date last accessed).

41. de Araújo Fonseca LG, Lima INDF, Gualdi LP. Characterization of Brazilian hospital admissions due to cardiovascular diseases: a longitudinal study. BMC Cardiovasc Disord 2020;20:311. https://doi.org/10.1186/s12872-020-01588-w

42. Hageman SHJ, Kaptoge S, Gynnild MN, Holtrop J, Pennells L, McEvoy JW, et al. Using SCORE2 with a risk chart or online calculator: impact on model performance, treatment eligibility, and cardiovascular disease prevention. Eur Heart J Qual Care Clin Outcomes 2025;12:213–20. https://doi.org/10.1093/ehjqcco/qcaf122

43. McCarthy CP, Rahimi K, McEvoy JW. Age-stratified risk categories for cardiovascular disease prevention therapies. JAMA Cardiol 2024;9:1069–70. https://doi.org/10.1001/jamacardio.2024.3544

44. Van Calster B, McLernon DJ, Van Smeden M, Wynants L, Steyerberg EW; Topic Group 'Evaluating diagnostic tests and prediction models' of the STRATOS initiative. Calibration: the Achilles heel of predictive analytics. BMC Med 2019;17:230. https://doi.org/10.1186/s12916-019-1466-7

45. SCORE2-Diabetes Working Group and the ESC Cardiovascular Risk Collaboration. SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. Eur Heart J 2023;44:2544–56. https://doi.org/10.1093/eurheartj/ehad260

46. Lookens J, Tymejczyk O, Rouzier V, Smith C, Preval F, Joseph I, et al. The Haiti cardiovascular disease cohort: study protocol for a population-based longitudinal cohort. BMC Public Health 2020;20:1633. https://doi.org/10.1186/s12889-020-09734-x

47. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham heart study. Circulation 2008;117:743–53. https://doi.org/10.1161/CIRCULATIONAHA.107.699579

48. Matsushita K, Kaptoge S, Hageman SHJ, Sang Y, Ballew SH, Grams ME, et al. Including measures of chronic kidney disease to improve cardiovascular risk prediction by SCORE2 and SCORE2-OP. Eur J Prev Cardiol 2023;30:8–16. https://doi.org/10.1093/eurjpc/zwac176

49. Hageman S, Petitjaen C, Pennells L, Kaptoge S, Pajouheshnia R, Tillmann T, et al. Improving 10-year cardiovascular risk prediction in apparently healthy people: flexible addition of risk modifiers on top of SCORE2. Eur J Prev Cardiol 2023;30:1705–14. https://doi.org/10.1093/eurjpc/zwad187

50. Berkelmans GFFN, Read SHH, Gudbjörnsdottir S, Wild SHH, Franzen S, van der Graaf Y, et al. Population median imputation was noninferior to complex approaches for imputing missing values in cardiovascular prediction models in clinical practice. J Clin Epidemiol 2022;145:70–80. https://doi.org/10.1016/j.jclinepi.2022.01.011

*Supplemental Materials

For Supplementary Material, please click here.

For Supplementary Appendix, please click here.

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