WORLD HEALTH ORGANIZATION CARDIOVASCULAR DISEASE RISK CHARTS REVISED MODELS TO ESTIMATE RISK IN 21 GLOBAL REGIONS

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World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions

The WHO CVD Risk Chart Working Group*

Summary

Background To help adapt cardiovascular disease risk prediction approaches to low-income and middle-income countries, WHO has convened an effort to develop, evaluate, and illustrate revised risk models. Here, we report the derivation, validation, and illustration of the revised WHO cardiovascular disease risk prediction charts that have been adapted to the circumstances of 21 global regions.

Methods In this model revision initiative, we derived 10-year risk prediction models for fatal and non-fatal cardiovascular disease (ie, myocardial infarction and stroke) using individual participant data from the Emerging Risk Factors Collaboration. Models included information on age, smoking status, systolic blood pressure, history of diabetes, and total cholesterol. For derivation, we included participants aged 40–80 years without a known baseline history of cardiovascular disease, who were followed up until the first myocardial infarction, fatal coronary heart disease, or stroke event. We recalibrated models using age-specific and sex-specific incidences and risk factor values available from 21 global regions. For external validation, we analysed individual participant data from studies distinct from those used in model derivation. We illustrated models by analysing data on a further 123 743 individuals from surveys in 79 countries collected with the WHO STEPwise Approach to Surveillance.

Findings Our risk model derivation involved 376 177 individuals from 85 cohorts, and 19 333 incident cardiovascular events recorded during 10 years of follow-up. The derived risk prediction models discriminated well in external validation cohorts (19 cohorts, 1 096 061 individuals, 25 950 cardiovascular disease events), with Harrell's C indices ranging from 0·685 (95% CI 0·629–0·741) to 0·833 (0·783–0·882). For a given risk factor profile, we found substantial variation across global regions in the estimated 10-year predicted risk. For example, estimated cardiovascular disease risk for a 60-year-old male smoker without diabetes and with systolic blood pressure of 140 mm Hg and total cholesterol of 5 mmol/L ranged from 11% in Andean Latin America to 30% in central Asia. When applied to data from 79 countries (mostly low-income and middle-income countries), the proportion of individuals aged 40–64 years estimated to be at greater than 20% risk ranged from less than 1% in Uganda to more than 16% in Egypt.

Interpretation We have derived, calibrated, and validated new WHO risk prediction models to estimate cardiovascular disease risk in 21 Global Burden of Disease regions. The widespread use of these models could enhance the accuracy, practicability, and sustainability of efforts to reduce the burden of cardiovascular disease worldwide.

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Introduction

By the year 2030, the UN Sustainable Development Goals[1] aim to reduce premature mortality from non-com- expansion of cardiovascular disease prevention and control efforts, WHO has developed tools and guidance, including risk prediction charts.[4,5]

WHO REVISED CARDIOVASCULAR RISK MODELS: OVERVIEW

- Global burden of cardiovascular diseases (CVD) especially high in low- and middle-income countries
- Existing risk prediction tools often not well calibrated for diverse populations
- WHO developed and recalibrated 10-year CVD risk models tailored to 21 global regions
- Models built using large-scale individual participant data for better accuracy
- Aim: Improve CVD risk estimation to guide prevention strategies worldwide
- Used data from 376,177 participants aged 40–80 without prior CVD, including key risk factors, to derive 10-year CVD risk models.
- Recalibrated models by region and validated externally using data from over 1 million individuals across diverse populations
- Good predictive performance (Harrell's C 0.69–0.83) across regions
- Substantial variation in predicted 10-year risk between regions for identical risk profiles
- Proportion with >20% risk ranges widely between countries (e.g., <1% Uganda, >16% Egypt)

INTRODUCTION

1. Global Burden of Cardiovascular Disease (CVD):
    - •Leading cause of non-communicable disease deaths (17.8 million in 2017)
    - •Over 75% of deaths occur in low- and middle-income countries
2. UN Sustainable Development Goal (SDG) 2030:
    - •Aim to reduce premature non-communicable disease mortality by one-third
    - •WHO commitment: Provide prevention and treatment to ≥50% of high-risk individuals aged 40+ by 2025
3. Role and Limitations of Existing Risk Prediction Models:
    - •Identify high-risk individuals for targeted interventions
    - •Existing models mainly based on high-income country data
    - •Poor calibration and applicability in low- and middle-income countries
4. WHO Efforts:
    - •Development and recalibration of updated, region-specific CVD risk models
    - •Use of routinely available data and sustainable updating methods
    - •Collaboration across academics, policymakers, and end-users for tailored solutions

STUDY DESIGN & DATA SOURCES

- Multi-step approach for model revision:
  - Derivation from 85 prospective cohorts (Emerging Risk Factors Collaboration - ERFC)
  - Recalibration to 21 global regions using Global Burden of Disease (GBD) & NCD Risk Factor Collaboration (NCD-RisC) data
  - External validation using 19 independent cohorts
  - Application on WHO STEPS survey data from 79 countries
- Inclusion criteria for cohorts:
  - Age 40–80, no prior CVD, baseline risk factor data (age, smoking, SBP, diabetes, cholesterol/BMI)
  - At least 1 year follow-up with well-defined cardiovascular outcomes

MODEL DEVELOPMENT AND VALIDATION

- Derived two risk models:
  - Laboratory-based (age, smoking, SBP, diabetes, total cholesterol)
  - Non-laboratory-based (age, smoking, SBP, BMI)
- Separate models for coronary heart disease and stroke; combined for overall CVD risk
- Cox proportional hazards models with study stratification
- Internal validation by leave-one-study-out cross-validation (Harrell's C-index)
- Recalibration by age, sex, and global region using updated incidence and risk factor data
-

EXTERNAL VALIDATION & APPLICATION

- External validation cohorts included Asia Pacific, New Zealand PREDICT, China, Thailand, Tehran, UK Biobank
- Assessment of discrimination (C-indices) and calibration in validation datasets
- Application of models to WHO STEPS surveys to estimate population-level risk distributions in 79 countries
- Comparison of laboratory vs non-laboratory model performance
- Compliance with TRIPOD guidelines and ethical approvals

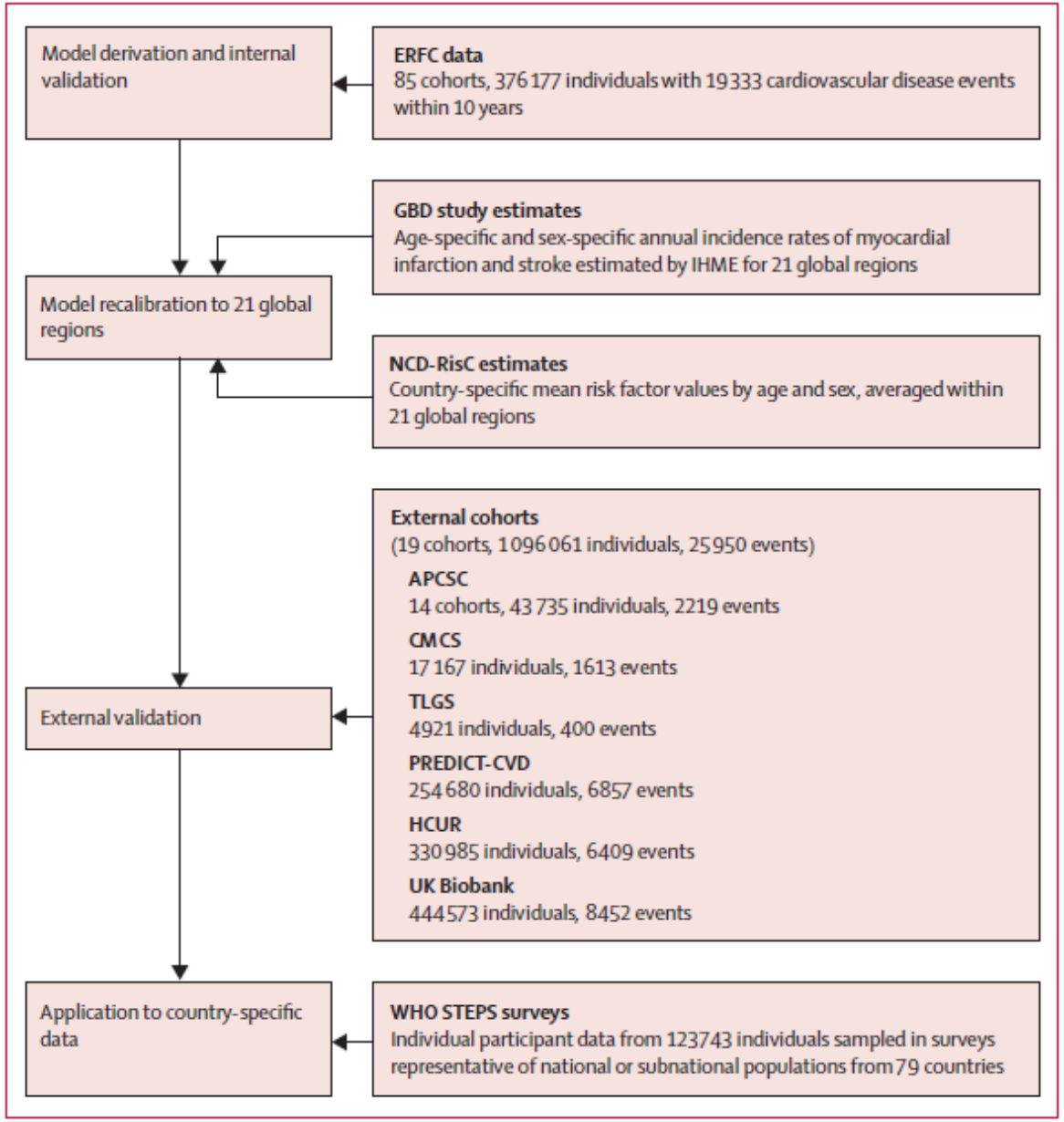

Figure 1: **Study design**

ERFC=Emerging Risk Factors Collaboration. GBD=Global Burden of Disease. IHME=Institute for Health Metrics and Evaluation. NCD-RisC=Non-Communicable Diseases Risk Factor Collaboration. APCSC=Asia Pacific Cohort Studies Collaboration. CMCS=Chinese Multi-Provincial Cohort Study. TLGS=Tehran Lipids and Glucose Study. PREDICT-CVD=New Zealand primary care-based PREDICT-CVD cohort. HCUR=Health Checks Ubon Ratchathani Study in Thailand. WHO STEPS=WHO STEPwise Approach to Surveillance.

	Men		Women	
	Main effect	Age interaction term*	Main effect	Age interaction term*
Laboratory-based models				
Fatal or non-fatal MI or CHD death				
Age at baseline per 5 years	1·43 (1·40–1·47)	..	1·67 (1·60–1·73)	..
Current smoking status	1·76 (1·68–1·84)	0·91 (0·89–0·93)	2·87 (2·64–3·11)	0·85 (0·81–0·88)
Systolic blood pressure per 20 mm Hg	1·30 (1·28–1·33)	0·98 (0·97–0·99)	1·37 (1·33–1·42)	0·99 (0·97–1·00)
History of diabetes	1·90 (1·76–2·04)	0·94 (0·91–0·97)	2·92 (2·60–3·28)	0·89 (0·84–0·94)
Total cholesterol per 1 mmol/L	1·26 (1·24–1·28)	0·98 (0·97–0·99)	1·23 (1·20–1·26)	0·97 (0·96–0·99)
Baseline survival estimate at 10 years†	0·954	..	0·989	..
Fatal or non-fatal stroke				
Age at baseline per 5 years	1·64 (1·58–1·70)	..	1·70 (1·63–1·76)	..
Current smoking status	1·65 (1·53–1·77)	0·93 (0·89–0·96)	2·11 (1·92–2·31)	0·90 (0·86–0·95)
Systolic blood pressure per 20 mm Hg	1·56 (1·51–1·61)	0·96 (0·95–0·97)	1·51 (1·46–1·56)	0·95 (0·94–0·97)
History of diabetes	1·87 (1·67–2·10)	0·88 (0·83–0·93)	2·36 (2·06–2·70)	0·90 (0·84–0·96)
Total cholesterol per 1 mmol/L	1·03 (1·00–1·06)	1·01 (0·99–1·02)	1·03 (0·99–1·06)	0·99 (0·97–1·01)
Baseline survival estimate at 10 years†	0·985	..	0·989	..
Non-laboratory-based models				
Fatal or non-fatal MI or CHD death				
Age at baseline per 5 years	1·44 (1·41–1·48)	..	1·69 (1·63–1·76)	..
Current smoking status	1·81 (1·73–1·90)	0·90 (0·88–0·93)	2·98 (2·75–3·24)	0·84 (0·81–0·88)
Systolic blood pressure per 20 mm Hg	1·31 (1·28–1·33)	0·98 (0·97–0·99)	1·40 (1·35–1·44)	0·98 (0·97–1·00)
BMI per 1 kg/m²	1·18 (1·15–1·22)	0·97 (0·96–0·99)	1·14 (1·10–1·18)	0·98 (0·97–1·00)
Baseline survival estimate at 10 years†	0·954	..	0·989	..
Fatal or non-fatal stroke				
Age at baseline per 5 years	1·63 (1·57–1·69)	..	1·69 (1·63–1·75)	..
Current smoking status	1·65 (1·53–1·78)	0·93 (0·89–0·96)	2·10 (1·91–2·30)	0·90 (0·86–0·95)
Systolic blood pressure per 20 mm Hg	1·58 (1·53–1·62)	0·96 (0·94–0·97)	1·54 (1·49–1·60)	0·95 (0·93–0·96)
BMI per kg/m²	1·08 (1·03–1·13)	0·99 (0·97–1·01)	1·02 (0·98–1·06)	1·00 (0·98–1·02)
Baseline survival estimate at 10 years†	0·985	..	0·989	..

Data are HRs (95% CI) from sex-specific Cox-proportional hazards models, stratified by study. Log HRs and heterogeneity statistics are given in appendix 1 (p 11). Age was centred at 60 years, systolic blood pressure at 120 mm Hg, total cholesterol at 6 mmol/L, and BMI at 25 kg/m². Smoking status was coded as current versus other, and history of diabetes as yes versus no. MI=myocardial infarction. CHD=coronary heart disease. BMI=body-mass index. HR=hazard ratio. *Age at baseline. †Baseline survival for each model was estimated by pooling the baseline survival at 10 years across studies with ≥10 years follow-up weighted by number of events by 10 years.

Table 2: **Summary of HRs for predictor variables in the WHO risk models derived with use of Emerging Risk Factors Collaboration data**

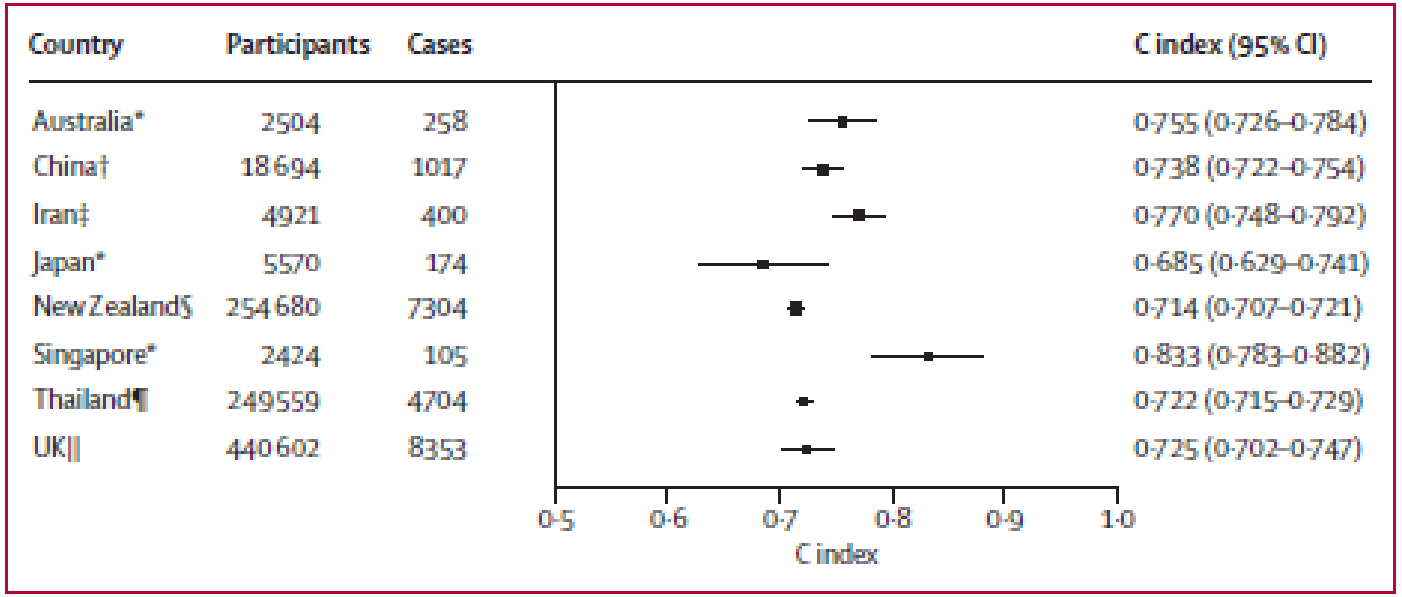

***Figure 3*: C index upon assessing ability of the laboratory-based WHO model to discriminate cardiovascular disease events in external validation cohorts**

Where multiple studies are used, country-specific estimates are the result of pooling study-specific C-index values, weighting by the number of events. APCSC=Asia Pacific Cohorts Studies Collaboration. *Calculated with data from studies from the APCSC. †Calculated with data from studies from the APCSC and the China Multi-Provincial Cohort Study. ‡Calculated with data from the Tehran Lipids and Glucose Study. §Calculated with data from studies from the APCSC and the PREDICT-CVD cohort. ¶Calculated with data from the Health Checks Ubon Ratchathani Study. ||Calculated with data from the UK Biobank.

STUDY POPULATION AND REGIONAL RISK CALIBRATION

- 376,177 participants aged 40-80 without prior CVD from mainly Europe & North America
- 19,333 CVD events during 10-year follow-up
- Risk factors: age, smoking, systolic BP, diabetes, cholesterol/BMI
- Risk factor effects decrease with age, especially diabetes & smoking in women
- Models recalibrated for 21 regions using regional disease rates and risk factor averages
- Example: 10-year CVD risk for a 60-year-old male smoker varies from 11% (Andean Latin America) to 30% (Central Asia)

EXTERNAL VALIDATION & MODEL APPLICATION

- Validated in 19 independent cohorts (1,096,061 participants, 25,950 events)
- Good discrimination: Harrell's C between 0.685 and 0.833
- Applied to WHO STEPS surveys in 79 countries; >20% risk ranged <1% (Uganda) to >16% (Egypt)
- Comparison of laboratory and non-laboratory models:
  - Non-lab model slightly less discriminative
  - Underestimates risk in diabetics but identifies most high-risk individuals at a lower threshold

Figure 4: **Distribution of 10-year cardiovascular disease risk according to recalibrated laboratory-based WHO risk prediction models for individuals aged 40–64 years from example countries**

Data from all countries are from adults aged 40–64 years with total cholesterol concentrations of 2·6–10·3 mmol/L and from samples representative of the national population, unless otherwise specified as subnational (S) or community based (C).

OVERVIEW AND KEY STRENGTHS OF THE REVISED WHO CVD RISK MODELS

- Developed and recalibrated models tailored for 21 global regions, mainly LMICs
- Integration into WHO HEARTS package to support prevention efforts
- Simple, scalable recalibration method using routine epidemiological data
- Models estimate combined fatal and non-fatal events, improving on previous calculators
- Applicable without reliance on complex laboratory data (non-lab models), suitable for resource-limited settings
- Open-access statistical tools provided for regular updates

IMPLICATIONS FOR POLICY AND PRACTICE

- Regional variation in risk highlights need for local data-informed decisions
- Enables better targeting of preventive resources based on more accurate risk stratification
- Non-laboratory models useful as initial screening tools, despite limitations in diabetics
- Revised risk charts with updated risk thresholds improve usability and communication
- Supports WHO goal to reduce premature mortality from non-communicable diseases
-

LIMITATIONS AND CONSIDERATIONS

- Model derivation primarily from cohorts in high-income countries due to data gaps in LMICs
- Recalibration relies on GBD and NCD-RisC estimates, which may lack country-level precision
- External validation includes mostly non-national cohorts, except one nationally representative dataset
- Possible over- or under-estimation of risk due to inclusion of recurrent cases and preventive treatment users
- Models do not include some risk factors available in high-income country equations
- Assumption that missing data are random minimizes bias but cannot fully eliminate it
- Future work needed to incorporate better data from LMICs and refine models accordingly

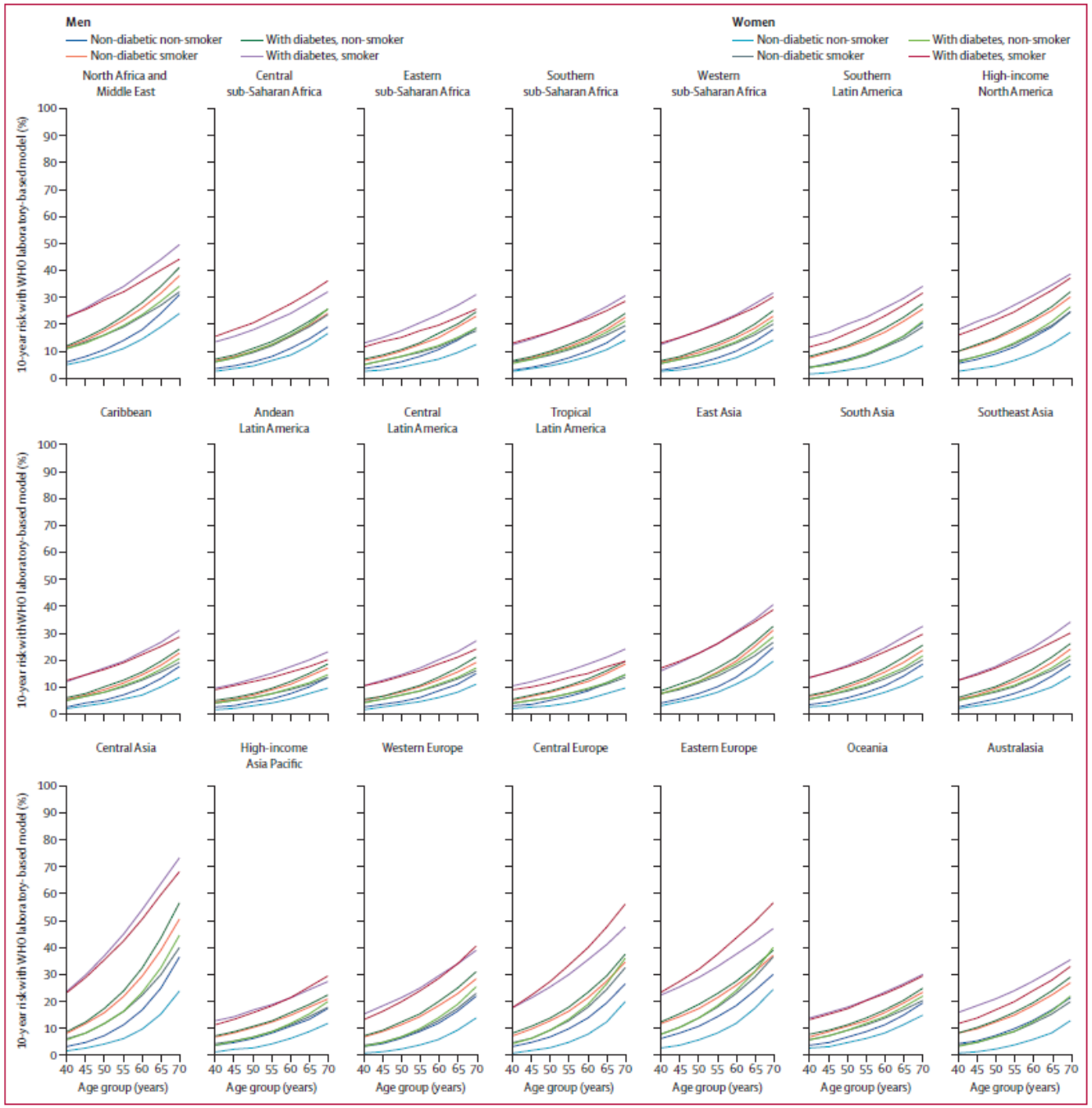

Figure 2: **Predicted 10-year cardiovascular disease risks for an individual with total cholesterol concentrations of 5 mmol/L and systolic blood pressure of 140 mm Hg, with the WHO laboratory-based model, for each region**

Countries included in the 21 regions defined by the Global Burden of Disease Study are provided in appendix 1 (p 39).

- THANKS FOR YOUR ATTENTION