HEARTS

Technical package for cardiovascular disease management in primary health care

Risk-based CVD management

World Health Organization

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Risk-based CVD management module

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Abbreviations

BMI	body mass index
CAD	coronary artery disease
CVD	cardiovascular disease
DM	diabetes mellitus
ESC	European Society of Cardiology
GBD	Global Burden of Disease
HTN	hypertension
HDL-C	high-density lipoprotein cholesterol
IHME	Institute for Health Metrics and Evaluation
IHRMS	INTERHEART Modifiable Risk Score
LMIC	low- and middle-income countries
MI	myocardial infarction
NCR-RisC	NCD Risk Factor Collaboration
PEN	Package of Essential Noncommunicable Disease Interventions
SBP	systolic blood pressure
TC	total cholesterol
WHO/ISH	World Health Organization / International Society of Hypertension

HEARTS Technical Package

More people die each year from cardiovascular diseases (CVDs) than from any other cause. Over three quarters of heart diseases and stroke-related deaths occur in low- and middle-income countries *(1).* The HEARTS technical package provides a strategic approach to improving cardiovascular health. It comprises six modules and an implementation guide. This package supports Ministries of Health to strengthen CVD management in primary care and aligns with World Health Organization's Package of Essential Non-communicable Disease Interventions (WHO PEN).

The WHO HEARTS modules are intended for use by policy-makers and programme managers at different levels within Ministries of Health who can influence CVD primary care delivery. Different sections of each module are aimed at different levels of the health system and different cadres of providers. All modules will require adaptation at country level.

The people who will find the modules most useful are:

- **National level** – Ministry of Health noncommunicable disease (NCD) policy-makers responsible for:
  - Developing strategies, policies and plans related to service delivery for CVD
  - Setting national targets on CVD, and monitoring and reporting progress
- **Subnational level** – Health/NCD programme managers responsible for:
  - Planning, training, implementing and monitoring service delivery
- **Primary care level** – Facility managers and primary health care providers and trainers responsible for:
  - Assigning tasks, organizing training and ensuring the facility is running smoothly
  - Collecting facility-level data on indicators of progress towards CVD targets.

Target users may vary, based on context, existing health systems and national priorities.

MODULES OF THE HEARTS TECHNICAL PACKAGE				
Module	**What does it include?**	**Who are the target users?**		
		National	**Subnational**	**Primary care**
Healthy-lifestyle counselling	Information on the four behavioural risk factors for CVD is provided. Brief interventions are described as an approach to providing counselling on risk factors and encouraging people to have healthy lifestyles.		✓	✓
Evidence-based protocols	A collection of protocols to standardize a clinical approach to the management of hypertension and diabetes.	✓	✓	✓
Access to essential medicines and technology	Information on CVD medicine and technology procurement, quantification, distribution, management and handling of supplies at facility level.	✓	✓	✓
Risk-based CVD management	**Information on a total risk approach to the assessment and management of CVD, including country-specific risk charts.**	✓	✓	✓
Team-based care	Guidance and examples on team-based care and task shifting related to the care of CVD. Some training materials are also provided.		✓	✓
Systems for monitoring	Information on how to monitor and report on the prevention and management of CVD. Contains standardized indicators and data-collection tools.	✓	✓	✓

Introduction

Development of cardiovascular disease (CVD) is influenced by risk factors such as: tobacco use, an unhealthy diet, physical inactivity, obesity (which can result from a combination of unhealthy diet, physical inactivity, and other factors), elevated blood pressure (hypertension), abnormal blood lipids (dyslipidaemia) and elevated blood glucose (diabetes mellitus). Continuing exposure to these risk factors leads to further progression of atherosclerosis, resulting in clinical manifestations of these diseases, including angina pectoris, myocardial infarction, heart failure and stroke. Total CVD risk depends on the individual's overall risk-factor profile.

In 2007, the WHO published Guidelines for the assessment and management of cardiovascular risk *(2)* that provide guidance for reducing disability and premature deaths from CVD in people at high risk who have not yet experienced a cardiovascular event. These 2007 guidelines were used as a framework for the development of national guidance on CVD prevention, and provide the WHO and International Society of Hypertension (WHO/ISH) cardiovascular (CVD) risk prediction charts for regional CVD risk prediction. WHO updated the CVD risk charts in 2019 *(3)*. This Risk-based CVD management module (HEARTS-R) will present the updated CVD risk charts for the assessment and management of CVD risk. Relevant information from the 2007 guidelines is reproduced.

Timely, affordable and sustained heathy-lifestyle interventions and, when needed, drug treatment will reduce the risk of heart attack and stroke in people with a high total risk of CVD, and hence will reduce premature morbidity, mortality and disability. Those who have their elevated blood pressure or cholesterol treated can reduce their risk by more than one-quarter to one-third *(4)* and have their risk reduced by half if both are treated *(5)*. For many years we have had inexpensive medications for hypertension (HTN). More recently, generic statins have been added to the WHO Essential Medicines list and have become available in many more countries. Despite the increased availability of drugs, less than 10% of the global population has its blood pressure controlled *(6)*.

Poor control of risk factors is in part a result of a lack of awareness among individuals of their risk status. The identification of risk level by health care providers is therefore a useful means of detecting those with high CVD risk and identifying who could benefit from treatment of high blood pressure, abnormal blood lipids and elevated blood glucose *(7)*. Recommendations for assessment and management of CVD risk factors have evolved over time in CVD guidelines.

This evolution in CVD recommendations and guidelines is a response to:

- an improved ability to quantify and identify those at highest risk
- an increase in the population affected by these risk factors
- changes in generic therapies available
- a recognition that despite these changes we are failing globally to significantly prevent CVD mortality, particularly in low- and middle-income countries (LMICs).

One change in guidelines has been a greater use of overall CVD risk levels to determine intensity of treatments. The additional focus on overall risk has occurred for three main reasons. First, there was recognition that an individual who has multiple risk factors, even if each factor is only moderately elevated, may, when all risk factors are taken into account, be at an overall higher risk than someone with an elevated level for a single risk factor. For example, a middle-aged female with moderate levels of several risk factors could have a 5- to 10-fold increased risk of having CVD in the next 10 years, when compared to a young male with an isolated elevated risk factor.

Second, targeting of those individuals at highest risk was recognized to lead to greater efficiency in benefit in terms of number of events avoided, because the relative risk reduction would be applied to a higher baseline risk *(8)*. Therefore, targeting patients with a high risk is the highest priority in a risk stratification approach *(9)*.

Third, improved computing and statistical methods have allowed researchers to pool large global data sets to create more accurate risk prediction tools for various populations.

As the cost of medicines is a significant component of total preventive health care costs, it is particularly important to base drug treatment decisions principally on an individual's risk level rather than on criteria such as ability to pay, or on blanket preventive strategies. In addition, guidelines based on total CVD risk, which use risk scoring methods, have been shown to be both less expensive and more effective than guidelines based on single risk-factor levels to treat the same number of patients *(10)*.

Drug therapy (including glycaemic control for diabetes mellitus, control of HTN and cholesterol, using a total risk approach) and counselling to individuals who have had a heart attack or stroke and to persons with high risk (≥20%) of a fatal and non-fatal cardiovascular event in the next 10 years is one of the "best buys" for tackling NCDs *(11)*. For those with a pre-existing condition such as prior CVD, risk identification is simple. For others, the use of clinical algorithms or "risk charts" can be used to further stratify patients.

A risk stratification approach is particularly suitable to settings with limited resources, where saving the greatest number of lives at lowest cost becomes imperative. However, in most guidelines, the use of risk tools has not replaced the knowledge needed to treat individual risk factors but has rather been used to augment the decision of whom to treat, so that those at the highest level of risk are easily identified for treatment. This module helps to identify those who would benefit from lifestyle changes and basic medical treatment to lower blood pressure, cholesterol, and manage diabetes mellitus in an integrated manner. Guidance on HTN and diabetes management can be found in other HEARTS Modules, as well.

Application of an approach that considers the total CVD risk will be better informed through country-level implementation research. Many areas, including the level of the facility at which CVD risk can be assessed, thresholds for treatment, adaptation of protocols, follow-up intervals and other logistics are best defined in the local context.

1 Updated WHO cardiovascular risk charts

2007 WHO/ISH cardiovascular risk prediction charts

Many risk-prediction models have been developed over the years. However, most equations are derived, recalibrated and validated in limited settings. The majority are derived from or recalibrated on populations of European descent living in high-income countries. As a result, these models might not be directly translatable or valid in low-resource and non-European settings. The WHO/ISH cardiovascular risk prediction charts were developed in 2007 to estimate 10-year risk of a fatal or non-fatal major cardiovascular event (myocardial infarction or stroke), according to age, sex, smoking status, blood pressure, total blood cholesterol and presence or absence of diabetes mellitus for 14 WHO epidemiological sub-regions *(12).* There are two sets of charts. One set could be used in settings where blood cholesterol can be measured, and the other in settings where blood cholesterol cannot be measured. Both sets require the status of diabetes in the individual to be known *(13)*.

2019 Updated WHO cardiovascular disease risk charts

The WHO updated the 2007 WHO/ISH cardiovascular risk prediction charts through the formation of a cross-sectorial collaboration of academics, policy-makers and end users of CVD risk scores. The model revision took place in three steps.

First, risk prediction algorithms were developed using individual-participant data from 85 prospective cohort studies with long-term follow-up in the Emerging Risk Factors Collaboration. Endpoint definitions of fatal and non-fatal CVD outcomes used for the model are described in Annex 4.

Second, to adjust the algorithms to the contemporary circumstances of different global regions, they were recalibrated using age-specific and gender-specific incidence rates and risk-factor values obtained from the Global Burden of Disease (GBD) Study *(14)* and the NCD Risk Factor Collaboration (NCD-RisC) *(15)*.

Third, performance of the algorithms was assessed by external validation, using individual-participant data from a further 19 prospective cohort studies (i.e. studies distinct from those used in the algorithm derivation) *(3).*

The updated WHO CVD risk prediction charts were developed and presented for 21 global regions, defined by GBD to maximize between-region variability and minimize heterogeneity in mortality and major drivers of health outcomes within each region *(3)* (Annex 1). The charts are intended to allow the introduction of a total risk-stratification approach for management of CVD. They are presented as laboratory-based and non-laboratory-based charts. Laboratory-based algorithms include information on age, sex, smoking status, systolic blood pressure, history or evidence of diabetes mellitus, and the total cholesterol value. In the non-laboratory-based algorithms, body mass index (BMI) is included; information on diabetes mellitus and cholesterol is not necessary for these charts.

Countries can find the charts relevant to them according to the appropriate GBD regional groups (Annex 2 and Annex 3).

WHO CVD risk (laboratory-based) charts

These are CVD risk charts that include measurements of total cholesterol and information on diabetes mellitus (Annex 2). The laboratory-based CVD risk charts should be used for treatment decisions. This is the indicated risk chart in a setting where laboratory facilities, and human and financial resources are accessible. These charts will facilitate health providers to initiate an intervention and treatment regimen, and to implement an appropriate follow-up plan based on the patient's total risk status. As an example, Figure 1 presents the WHO CVD risk charts for North Africa and Middle East Region for use when information on total cholesterol and diabetes is available.

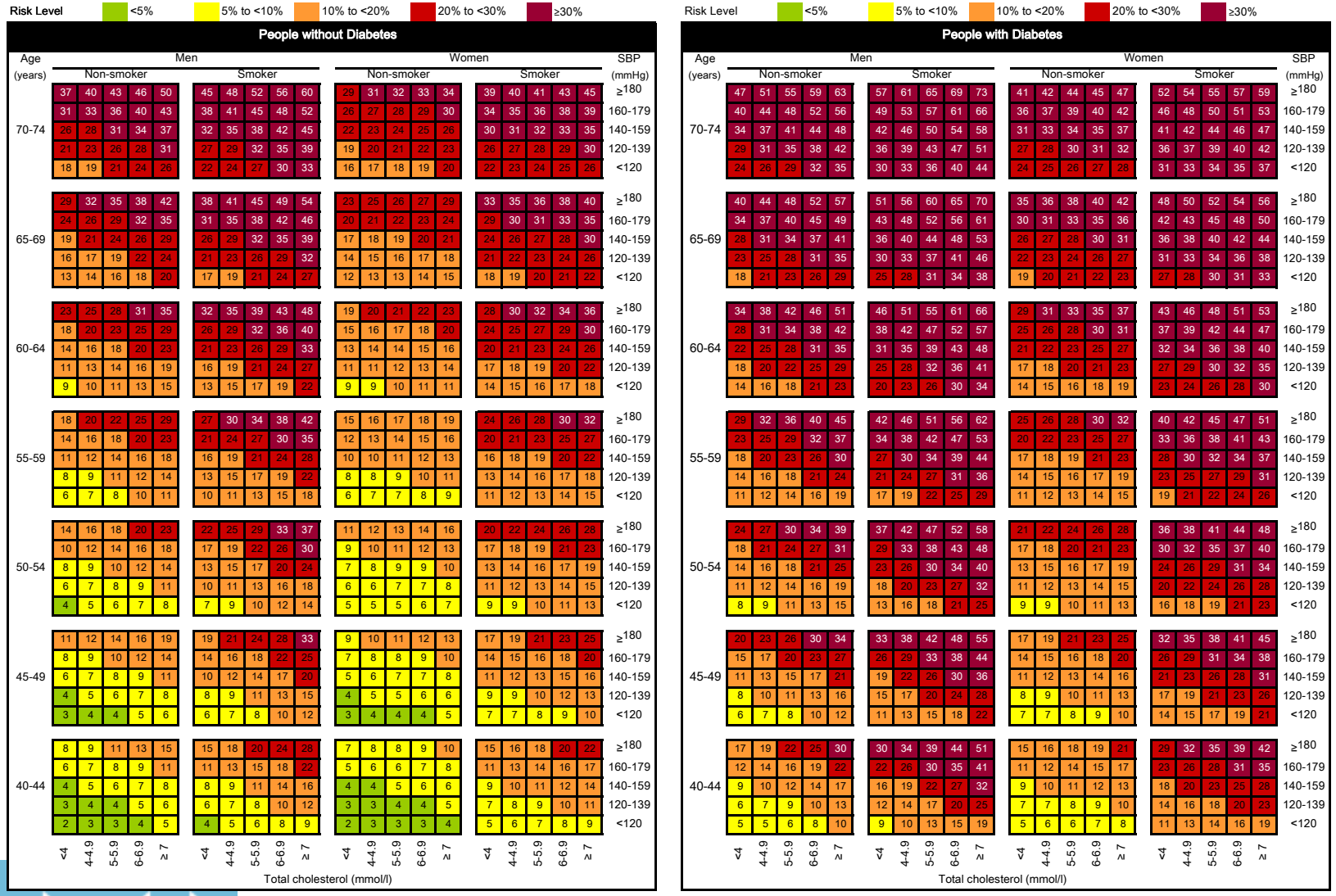
WHO CVD risk (non-laboratory-based) charts

Many low-resource settings have limited testing facilities or limited financial and physical capacity for biochemical measurements (e.g. blood sugar determination and cholesterol assays). WHO CVD risk (non-laboratory-based) charts can be used to predict total CVD risk without information on total cholesterol and diabetes (Annex 3). Only age, sex, smoking status, systolic blood pressure and body mass index (BMI) will be needed to predict cardiovascular risk. These non-laboratory-based WHO CVD risk charts are aimed at stratification in low-resource communities and office settings and can be used for decisions regarding referral. In population samples, there was moderate agreement between WHO CVD risk predictions using laboratory and non-laboratory algorithms. Of those at >20% risk using the laboratory-based algorithm, >97% of men and women were also identified at >10% by using the non-laboratory-based algorithm. However, when using a 20% threshold with non-laboratory-based algorithm, only approximately 65% of men and 35% of women were identified as at the same level of risk when compared to the laboratory-based algorithm. This discrepancy is largely due to the fact that the non-laboratory-based algorithm does not allow for the extra CVD risk associated with diabetes mellitus and substantially underestimates CVD risk in individuals with diabetes mellitus. For example, among individuals with diabetes classified as being at greater than 20% risk with the laboratory-based models, about 45% of men and 25% of women were classified as being at greater than 20% risk with the non-laboratory-based models (whereas in individuals without diabetes, about 85% of men and 95% of women showed such agreement) *(3).* As an example, Figure 2 is the WHO CVD risk (non-laboratory-based) charts for North Africa and Middle East.

Figure 1: Example of WHO CVD risk (laboratory-based) chart

North Africa and Middle East

Afghanistan, Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, occupied Palestinian territory, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen

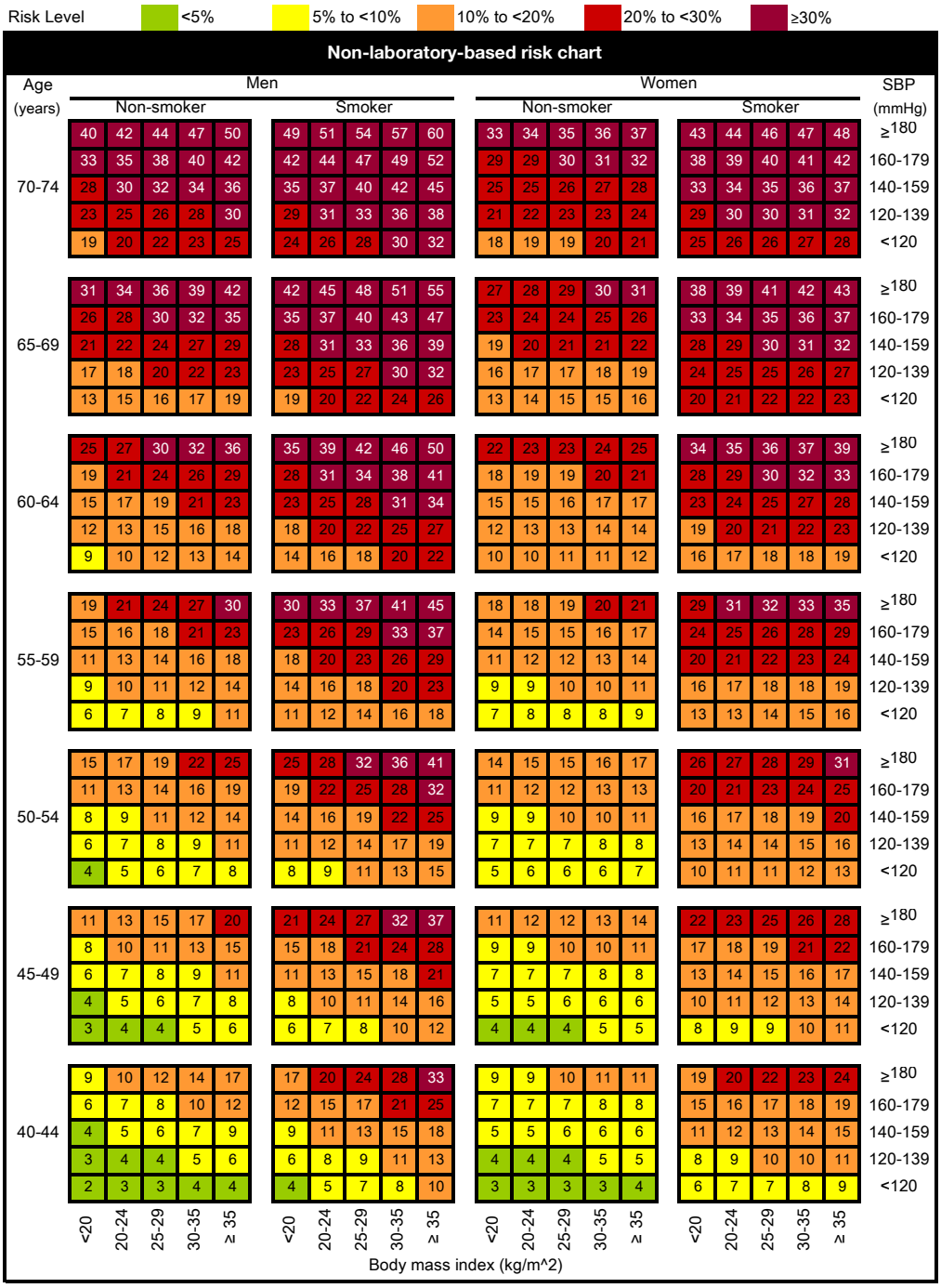


North Africa and Middle East

Figure 2: Example of WHO CVD risk (non-laboratory-based) chart

North Africa and Middle East

Afghanistan, Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, occupied Palestinian territory, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen



North Africa and Middle East

Comparison between 2007 WHO/ISH risk prediction charts and 2019 WHO CVD risk charts

The updated CVD risk charts are presented in an analogous manner to the previous WHO/ISH risk charts to facilitate their continuity of use with some adaptation. However, there are several advantages of the updated WHO CVD risk charts over the previous WHO/ISH risk prediction charts and other global, regional and national CVD risk prediction models available (Table 1).

First, compared with the 2007 charts, the new risk charts use data with more scientific rigour, from diverse populations, which is much more globally relevant.

Second, the charts use more contemporary estimates of CVD incidence and risk factors. This, together with simple and generalizable methods, allows for recalibration of the models for many different populations. This means that the CVD risk estimate for an individual in a given country is likely to be much more accurate than in the older charts.

Third, the recalibration approach used allows for rapid revision of CVD models, enabling a flexible updating of models as new relevant epidemiological data for geographical areas arise.

Fourth, the new charts produce estimates for 21 Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) regions compared to the 14 WHO regions in the old charts.

The risk stratification for the updated WHO charts differs from those used in the 2007 WHO/ISH CVD risk prediction charts to recognize changes in reported GBD CVD incidence. Stratification is now as follows: <5% (green), 5% to <10% (yellow), 10% to <20% (orange), 20% to <30% (red), and ≥30% (dark red). The category >40% is not retained in the updated charts as fewer people in the new risk charts were in that group. This risk stratification is aligned to the WHO recommendations for management of CVD risk.

Annexes 5a, 5b and 6 present the comparison of different risk charts and an approach to identifying suitable risk charts.

Table 1: Comparison between 2007 WHO/ISH risk prediction charts with 2019 WHO CVD risk charts

Parameter	2007 WHO/ISH risk prediction charts	2019 WHO CVD risk charts
Presentation	For 14 WHO epidemiological subregions	21 IHME GBD regions with more homogenous grouping of countries
Types of charts	Two sets: One set can be used in settings where blood cholesterol can be measured. The other set is for settings in which blood cholesterol cannot be measured.	Two sets: Laboratory-based charts Non-laboratory-based charts
Variables	1. With individual cholesterol value: • age • sex • smoking • systolic blood pressure • presence or absence of diabetes • total cholesterol 2. Without individual cholesterol value: • age • sex • smoking • systolic blood pressure • presence or absence of diabetes • national average cholesterol value	1. Laboratory-based: • age • sex • smoking • systolic blood pressure • presence or absence of diabetes • total cholesterol 2. Non-laboratory-based: • age • sex • smoking • systolic blood pressure • BMI
Risk levels and colour code	2007	2019
	Green <10%	Green <5%
	Yellow 10% to <20%	Yellow 5% to <10%
	Orange 20% to <30%	Orange 10% to <20%
	Red 30% to <40%	Red 20% to <30%
	Deep red >40%	Deep red ≥30%
Difference in interpretation of risk levels	Green was <10%	Green is <5% and corresponding changes in other risk levels.

2 Assessment and management of total CVD risk

This section is based on Protocol 1 in the WHO Package of Essential NCD interventions *(16).* This protocol remains current except for the change in the risk level in the updated WHO cardiovascular (CVD) risk charts. Assessment of total CVD risk can be used for routine management of hypertension (HTN) and diabetes mellitus (DM), and for targeting the following categories of people:

- age >40 years
- smokers
- obesity
- known to have HTN
- known to have DM
- history of premature CVD in first-degree relative
- history of DM or kidney disease in first-degree relative.

Instructions for using the WHO CVD risk (laboratory- based) charts

Table 2 and Figure 3 present a step-by-step guide to applying the WHO CVD (laboratory-based) risk charts. These charts are to be used only for individuals whose status regarding diabetes and total cholesterol is available. Tests for diabetes and cholesterol can be carried out at the time of assessment. If the information on diabetes and total cholesterol is not available, then refer to the instructions on use of non-laboratory-based risk charts.

Table 2: Using the WHO CVD risk (laboratory-based) charts

Action			
Select the regional chart covering your country: • REGION NAME is printed at the top of the charts. • Countries included in each region can be found in Annex 1.			
Have the following information ready: • age • sex • smoker* or non-smoker • presence or absence of diabetes† • systolic blood pressure • total blood cholesterol‡			
Using the charts			
STEP 1: Select the section of the chart as relevant for people with or without diabetes.			
STEP 2: Select the table for men or women, as appropriate.			
STEP 3: Select smoker or non-smoker column.			
STEP 4: Select age-group.			
STEP 5: Within the selected box find the cell where the person's systolic blood pressure and total blood cholesterol intersect.			
STEP 6: The colour of the cell indicates the 10-year risk of a fatal or non-fatal CVD event. The value within the cell is the risk percentage. Colour coding is based on the grouping.		Green	<5%
		Yellow	5% to <10%
		Orange	10% to <20%
		Red	20% to <30%
		Deep red	≥30%
STEP 7: Record CVD risk percentage in person's chart.			
STEP 8: Counsel, treat and refer according to risk level			

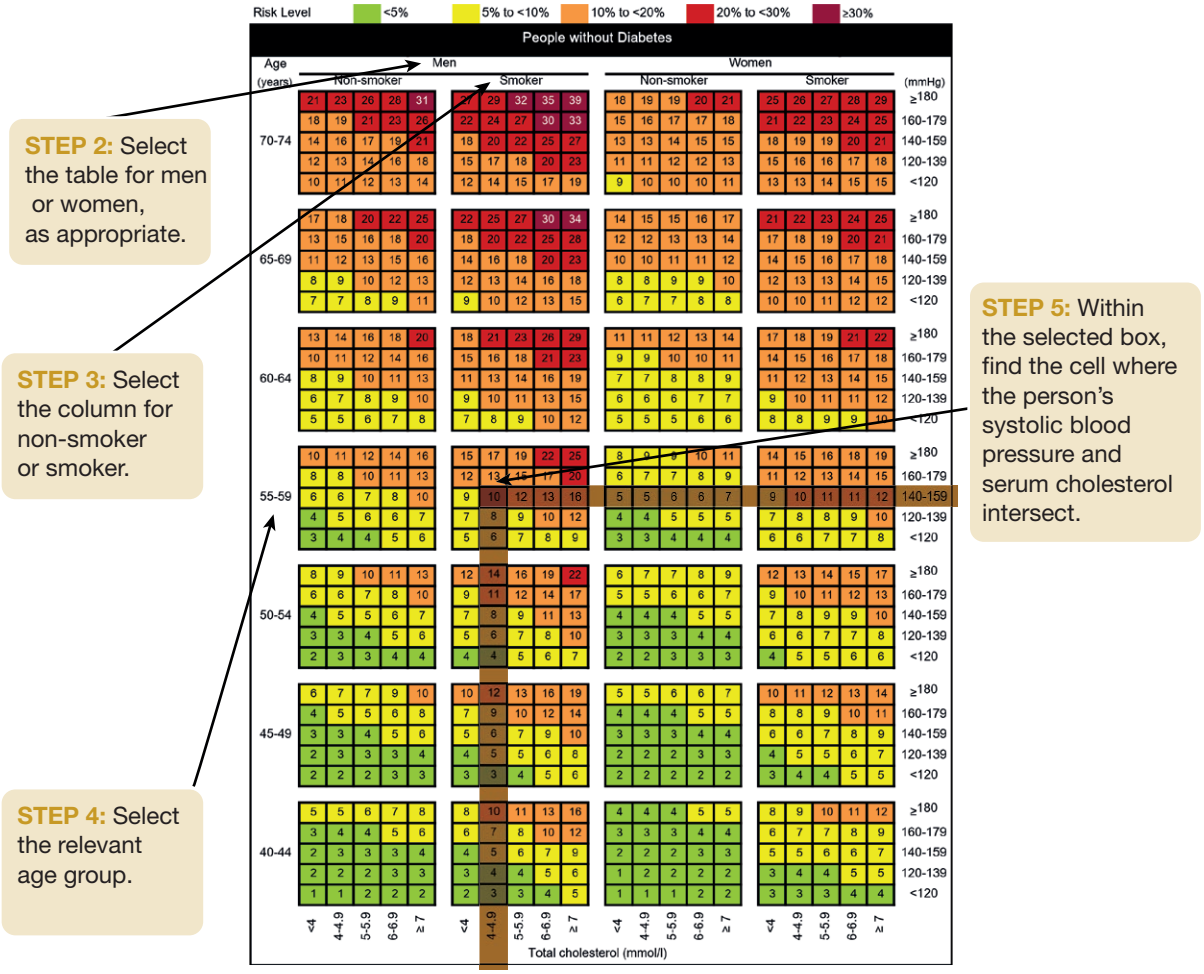
* Current smoker

† Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL), or 2-h plasma glucose ≥11.1 mmol/L (200 mg/dL), or HbA1c ≥6.5% or known diabetes

‡ Cholesterol values are to be entered in the chart as mmol/L (To convert mg/dL to mmol/L, multiply by 0.02586. e.g 200 mg/dL x 0.02586 = 5.172 mmol/L.)

Figure 3: Illustration of how to use the WHO CVD risk (laboratory-based) chart

STEP 1: Select the section of the chart for people with or without diabetes.



Integrated management of total CVD risk

Management of total CVD risk in people with different risk thresholds is presented in Table 3. This is based on the WHO PEN Protocol *(16)* except for the change in risk levels, which are adjusted to the updated CVD risk charts. The purpose of management is to motivate and assist individuals with high risk levels to lower their total CVD risk. All individuals with blood pressure at or above 160/100 mmHg, or blood pressure raised to a lesser degree but with target organ damage should have drug treatment and specific lifestyle advice to lower their blood pressure and risk of CVD.

All patients should receive counselling on diet (which includes lipid-lowering diet and low sodium), physical activity, tobacco cessation (smoking and smokeless) and avoiding harmful use of alcohol *(1).* For further details on counselling please refer to the HEARTS Module "H" on Healthy-lifestyle counselling *(17).*

Table 3: Management guidance for total CVD risk

Management of total CVD risk (adapted from WHO PEN Protocol 1)	
Risk <10%	Counsel on diet, physical activity, smoking cessation and avoiding harmful use of alcohol. If risk <5%, follow up in 12 months. If risk 5% to <10%, follow up every 3 months until targets are met, then 6–9 months thereafter.
Risk 10% to <20%	Counsel on diet, physical activity, smoking cessation and avoiding harmful use of alcohol. Persistent BP ≥140/90 mmHg consider drugs (see below). Follow up every 3–6 months.
Risk >20%	Counsel on diet, physical activity, smoking cessation and avoiding harmful use of alcohol. Persistent BP ≥130/80, consider drugs (see below). Give a statin. Follow up every 3 months. If there is no reduction in cardiovascular risk after six months of follow-up refer to next level.
Important practical points	Management of hypertension and diabetes: • For management of hypertension refer to HEARTS technical package E module *(18):* https://www.who.int/cardiovascular_diseases/hearts/en/ • For management of diabetes mellitus type 2, refer to the HEARTS module Diagnosis and management of diabetes *(19)*: https://www.who.int/publications-detail/who-ucn-ncd-20.1
	Consider drug treatment for following categories: • All patients with established DM and CVD (coronary heart disease, myocardial infarction, transient ischaemic attacks, cerebrovascular disease or peripheral vascular disease), renal disease. If stable, should continue the treatment already prescribed and be considered as having risk >20%. • People with albuminuria, retinopathy, left ventricular hypertrophy. • All individuals with persistent raised BP ≥160/100 mmHg. • All individuals with total cholesterol at or above 8 mmol/L (320 mg/dL).
	Follow-up visits: • Ask about: new symptoms, adherence to advice on tobacco and alcohol use, physical activity, healthy diet, medications etc. • Assess (physical exam). • Estimate cardiovascular risk. • Refer if necessary. • Counsel all and treat as shown in protocol.

Countries may set different thresholds for initiating treatment, based on the distribution of CVD risk in the population (Annex 7). If, after a reasonable amount of time, the non-drug treatment alone is not able to meet the hypertension (HTN) control goals, consider drug treatment.

Follow-up

Follow-up frequency will depend on the capacity of the health system and will have to be decided based on the local context. National protocols are important for the management as they will help to standardize the treatment and bring about efficiencies. A schedule of follow-up based on WHO PEN Protocol 1 is provided. If risk is <5%, follow up in 12 months. If risk is 5%–10%, follow up every 3 months, then 6–9 months thereafter *(16)*. For patients who are not at high enough risk for medical therapy, CVD risk should be reassessed every 12 months, or earlier if clinical symptoms develop.

Instructions for using WHO CVD risk (non-laboratory-based) charts

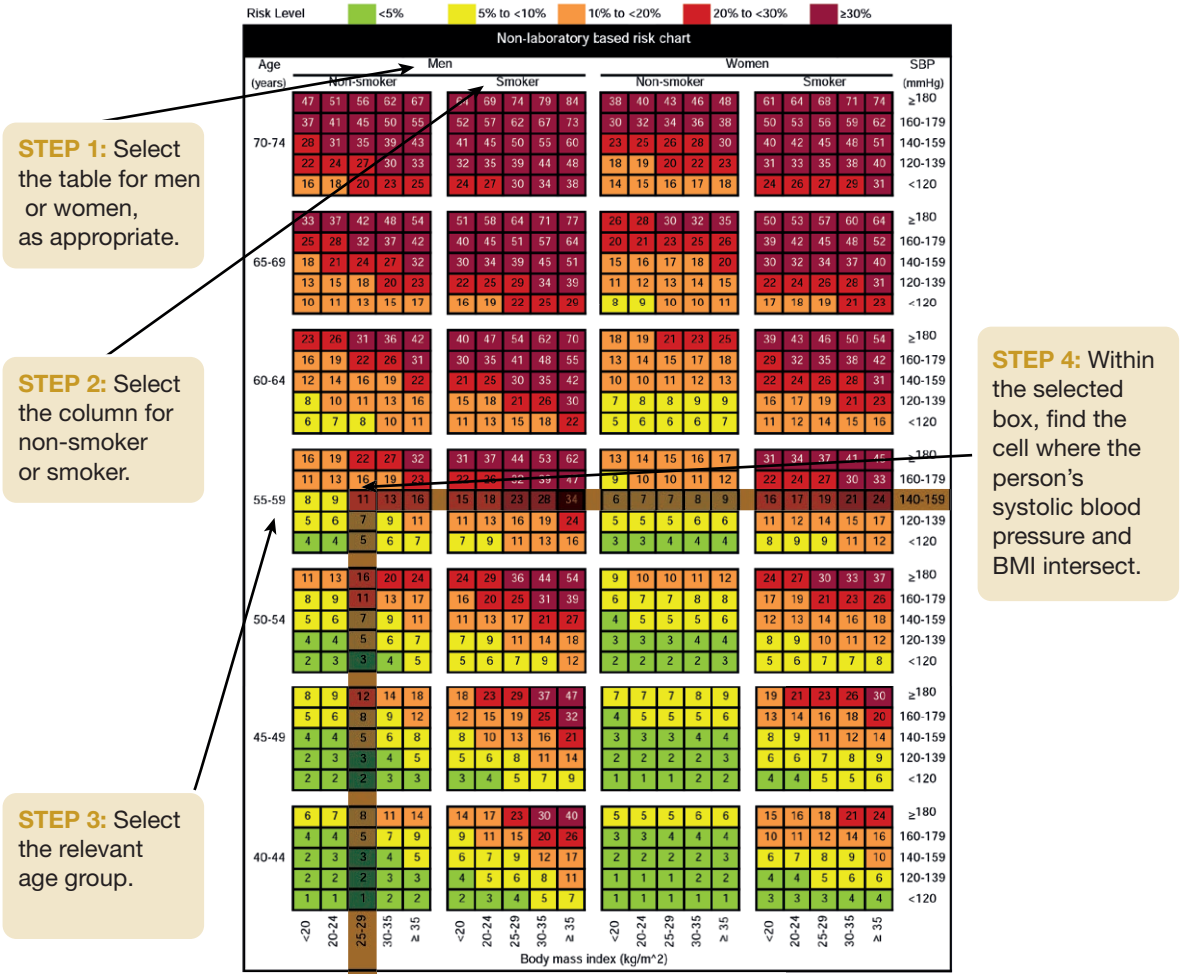
These charts are for the use of settings where diabetes and cholesterol cannot be measured. They can also be used to identify people at high risk who can be taken up for further investigations. Table 4 and Figure 4 present the steps to apply the non-laboratory WHO CVD risk charts.

Table 4: Using the WHO CVD risk (non-laboratory-based) charts

Action			
Select the regional chart covering your country: • REGION NAME is printed at the top of the charts. • Countries included in each region can be found in Annex 1.			
Have the following information ready: • age • sex • smoker* or non-smoker • systolic blood pressure • BMI (body mass index) = weight (kg) ÷ height (m)^2			
Using the charts			
STEP 1: Select the table for men or women, as appropriate.			
STEP 2: Select smoker or non-smoker column.			
STEP 3: Select age-group.			
STEP 4: Within the selected box find the cell where the person's systolic blood pressure and body mass index (BMI) intersect.			
STEP 5: The colour of the cell indicates the 10-year risk of a fatal or non-fatal CVD event. The value within the cell is the risk percentage. Colour coding is based on the grouping.		Green	<5%
		Yellow	5% to <10%
		Orange	10% to <20%
		Red	20% to <30%
		Deep red	≥30%
STEP 6: Record CVD risk percentage in person's chart.			
STEP 7: Counsel, treat and refer according to risk level			

* Current smoker

Figure 4: Illustration of how to use the WHO CVD risk (non-laboratory-based) chart



Use of WHO CVD risk (non-laboratory-based) charts

Currently, the WHO CVD risk (non-laboratory-based) charts can be considered for identifying a subset of the population who might benefit from laboratory-based risk assessment. Where laboratory testing may be available but extremely limited due to costs or distance, use of the non-laboratory charts could allow for a two-stage process that reduces the number of people at lower levels of risk who are subjected to unwarranted testing. Additionally, the non-laboratory risk charts can be used for education and advocacy regarding total CVD risk in areas where lab testing remains currently unavailable. In these areas, health care providers and policy-makers can use the non-laboratory risk charts to assess the general risk of the population, and to advocate for more resources if risk appears high. Lastly, some studies have shown that use of the non-laboratory-based tool for determining future risk performs as well as laboratory-based tools and may even be cost-effective for decisions regarding medical therapy *(4, 5)*. As more data become available to confirm these findings, the WHO CVD risk (non-laboratory-based) charts may be recommended for use in treatment decisions as well. Individuals with a total CVD risk level of 10% and above should receive an assessment using laboratory-based charts after measurement for diabetes and cholesterol. Advice on lifestyle modification should be given as needed.

Annex 1: GBD regions

The first step when using the WHO CVD risk charts is to identify which Global Burden of Disease (GBD) region a country is in (Table 5).

Table 5: GBD regional groups

GBD region	Countries	Page number of charts	
		Lab-based	Non-lab-based
High-income North America	Canada, Greenland, United States of America	25	46
Caribbean	Antigua and Barbuda, Bahamas, Barbados, Belize, Bermuda, Cuba, Dominica, Dominican Republic, Grenada, Guyana, Haiti, Jamaica, Puerto Rico, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago	26	47
Central Latin America	Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Venezuela (Bolivarian Republic of)	27	48
Andean Latin America	Bolivia, Ecuador, Peru	28	49
Tropical Latin America	Brazil, Paraguay	29	50
Southern Latin America	Argentina, Chile, Uruguay	30	51
Western Europe	Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom	31	52
Central Europe	Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Montenegro, North Macedonia, Poland, Romania, Serbia, Slovakia, Slovenia	32	53
Eastern Europe	Belarus, Estonia, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine	33	54
North Africa and Middle East	Afghanistan, Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, occupied Palestinian territory, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen	34	55

GBD region	Countries	Page number of charts	
		Lab-based	Non-lab-based
Western Sub-Saharan Africa	Benin, Burkina Faso, Cabo Verde, Cameroon, Chad, Cote d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo	35	56
Central Sub-Saharan Africa	Angola, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon	36	57
Eastern Sub-Saharan Africa	Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, Uganda, United Republic of Tanzania, Zambia	37	58
Southern Sub-Saharan Africa	Botswana, Eswatini, Lesotho, Namibia, South Africa, Zimbabwe	38	59
Central Asia	Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan	39	60
East Asia	China, Democratic People's Republic of Korea	40	61
South Asia	Bangladesh, Bhutan, India, Nepal, Pakistan	41	62
South-East Asia	Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Maldives, Mauritius, Myanmar, Philippines, Seychelles, Sri Lanka, Thailand, Timor-Leste, Viet Nam	42	63
High-income Asia Pacific	Brunei Darussalam, Japan, Republic of Korea, Singapore	43	64
Australasia	Australia, New Zealand	44	65
Oceania	Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu	45	66

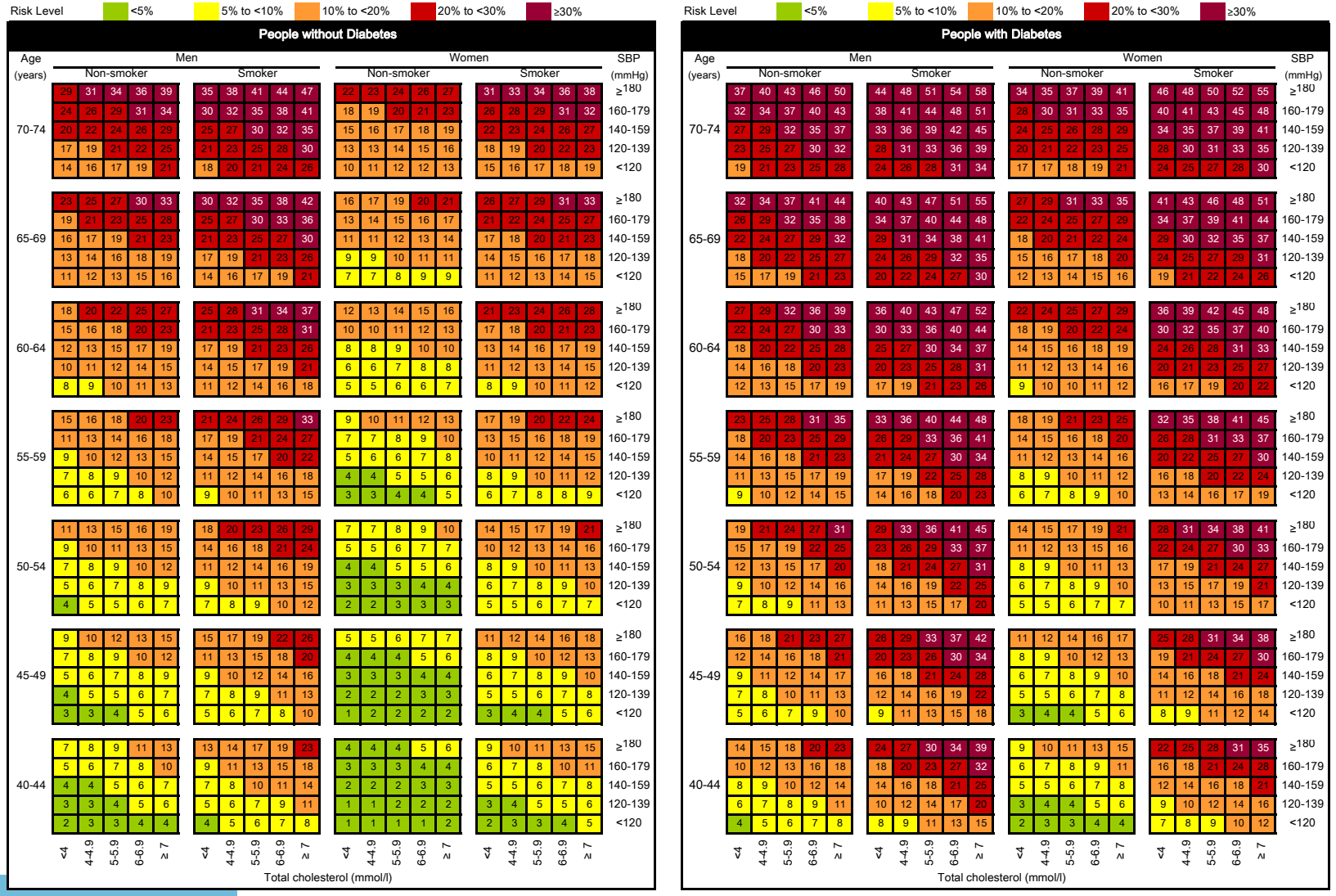
WHO CVD risk charts for a specific region can be downloaded from: https://www.who.int/news-room/detail/02-09-2019-who-updates-cardiovascular-risk-charts

Annex 2: WHO CVD risk (laboratory-based) charts

WHO cardiovascular disease risk laboratory-based charts

High-income North America

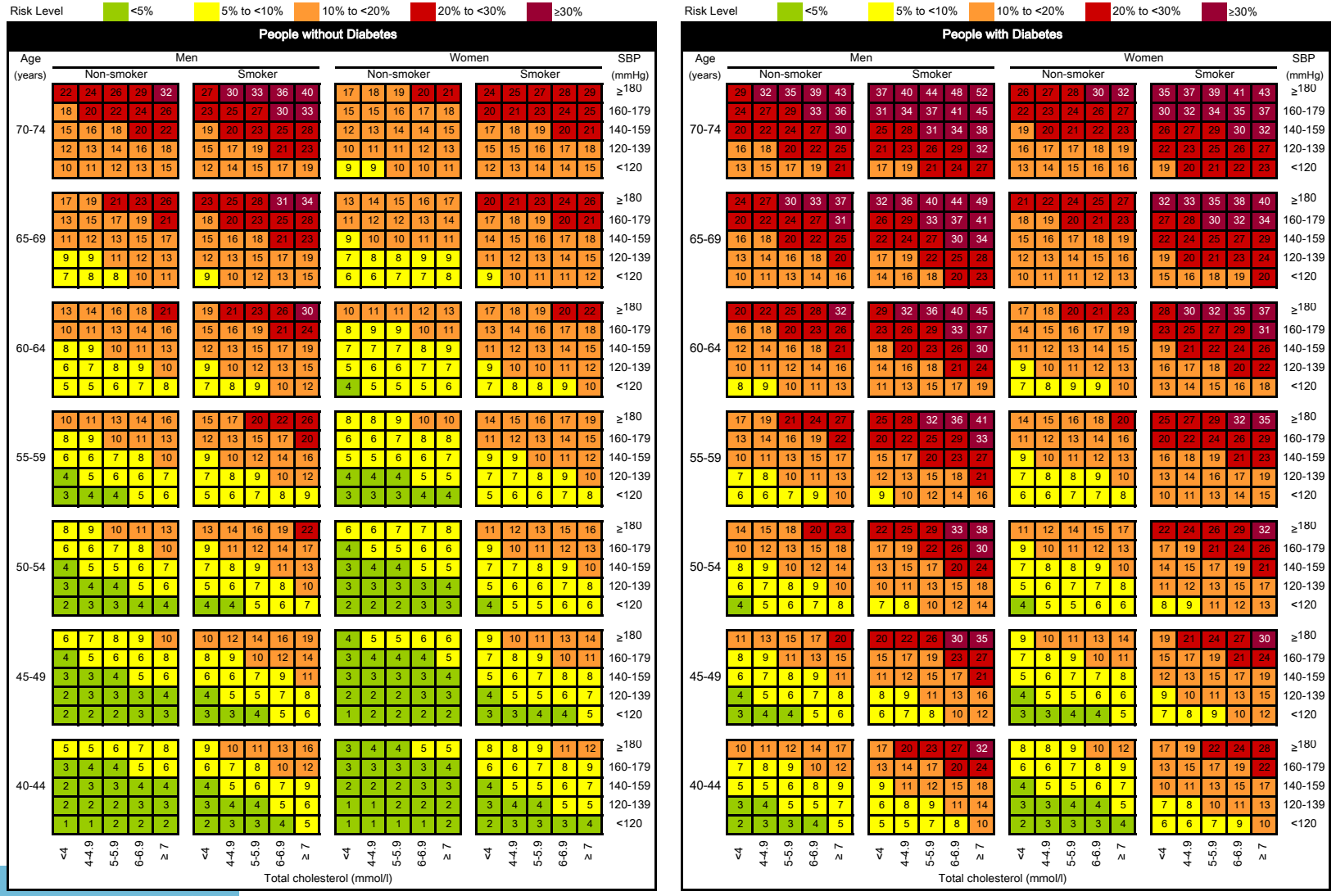
Canada, Greenland, United States of America



WHO cardiovascular disease risk laboratory-based charts

Caribbean

Antigua and Barbuda, Bahamas, Barbados, Belize, Bermuda, Cuba, Dominica, Dominican Republic, Grenada, Guyana, Haiti, Jamaica, Puerto Rico, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago

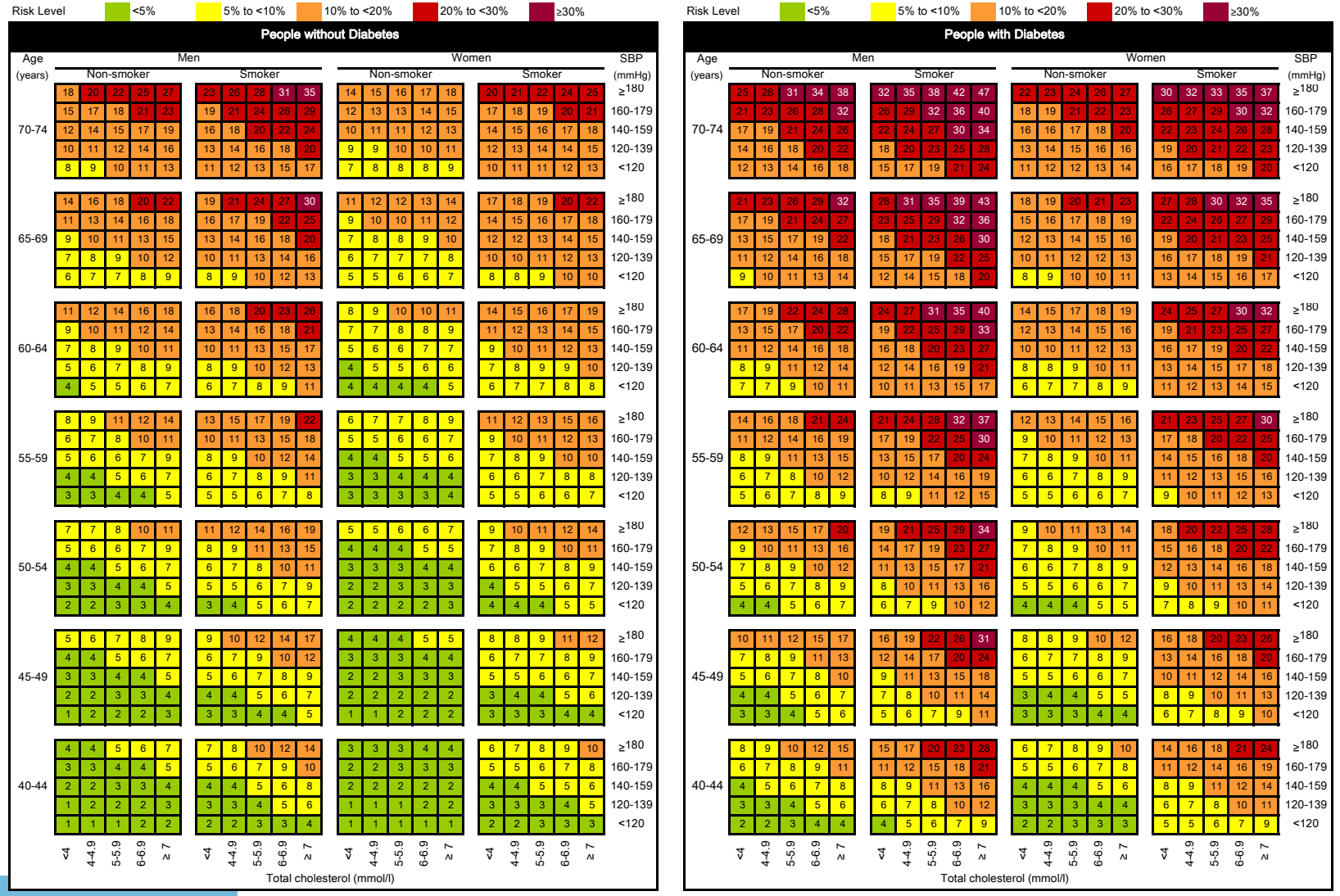


Caribbean

WHO cardiovascular disease risk laboratory-based charts

Central Latin America

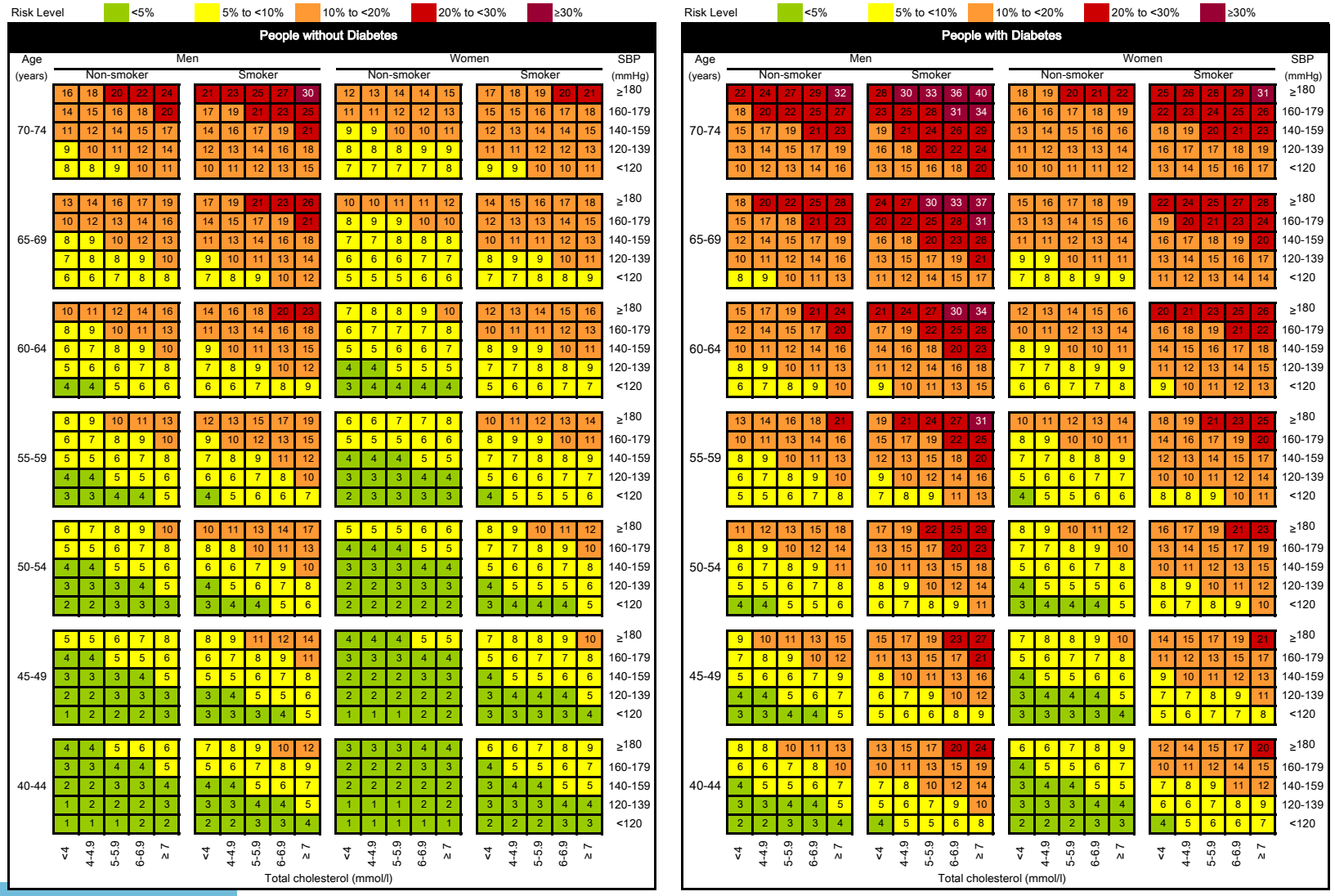
Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Venezuela (Bolivarian Republic of)



WHO cardiovascular disease risk laboratory-based charts

Andean Latin America

Bolivia, Ecuador, Peru

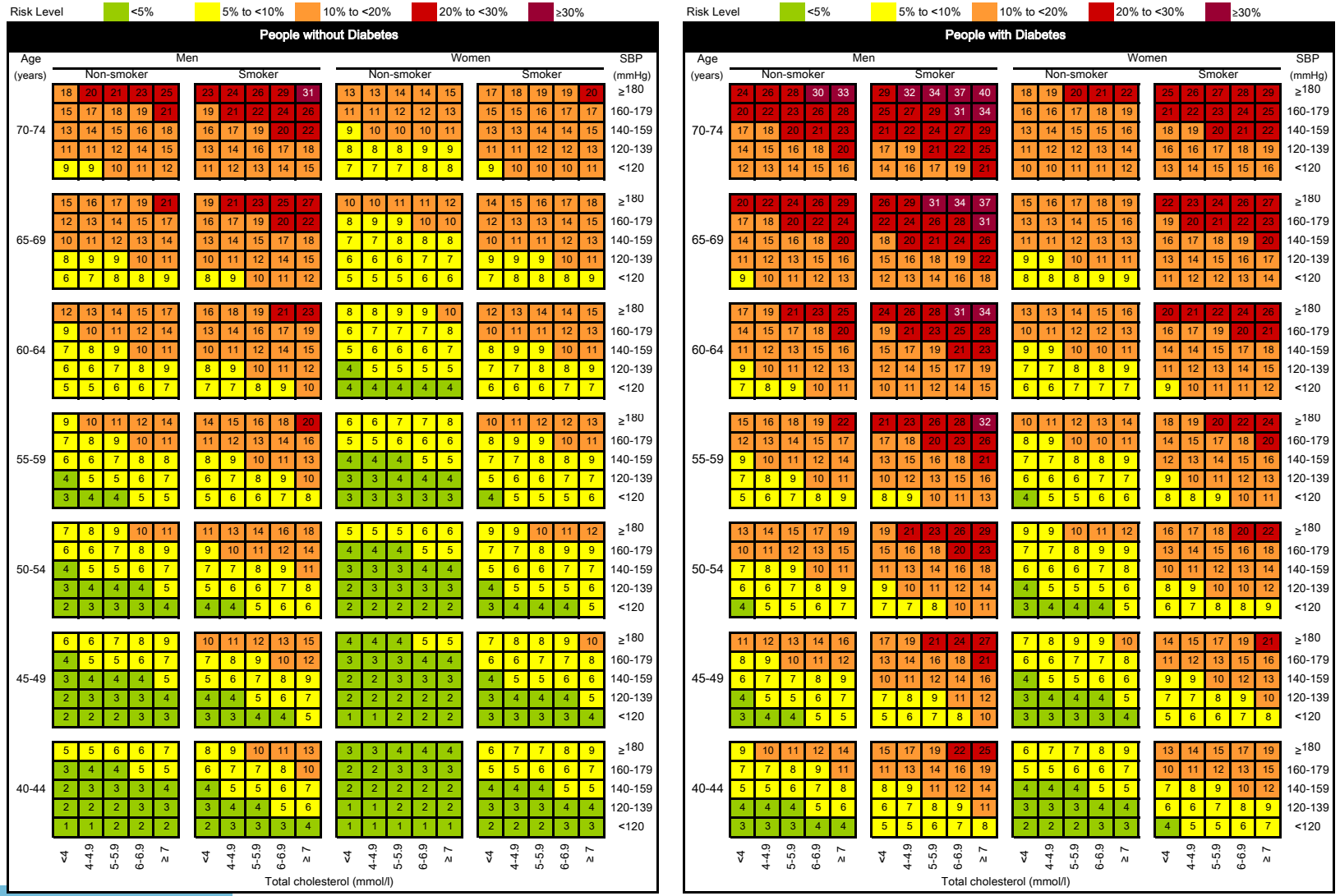


Andean Latin America

WHO cardiovascular disease risk laboratory-based charts

Tropical Latin America

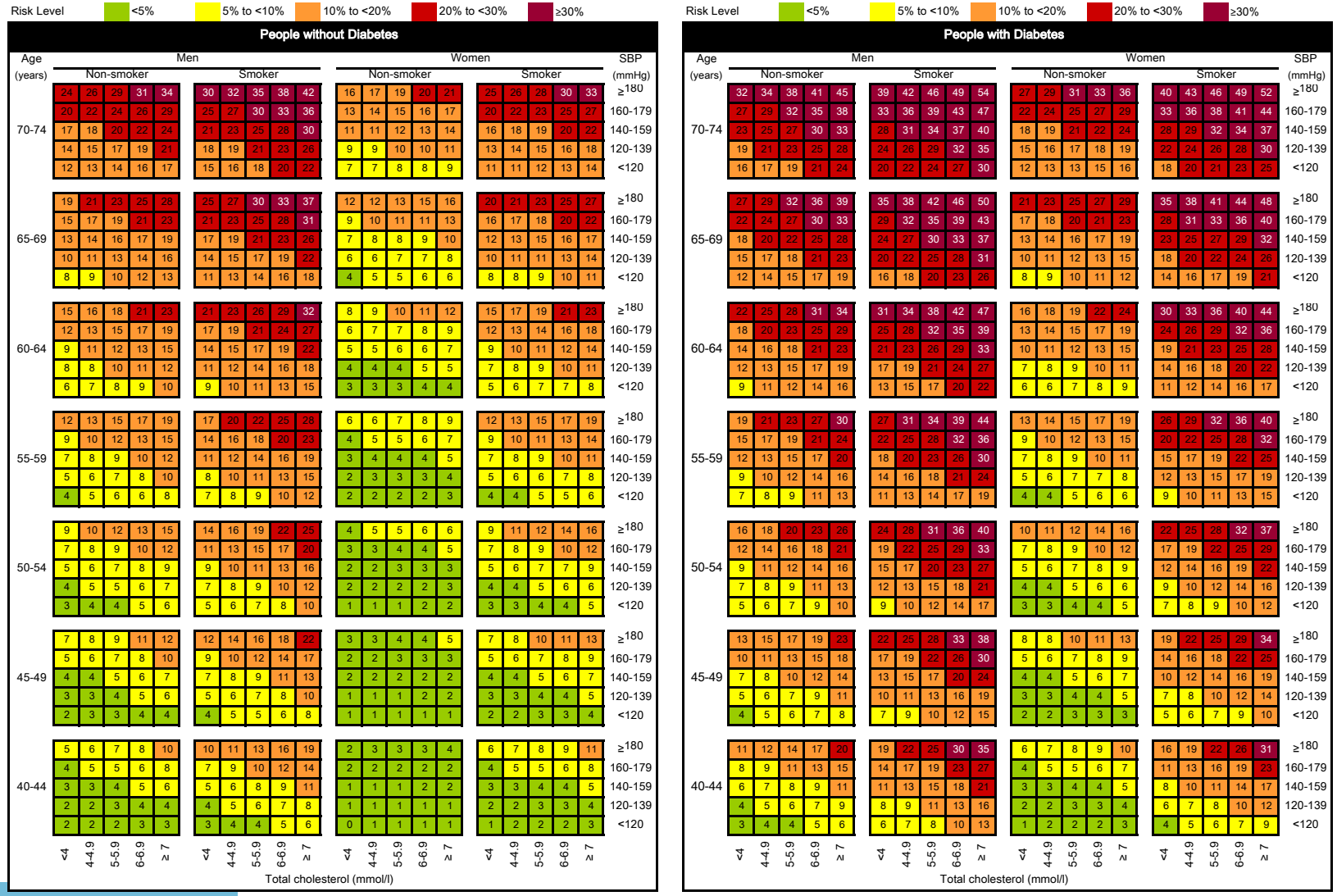
Brazil, Paraguay



WHO cardiovascular disease risk laboratory-based charts

Southern Latin America

Argentina, Chile, Uruguay

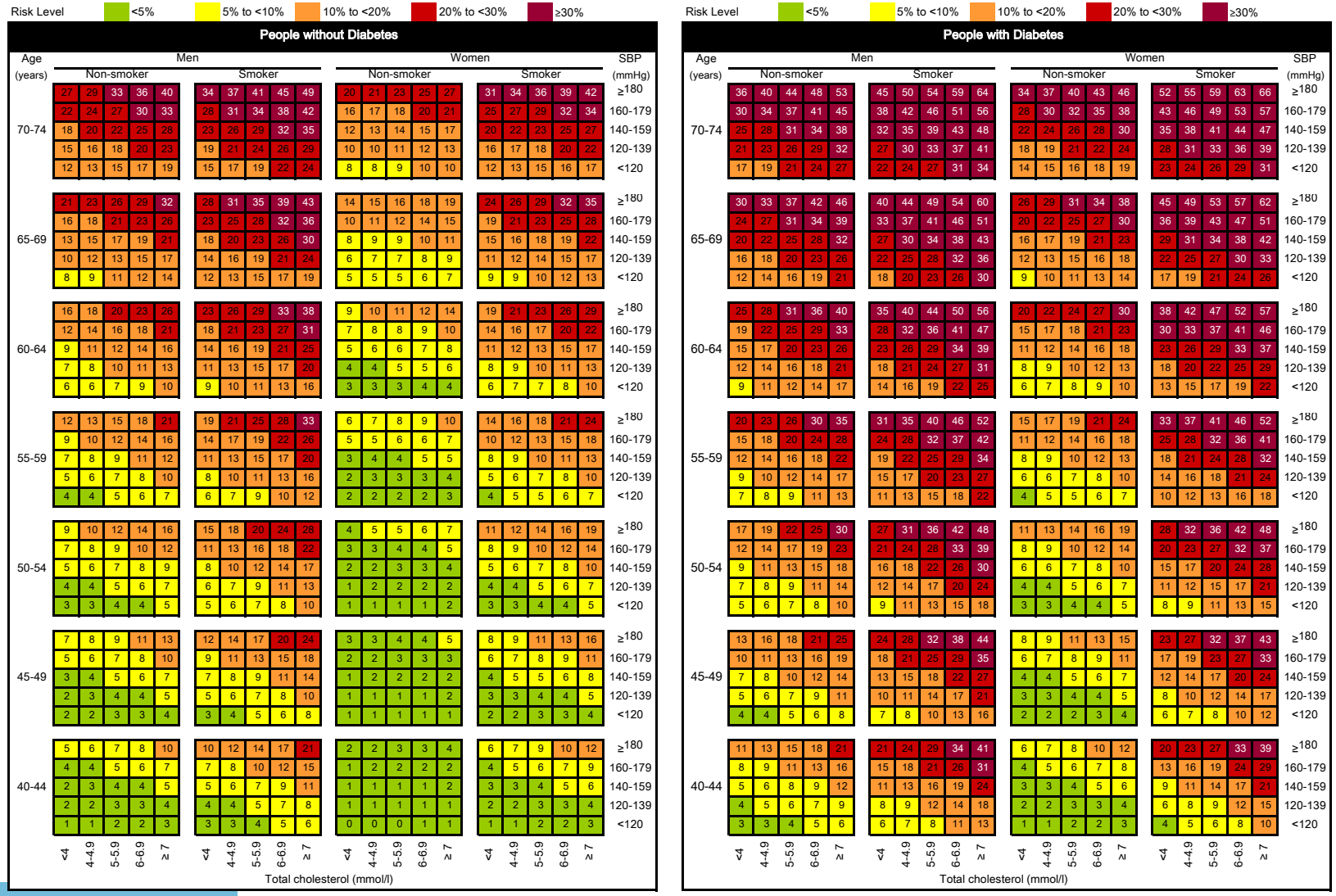


Southern Latin America

WHO cardiovascular disease risk laboratory-based charts

Western Europe

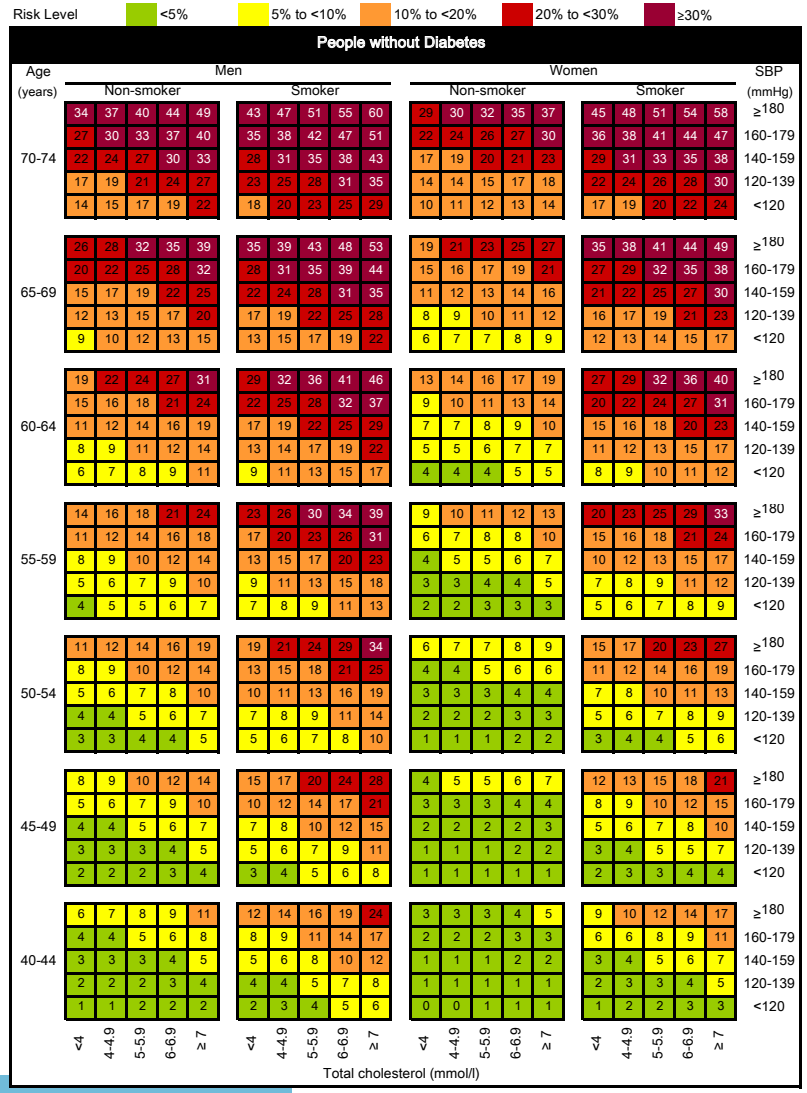
Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom

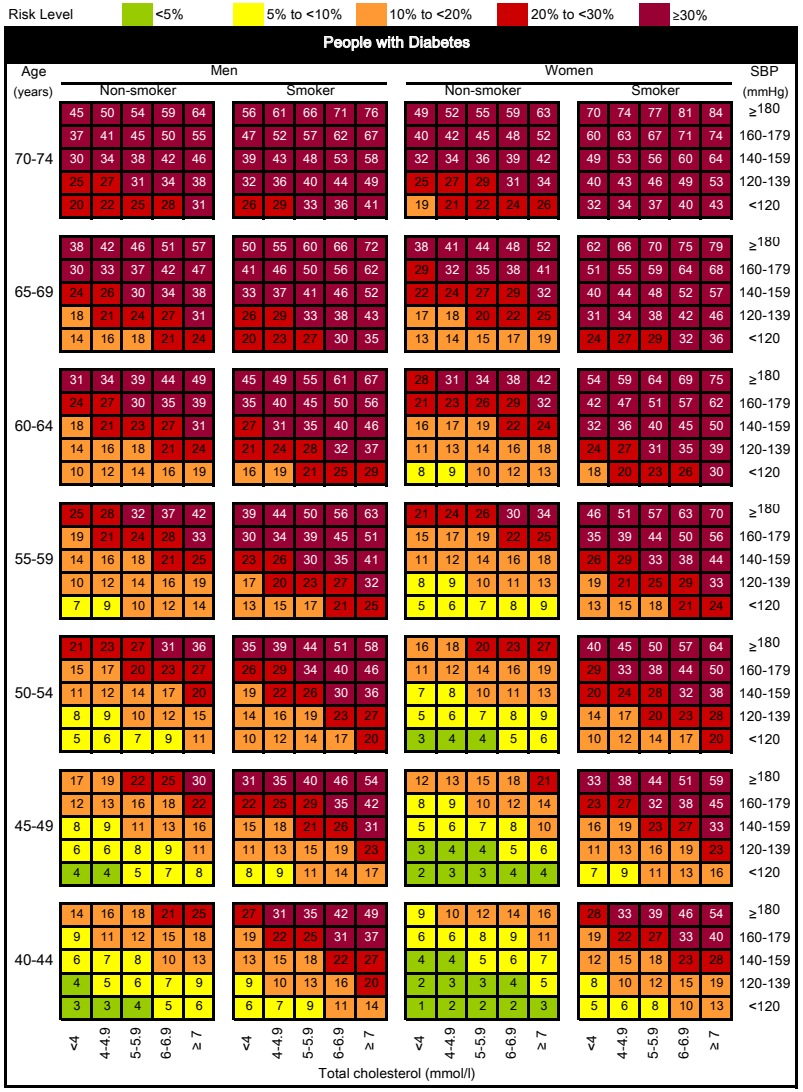


WHO cardiovascular disease risk laboratory-based charts

Central Europe

Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Montenegro, North Macedonia, Poland, Romania, Serbia, Slovakia, Slovenia



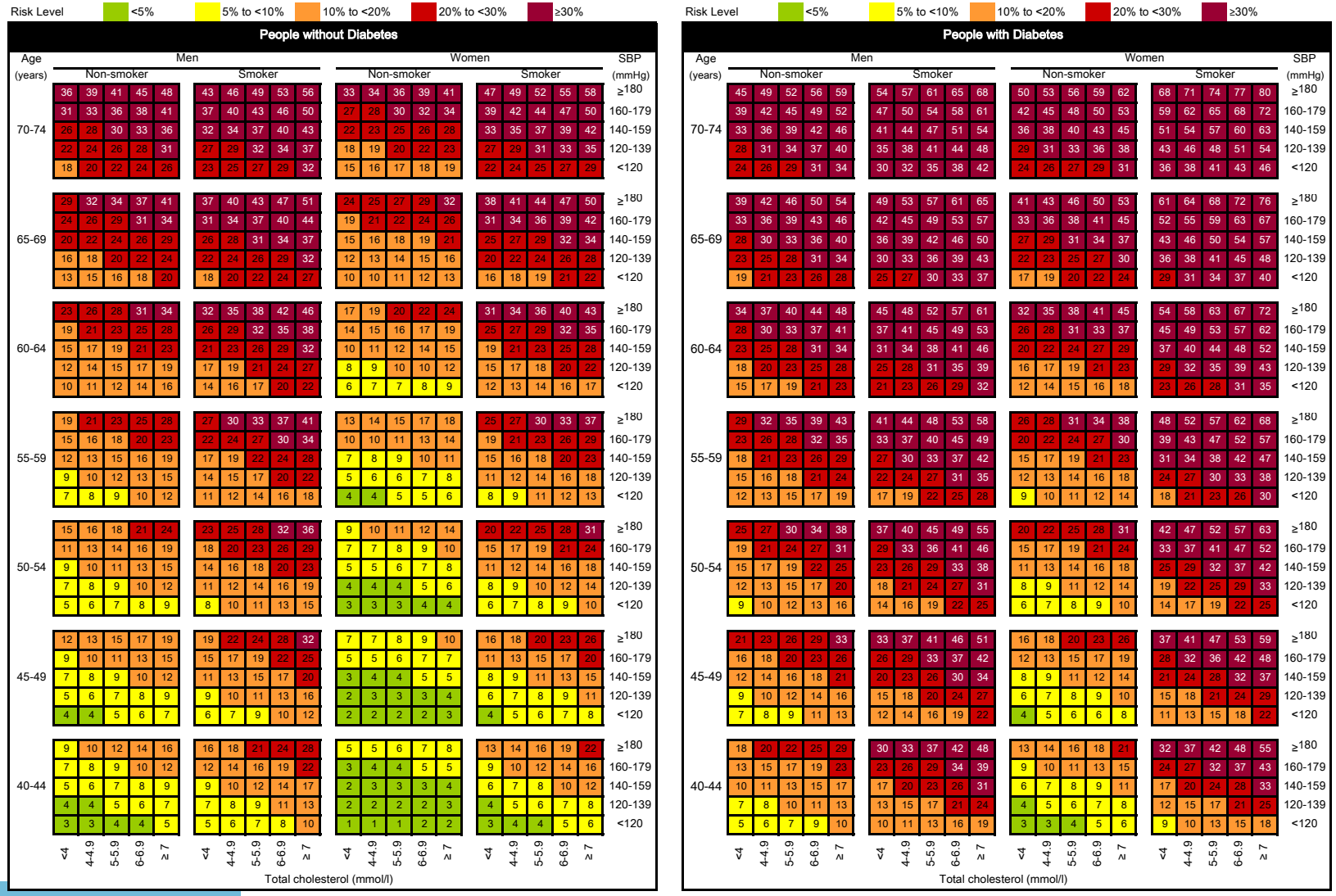


Central Europe

WHO cardiovascular disease risk laboratory-based charts

Eastern Europe

Belarus, Estonia, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine

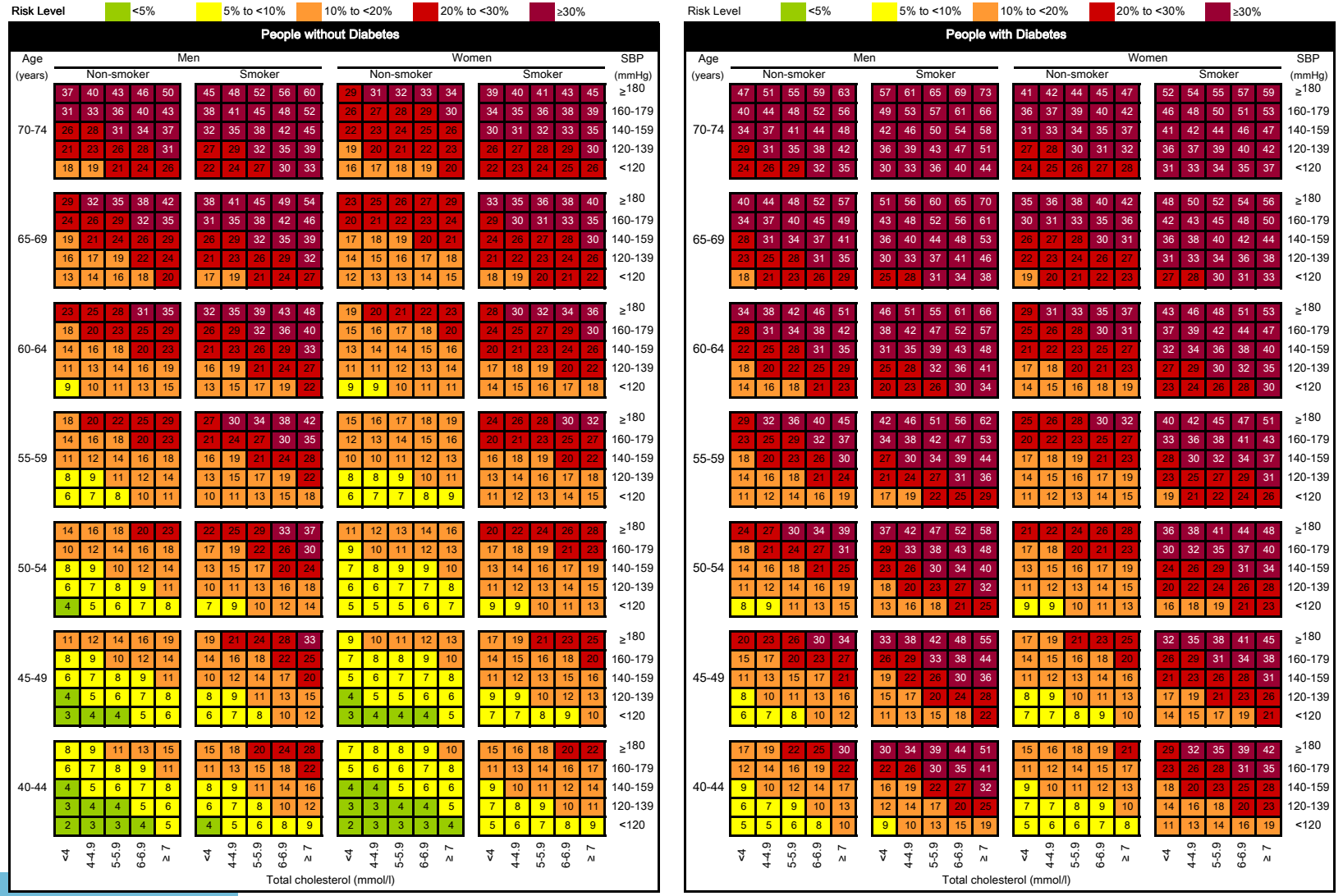


Eastern Europe

WHO cardiovascular disease risk laboratory-based charts

North Africa and Middle East

Afghanistan, Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, occupied Palestinian territory, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen

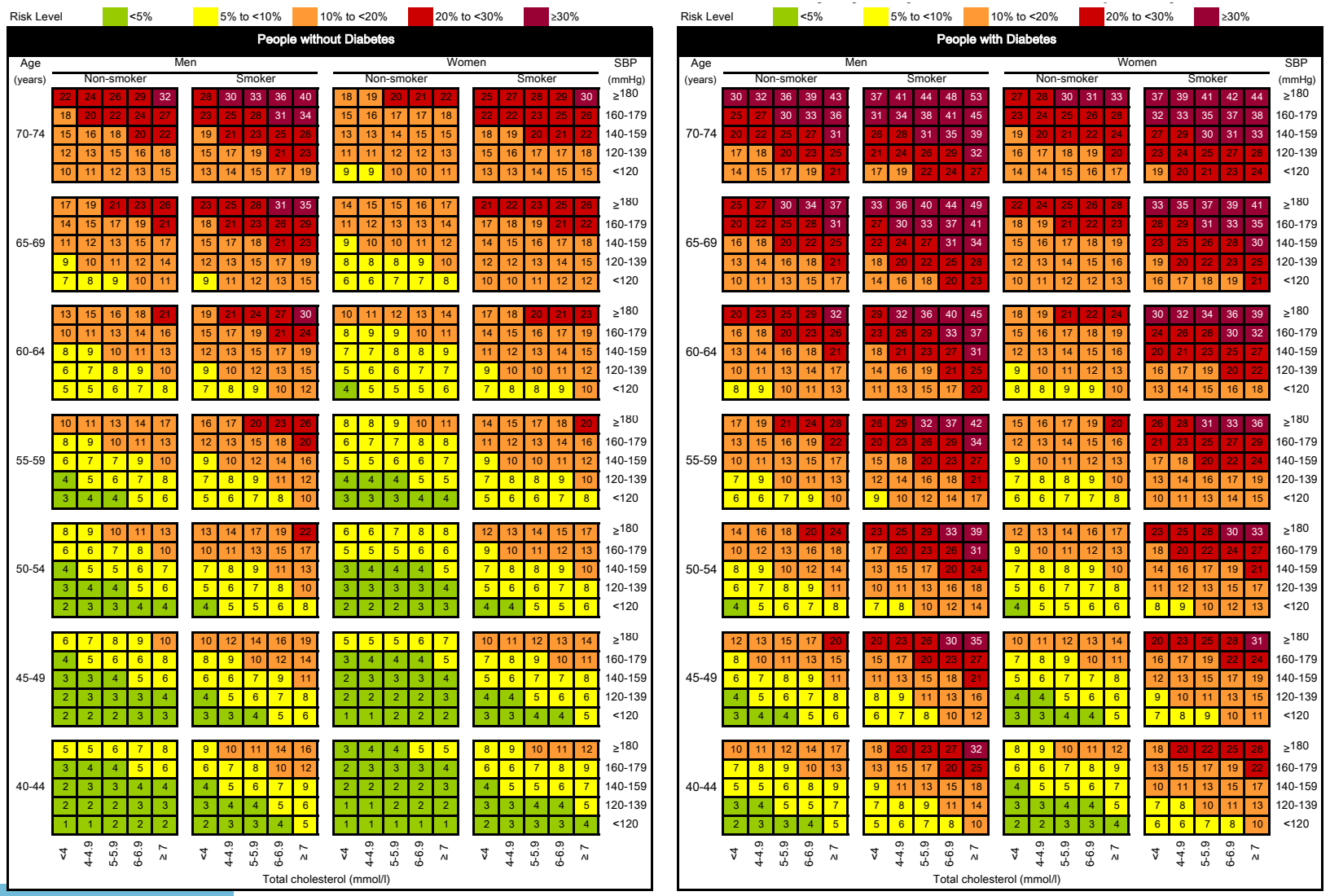


North Africa and Middle East

WHO cardiovascular disease risk laboratory-based charts

Western Sub-Saharan Africa

Benin, Burkina Faso, Cabo Verde, Cameroon, Chad, Cote d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo

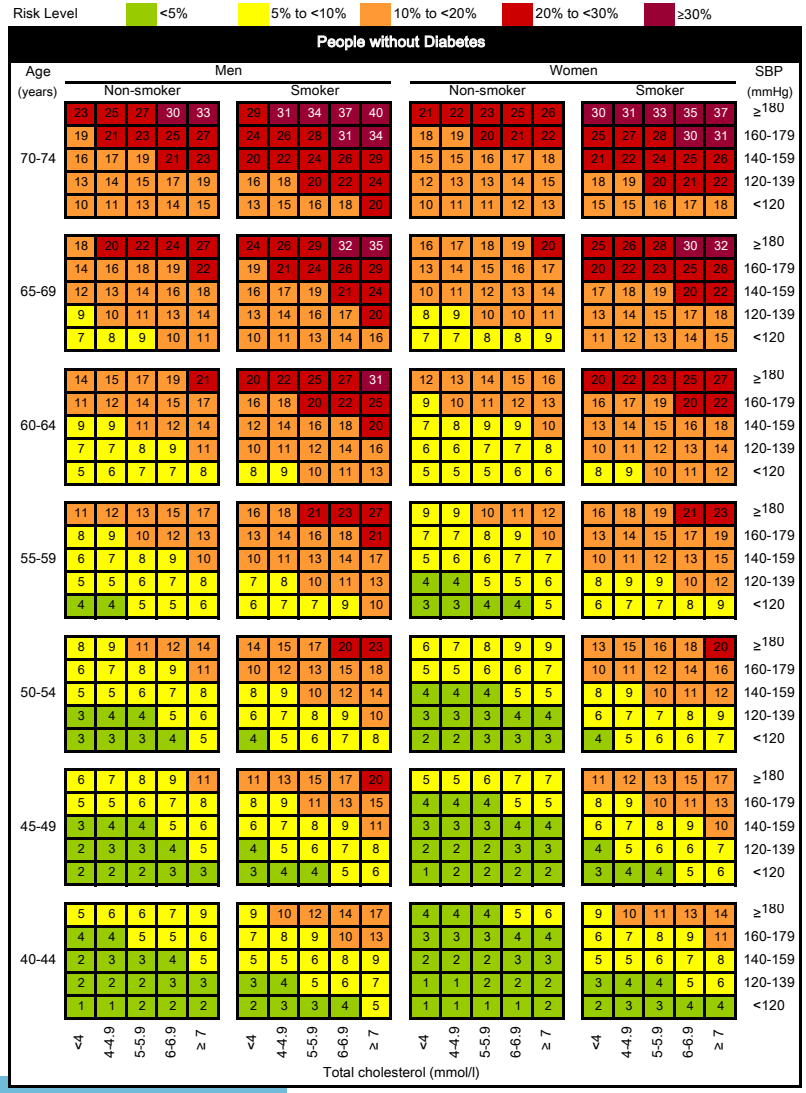


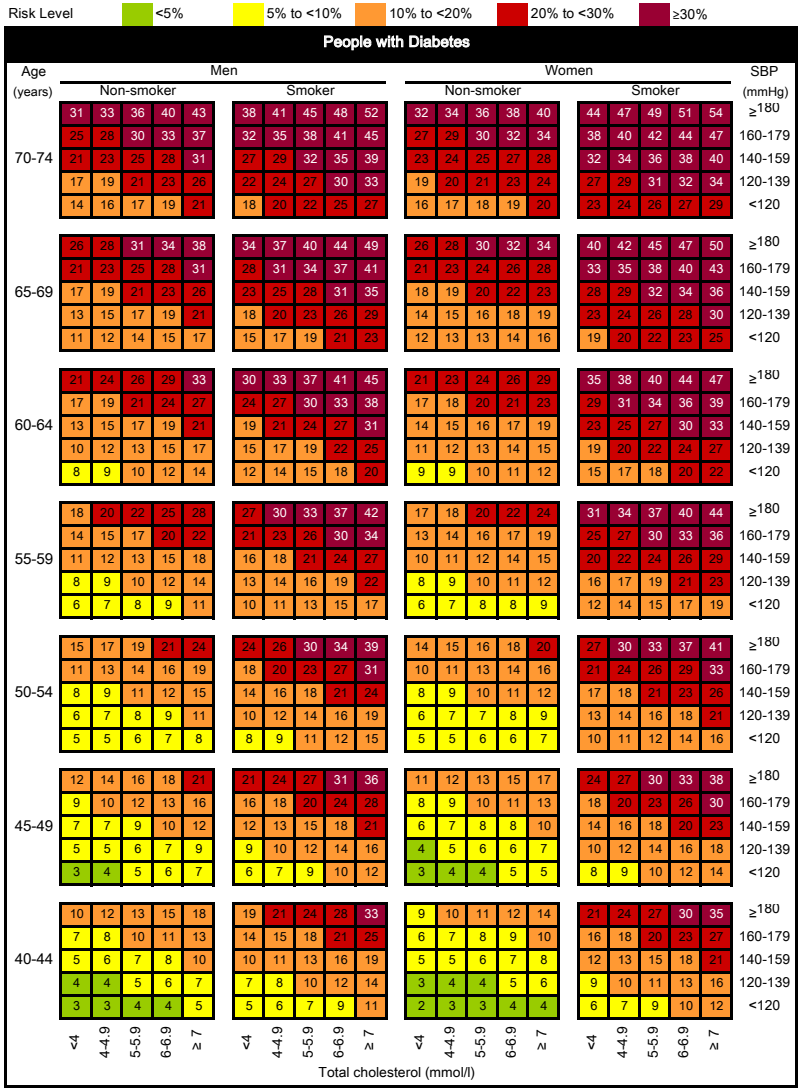
Western Sub-Saharan Africa

WHO cardiovascular disease risk laboratory-based charts

Central Sub-Saharan Africa

Angola, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon

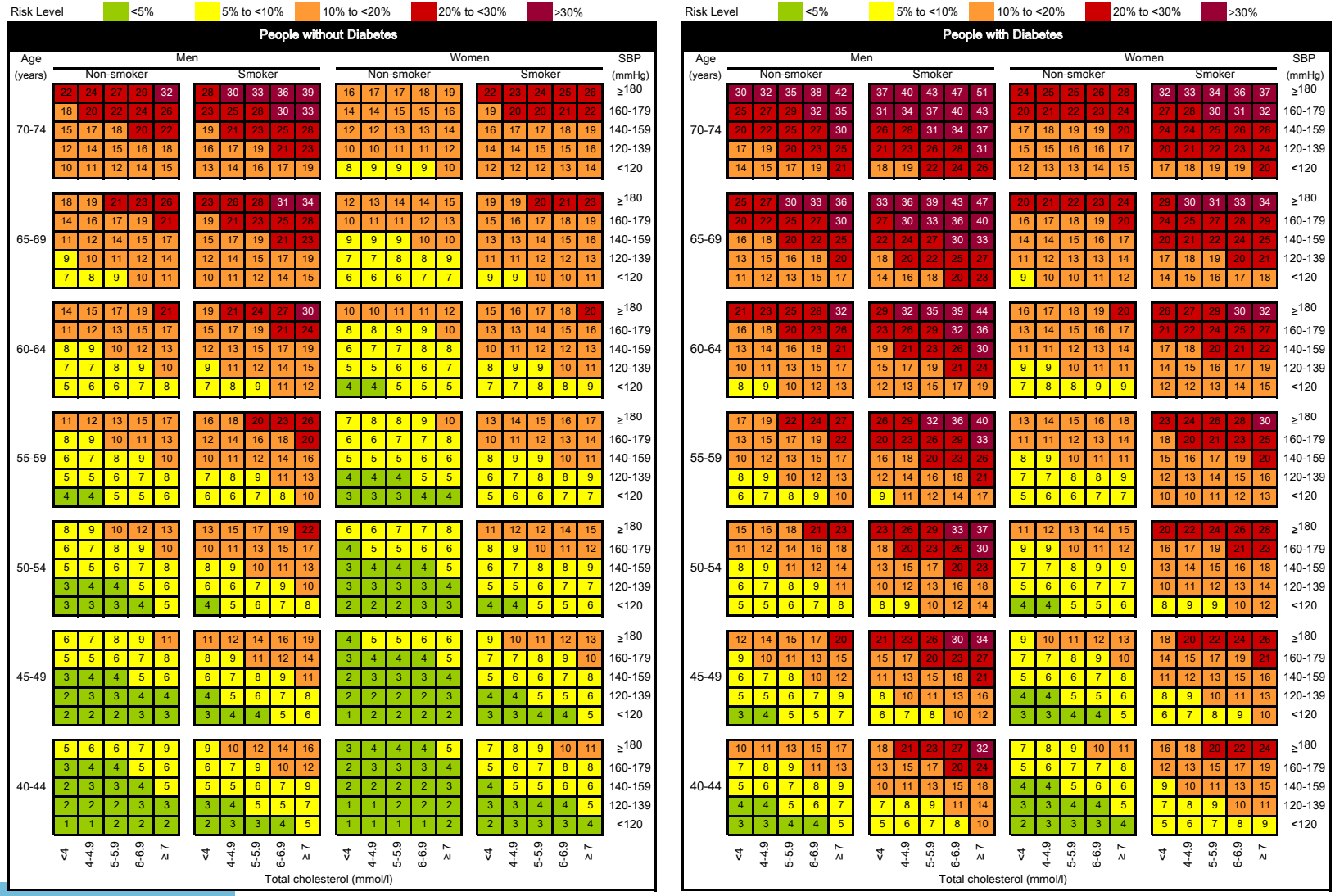




WHO cardiovascular disease risk laboratory-based charts

Eastern Sub-Saharan Africa

Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, Uganda, United Republic of Tanzania, Zambia

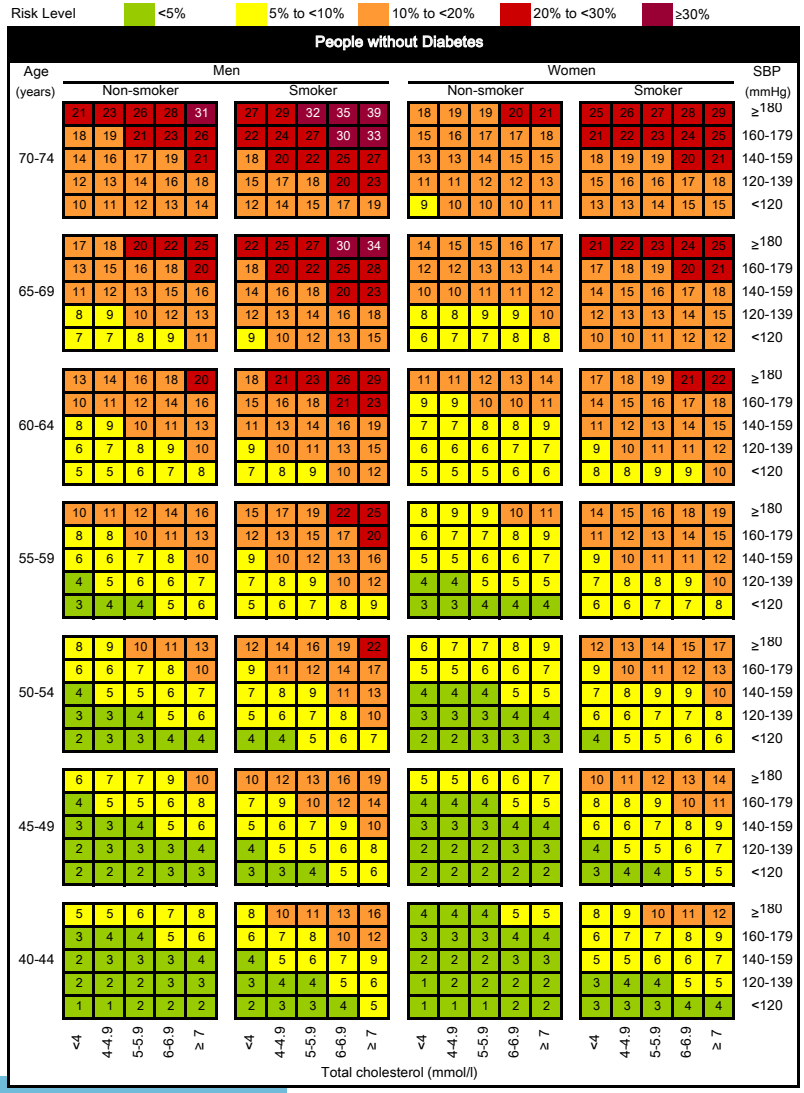


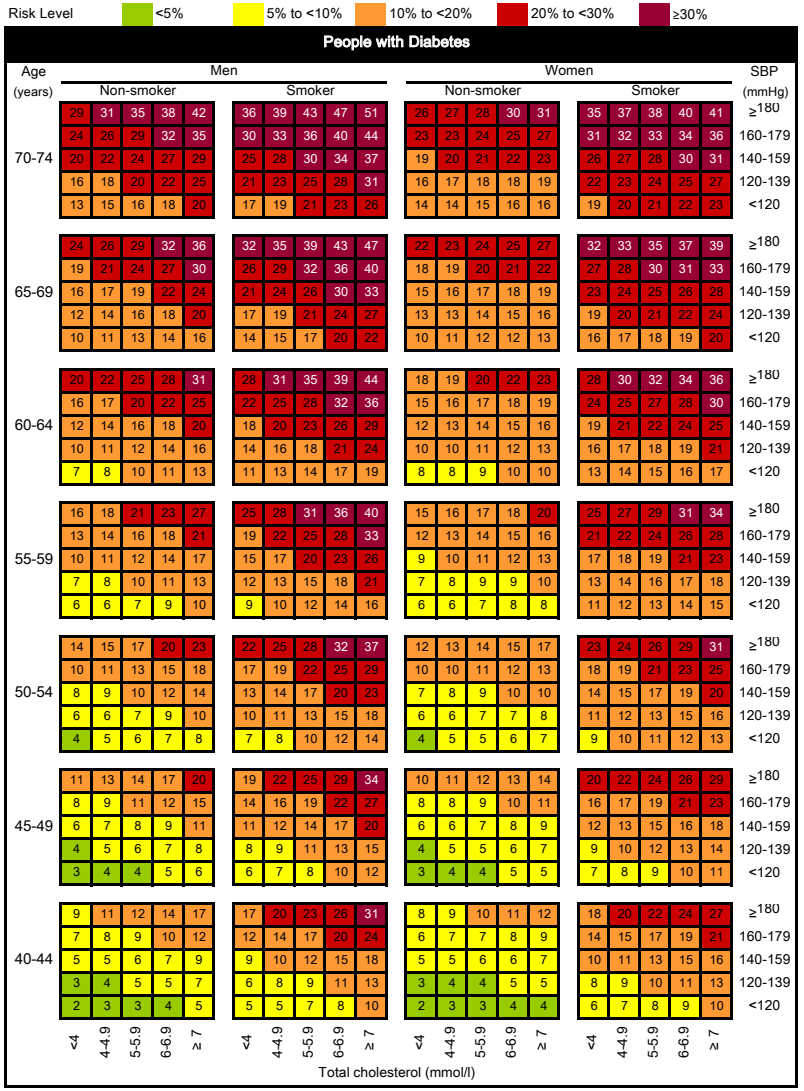
Eastern Sub-Saharan Africa

WHO cardiovascular disease risk laboratory-based charts

Southern Sub-Saharan Africa

Botswana, Eswatini, Lesotho, Namibia, South Africa, Zimbabwe

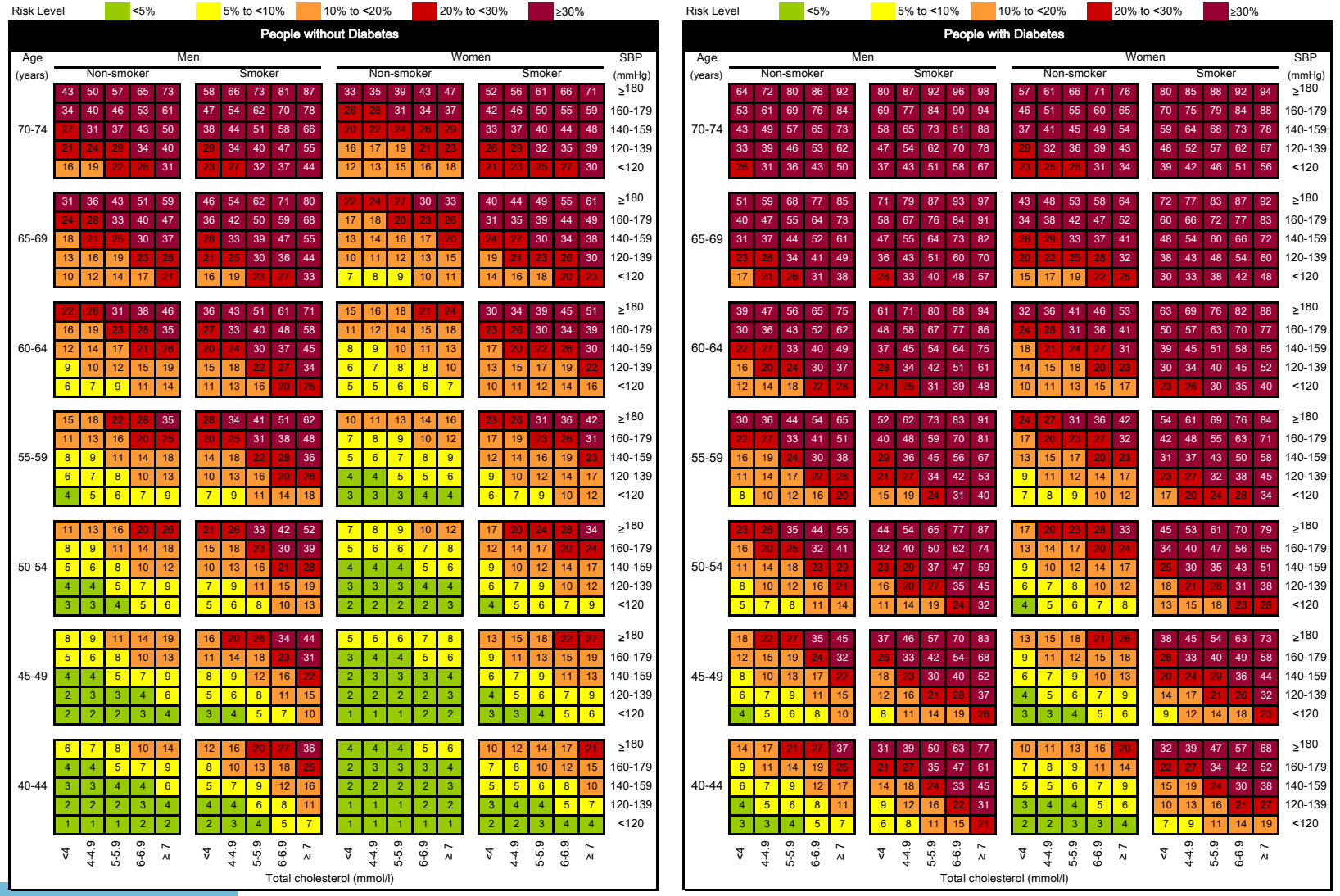




WHO cardiovascular disease risk laboratory-based charts

Central Asia

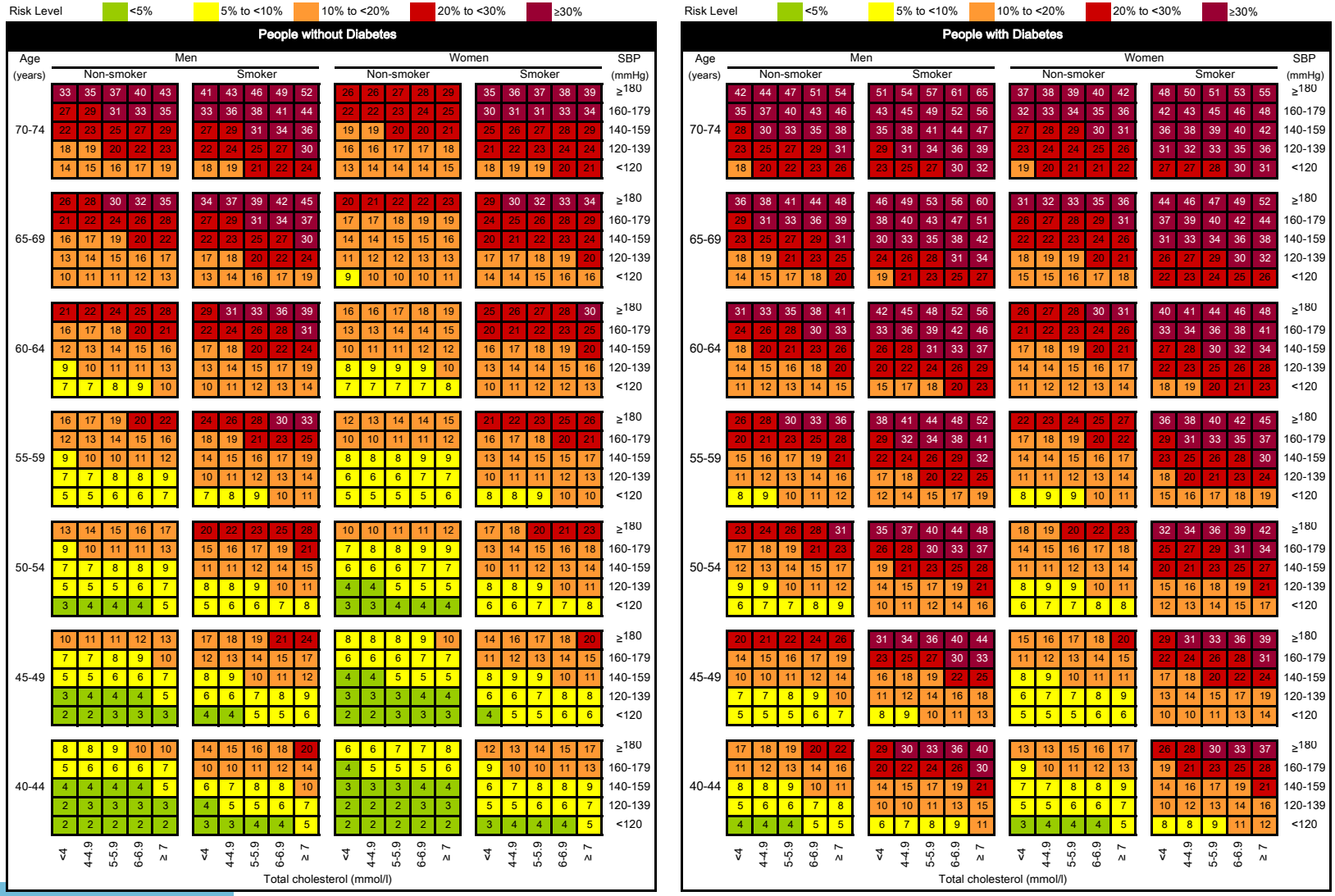
Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan



WHO cardiovascular disease risk laboratory-based charts

East Asia

China, Democratic People's Republic of Korea

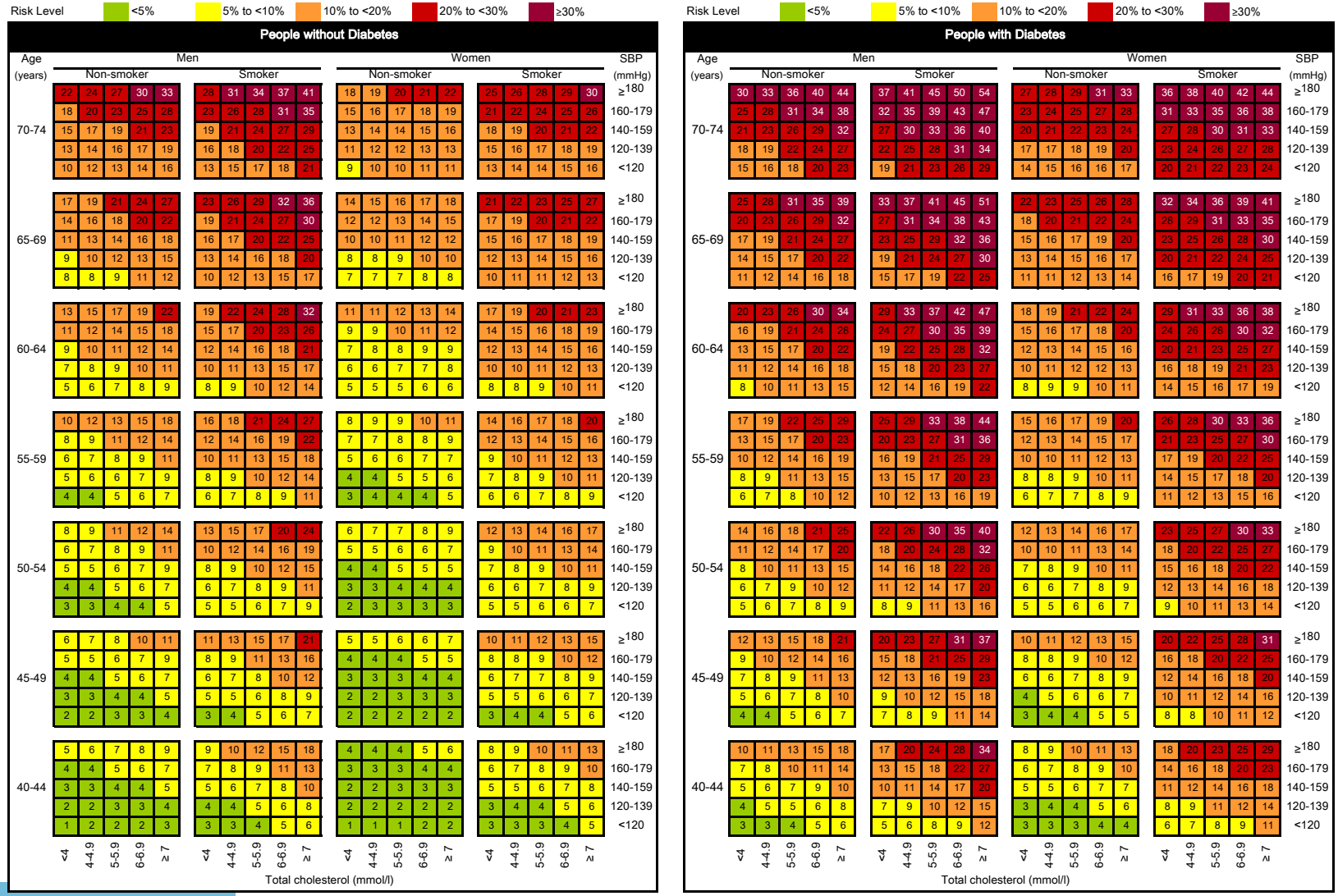


East Asia

WHO cardiovascular disease risk laboratory-based charts

South Asia

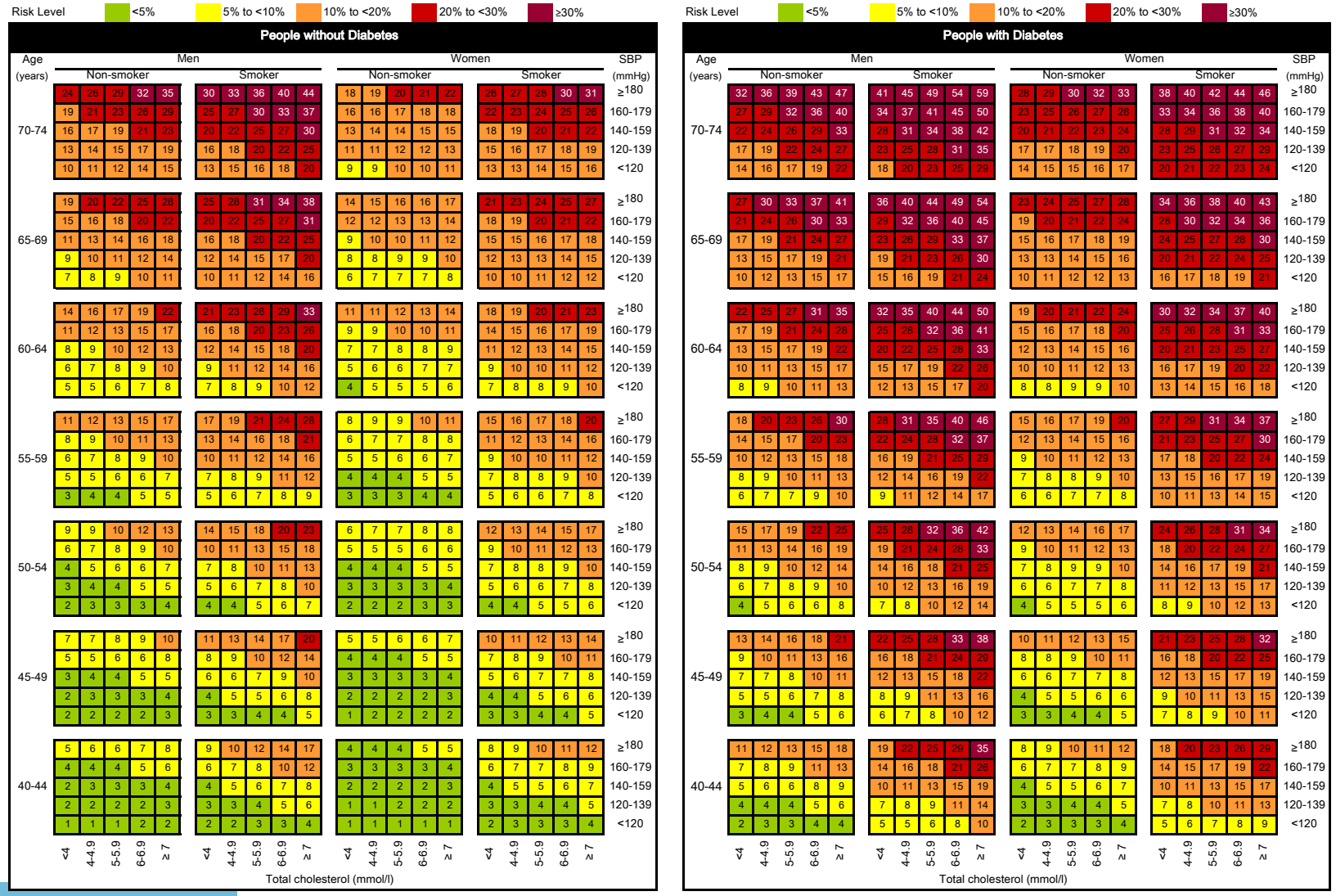
Bangladesh, Bhutan, India, Nepal, Pakistan



WHO cardiovascular disease risk laboratory-based charts

South-East Asia

Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Maldives, Mauritius, Myanmar, Philippines, Seychelles, Sri Lanka, Thailand, Timor-Leste, Viet Nam

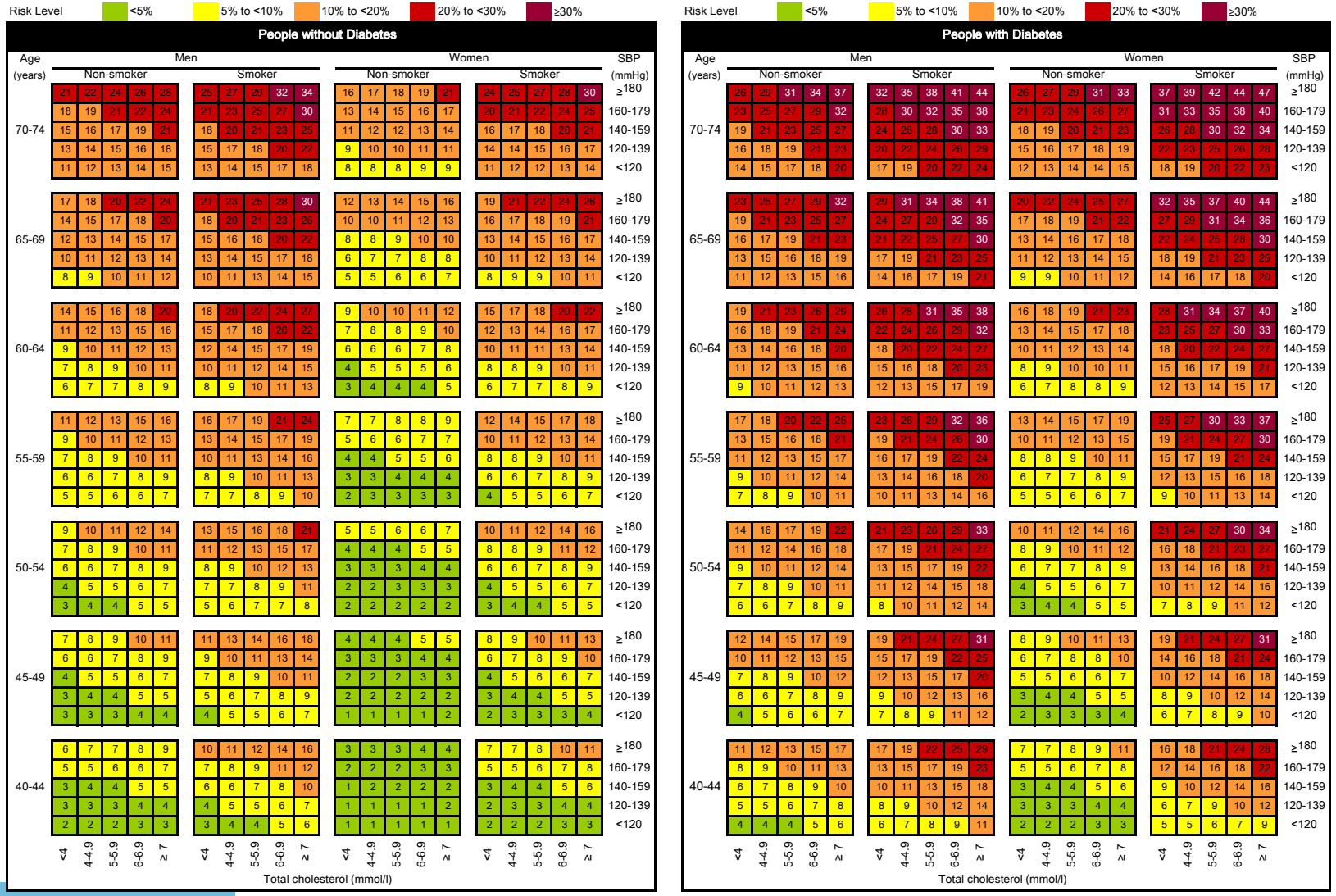


South-East Asia

WHO cardiovascular disease risk laboratory-based charts

High-income Asia Pacific

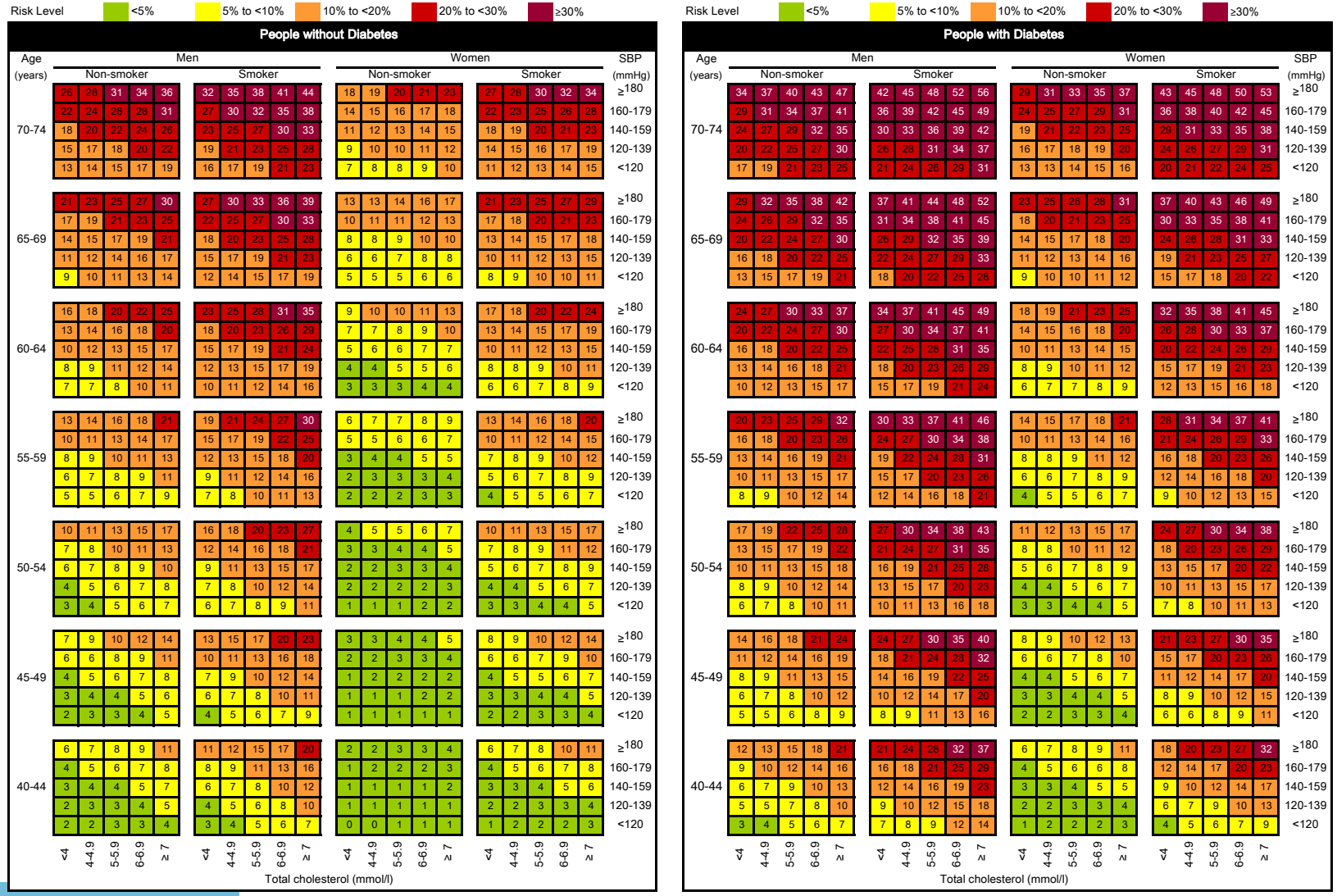
Brunei Darussalam, Japan, Republic of Korea, Singapore



WHO cardiovascular disease risk laboratory-based charts

Australasia

Australia, New Zealand

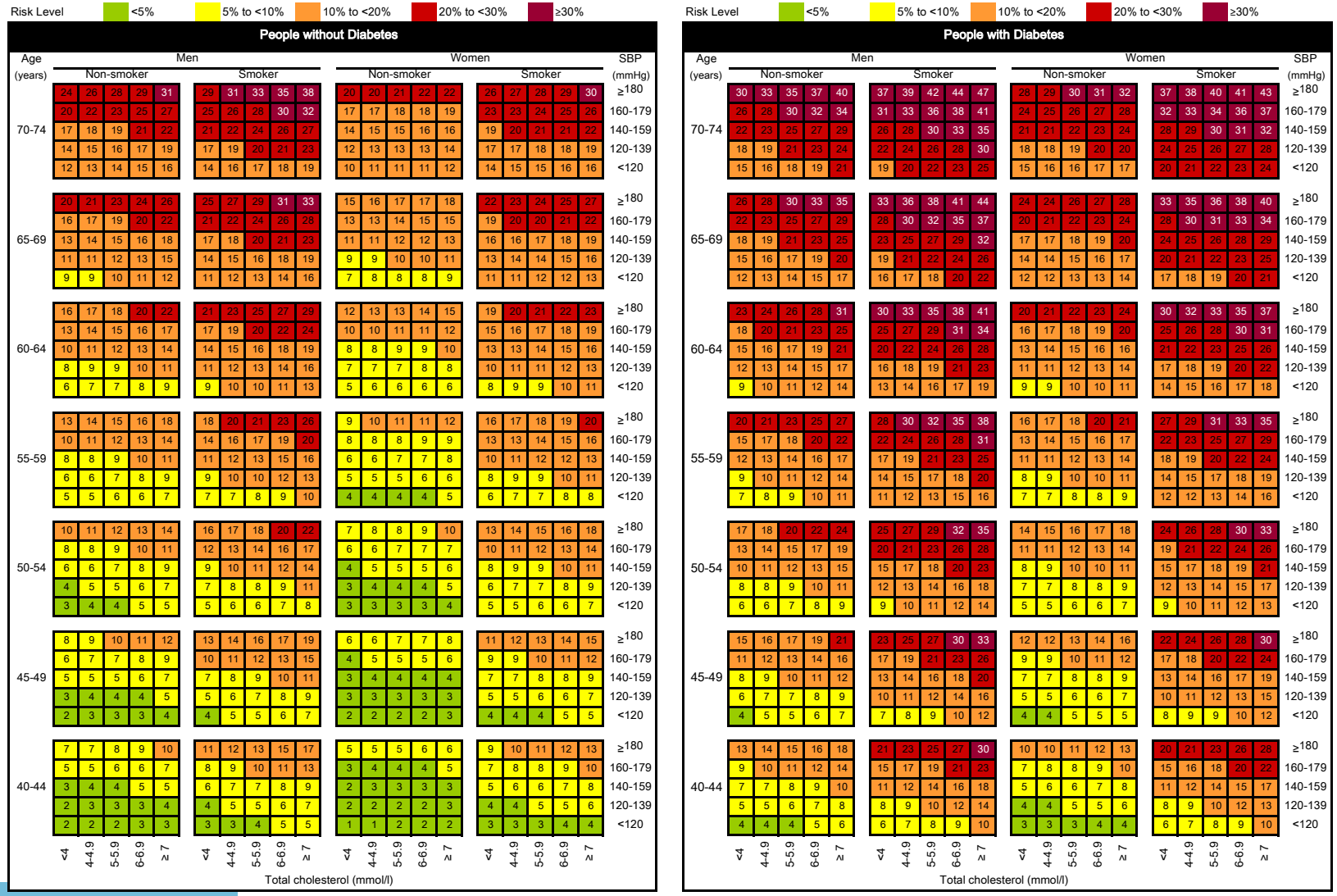


Australasia

WHO cardiovascular disease risk laboratory-based charts

Oceania

Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu

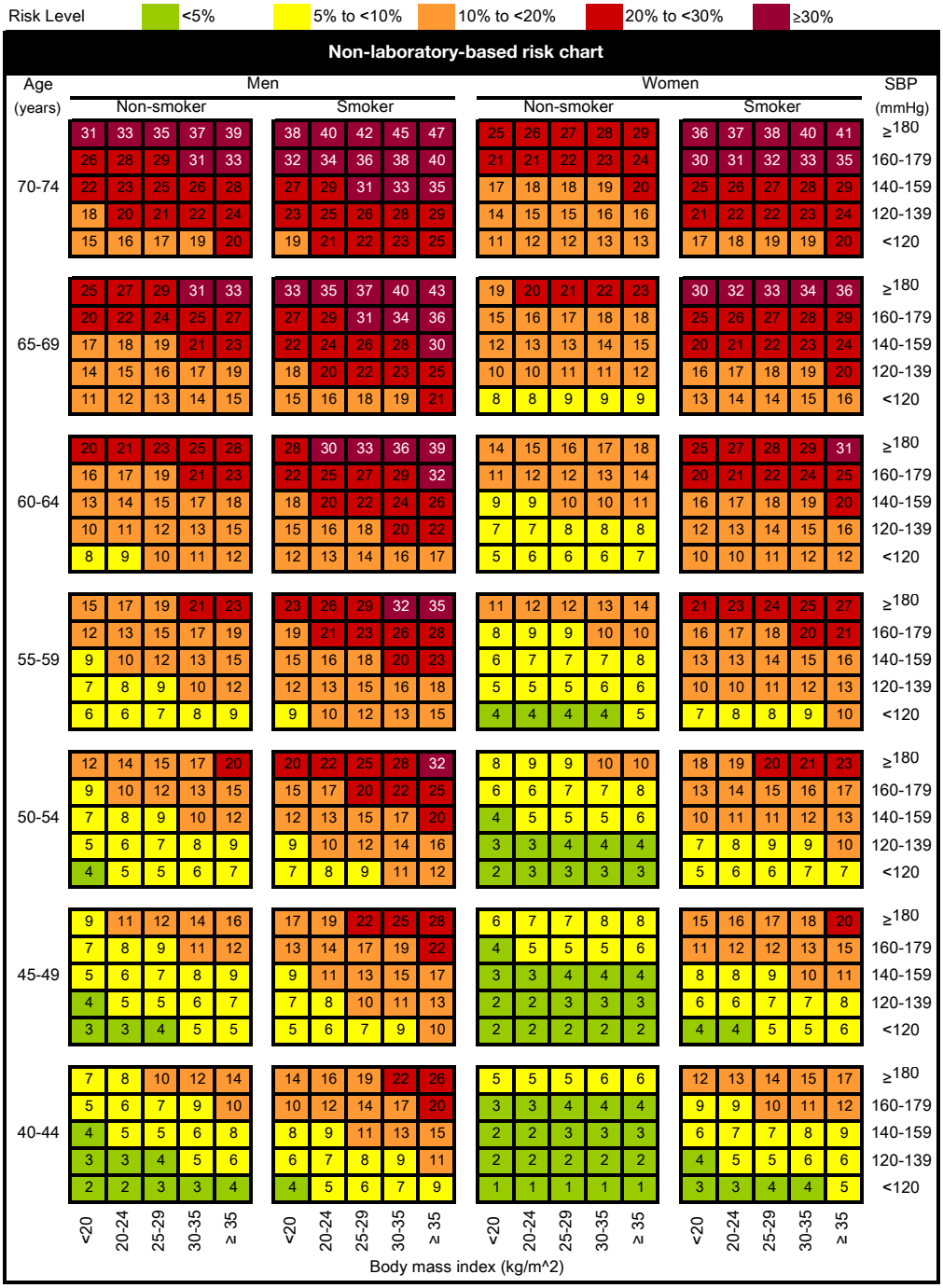


Annex 3: WHO CVD risk (non-laboratory-based) charts

WHO cardiovascular disease risk non-laboratory-based charts

High-income North America

Canada, Greenland, United States of America

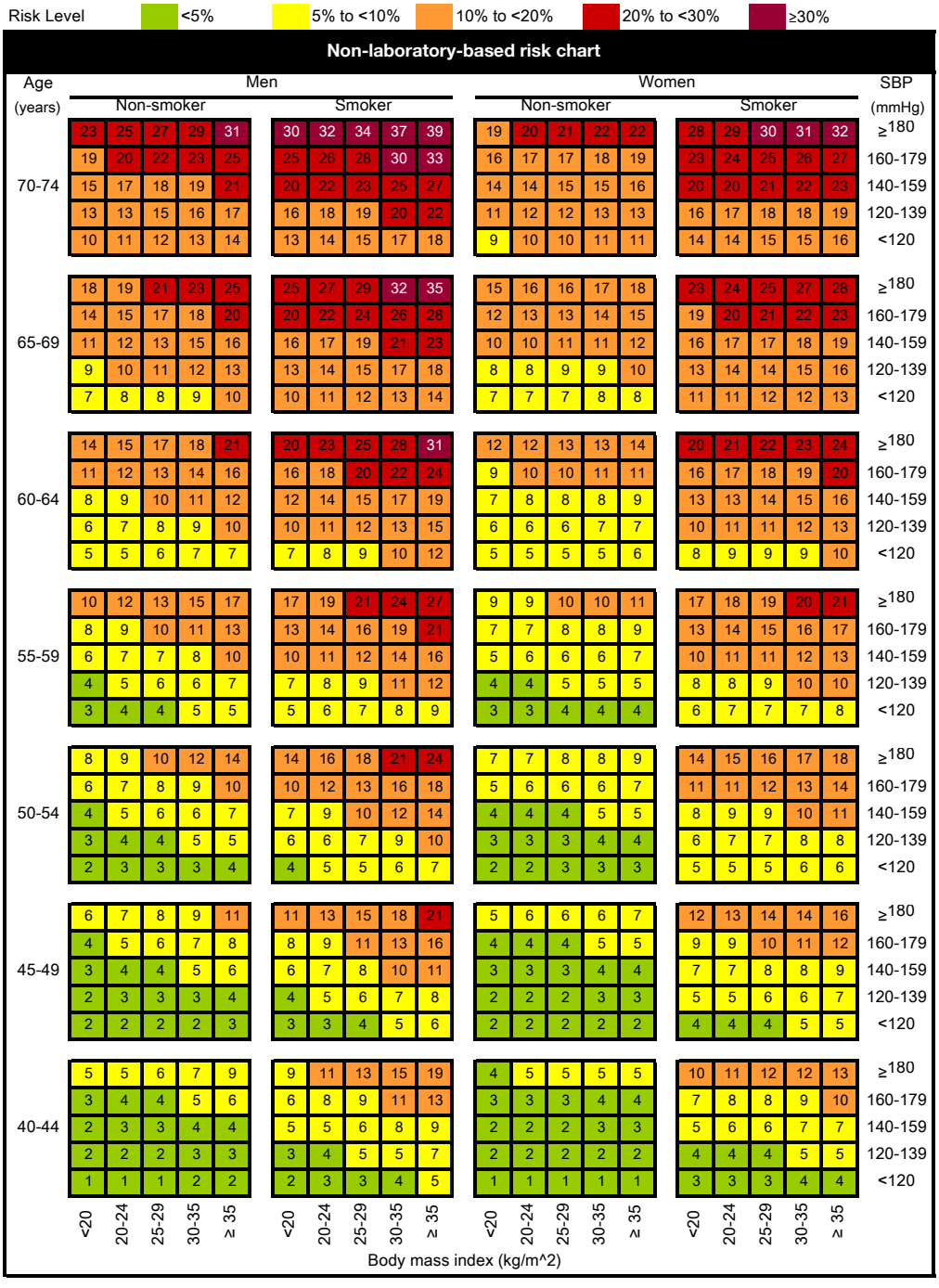


High-income North America

WHO cardiovascular disease risk non-laboratory-based charts

Caribbean

Antigua and Barbuda, Bahamas, Barbados, Belize, Bermuda, Cuba, Dominica, Dominican Republic, Grenada, Guyana, Haiti, Jamaica, Puerto Rico, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago

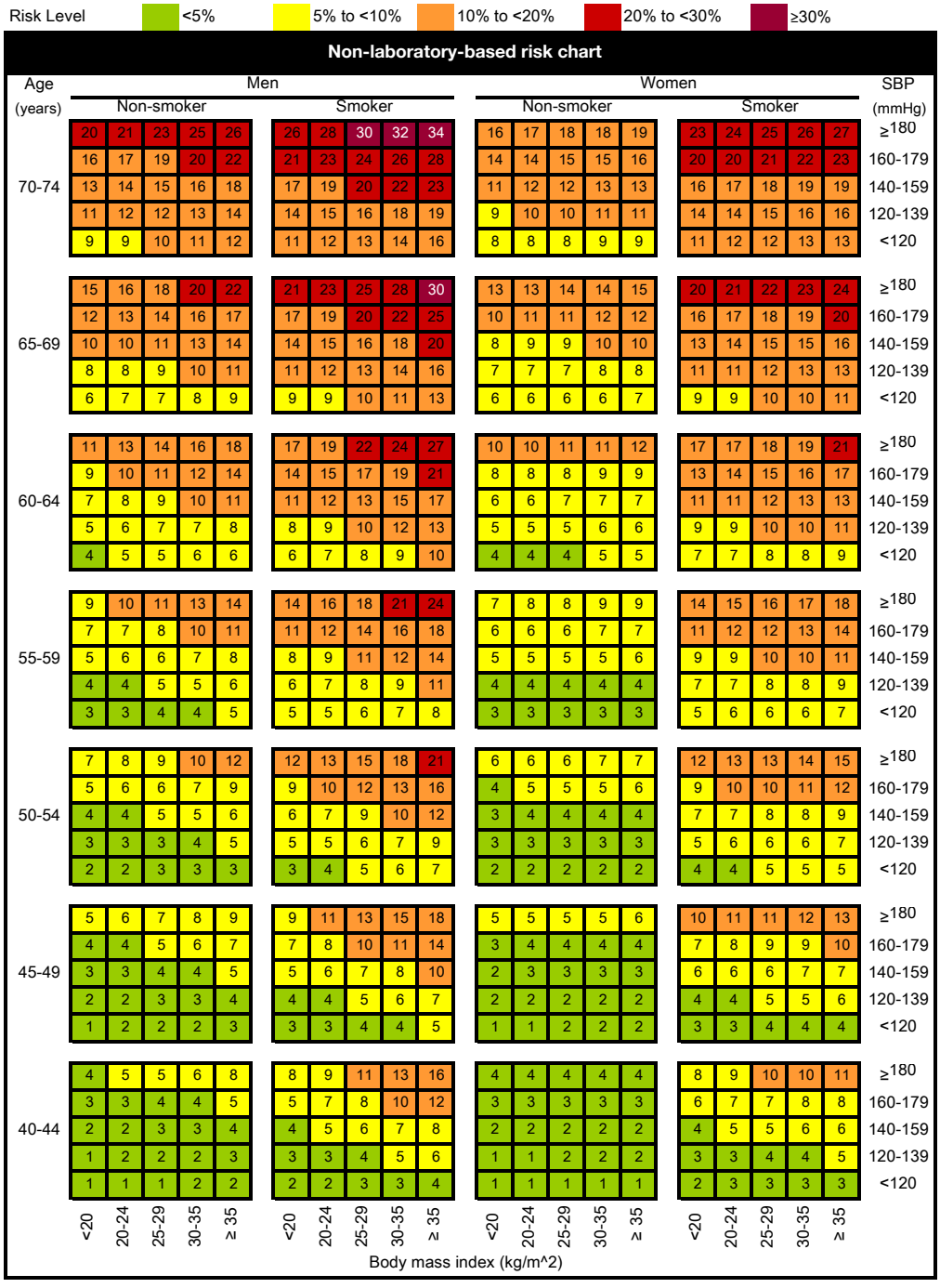


Caribbean

WHO cardiovascular disease risk non-laboratory-based charts

Central Latin America

Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Venezuela (Bolivarian Republic of)

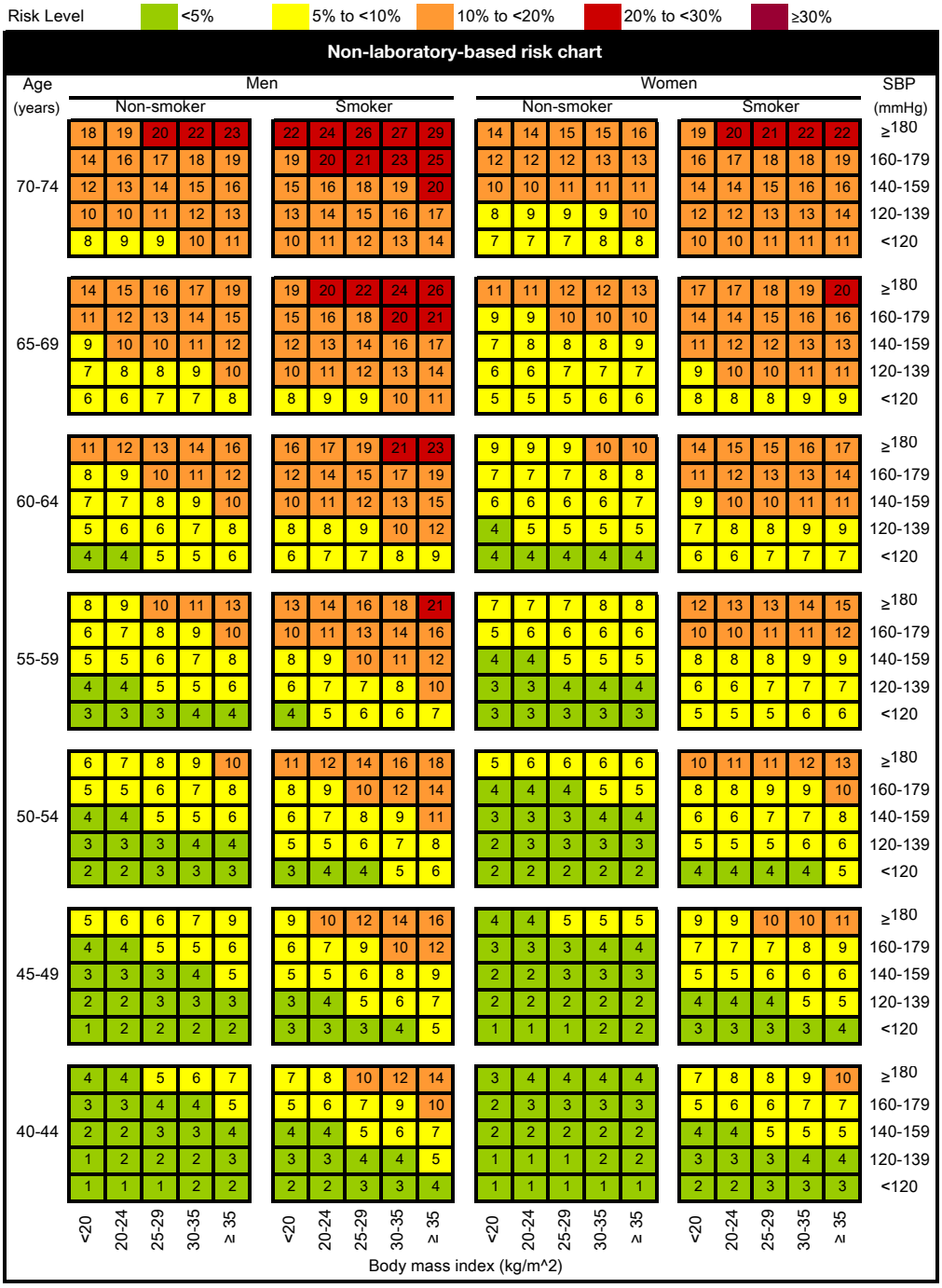


Central Latin America

WHO cardiovascular disease risk non-laboratory-based charts

Andean Latin America

Bolivia, Ecuador, Peru

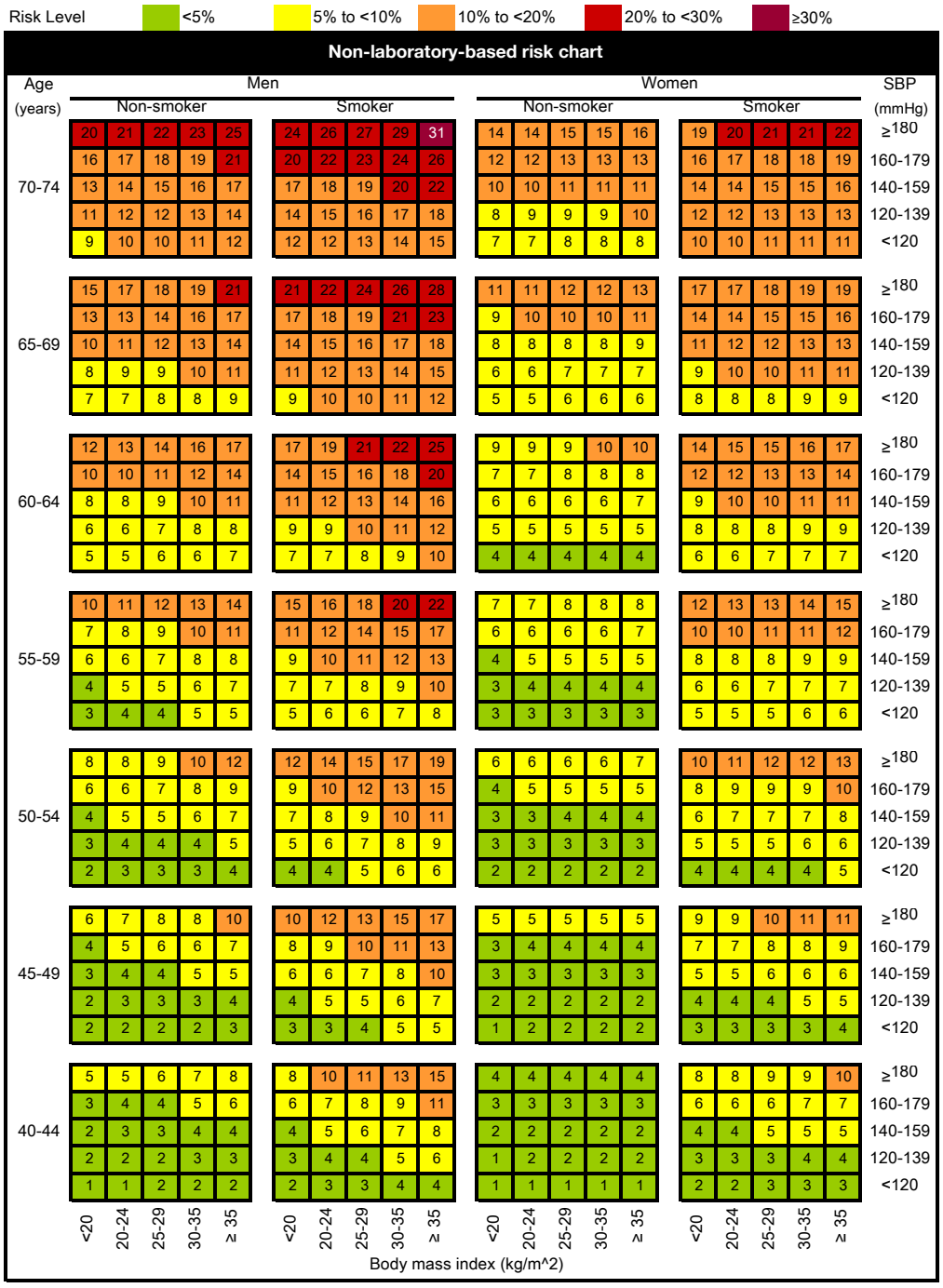


Andean Latin America

WHO cardiovascular disease risk non-laboratory-based charts

Tropical Latin America

Brazil, Paraguay

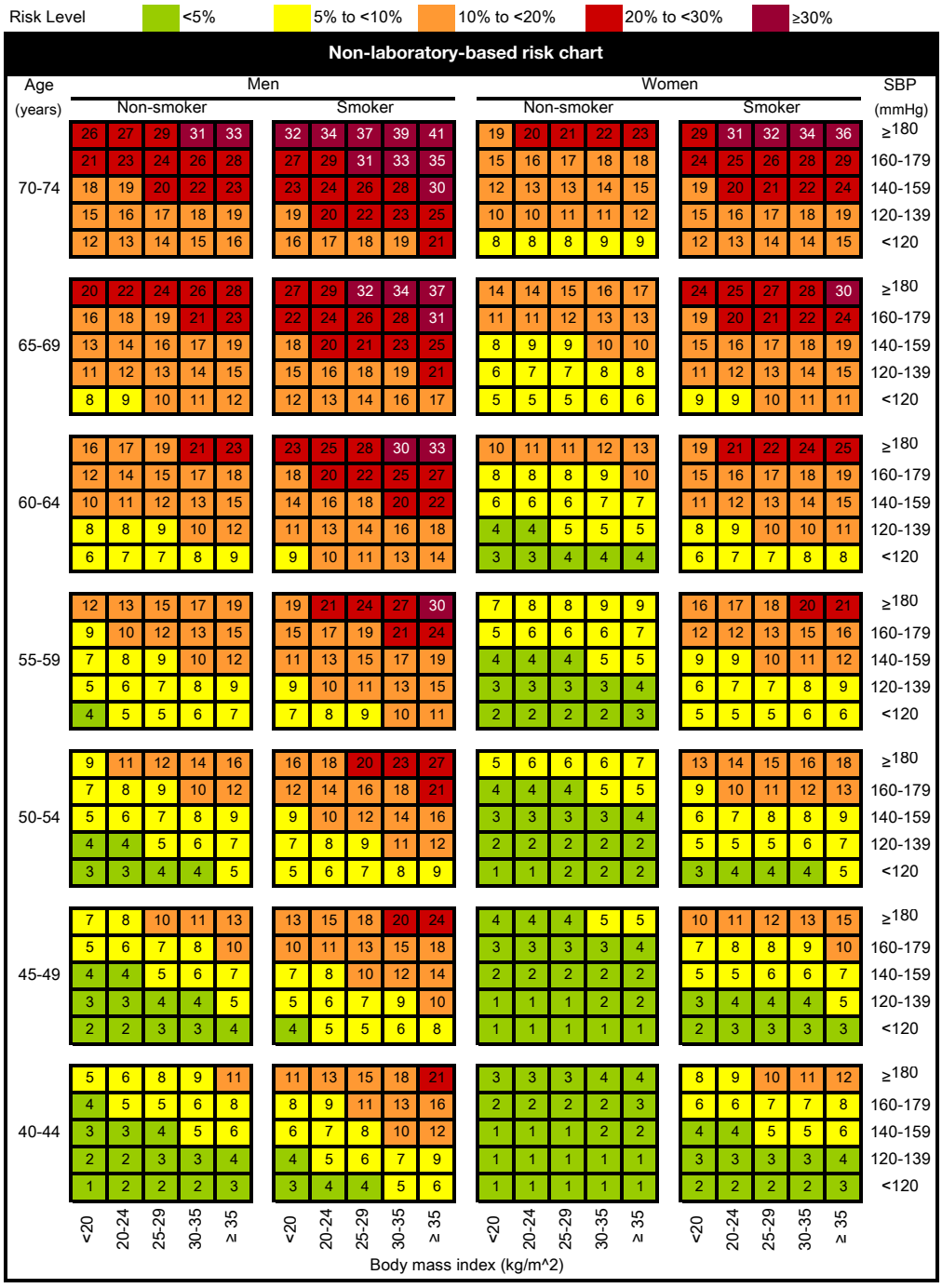


Tropical Latin America

WHO cardiovascular disease risk non-laboratory-based charts

Southern Latin America

Argentina, Chile, Uruguay

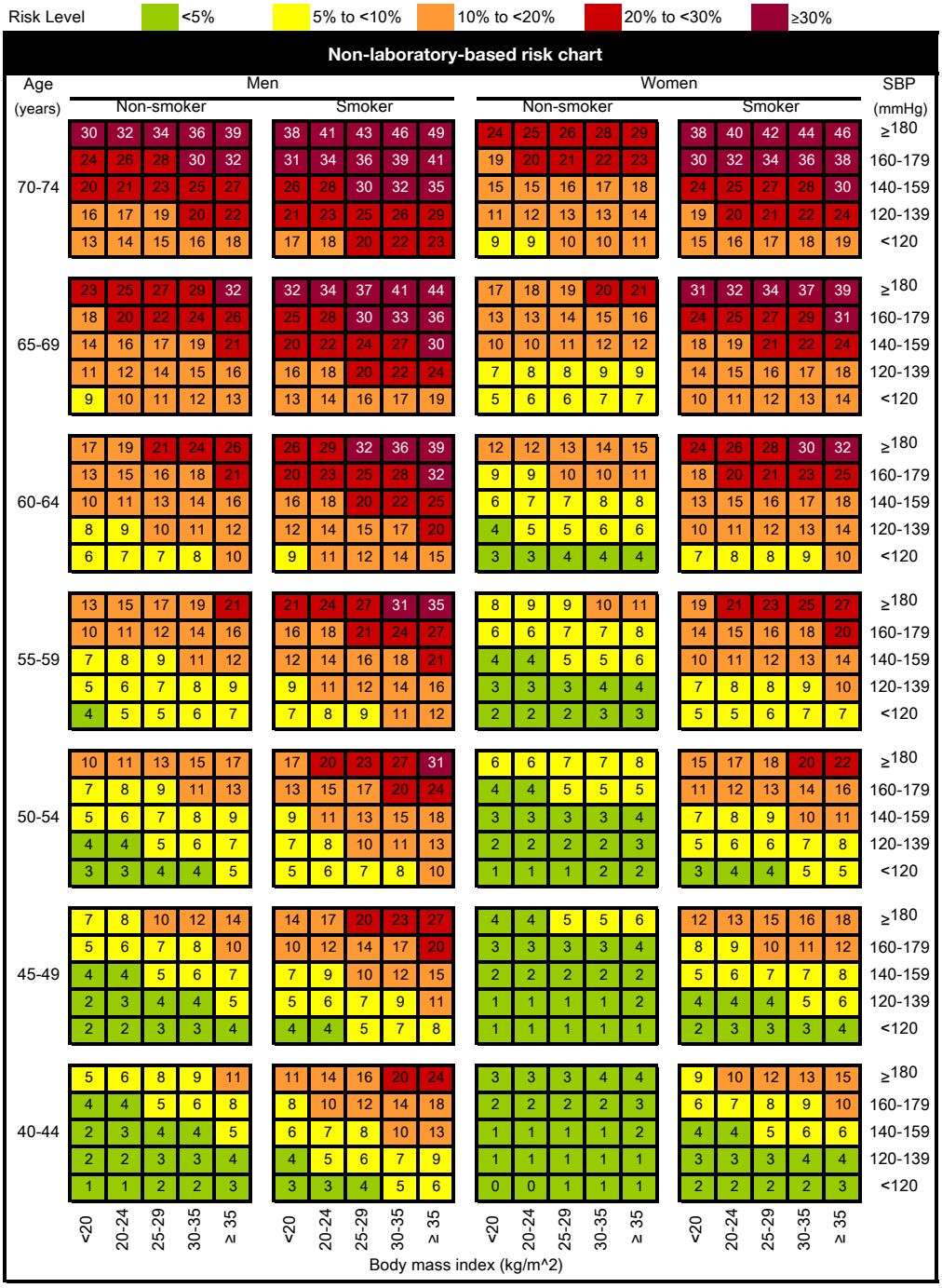


Southern Latin America

WHO cardiovascular disease risk non-laboratory-based charts

Western Europe

Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom

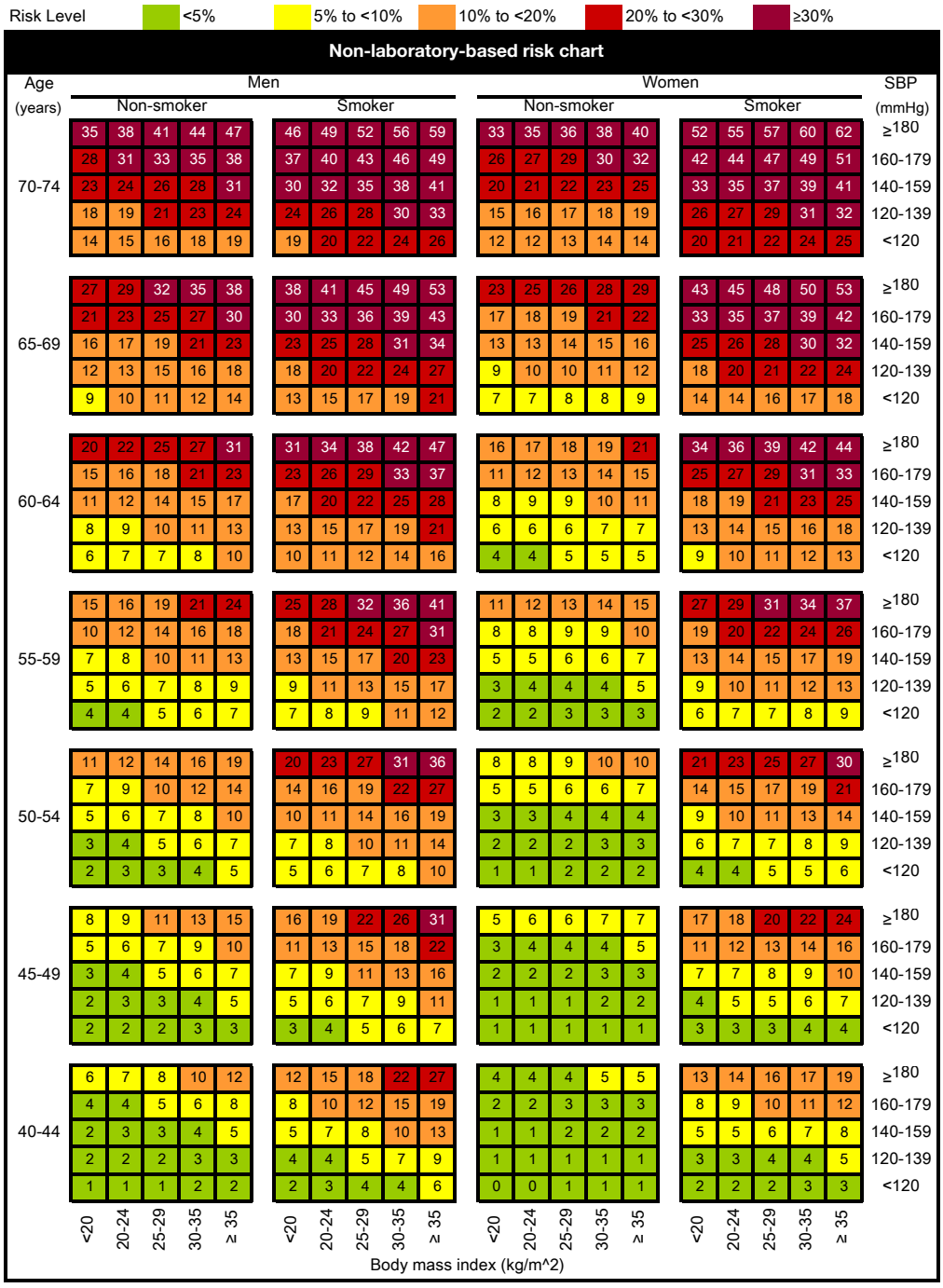


Western Europe

WHO cardiovascular disease risk non-laboratory-based charts

Central Europe

Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Montenegro, North Macedonia, Poland, Romania, Serbia, Slovakia, Slovenia

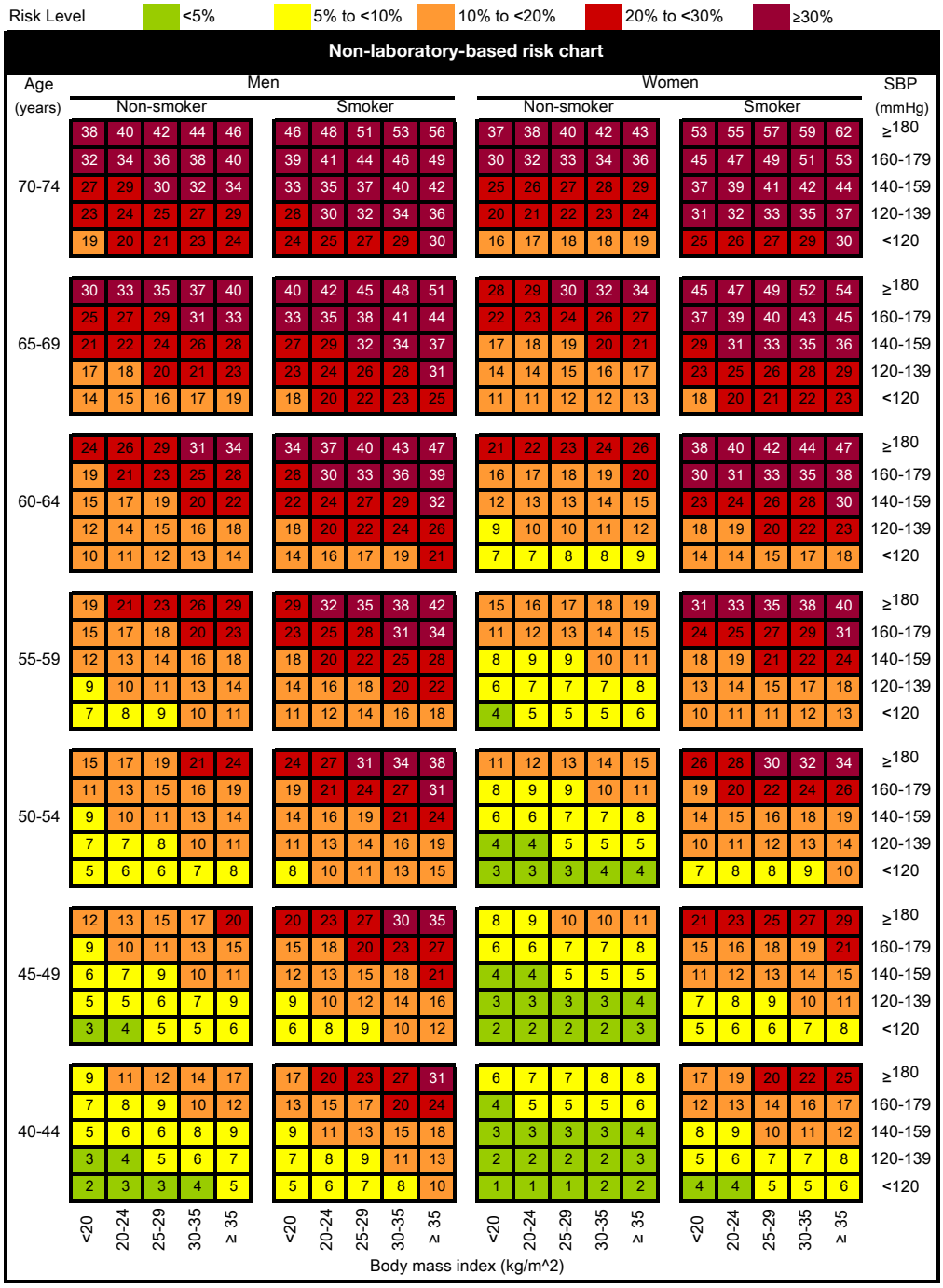


Central Europe

WHO cardiovascular disease risk non-laboratory-based charts

Eastern Europe

Belarus, Estonia, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine

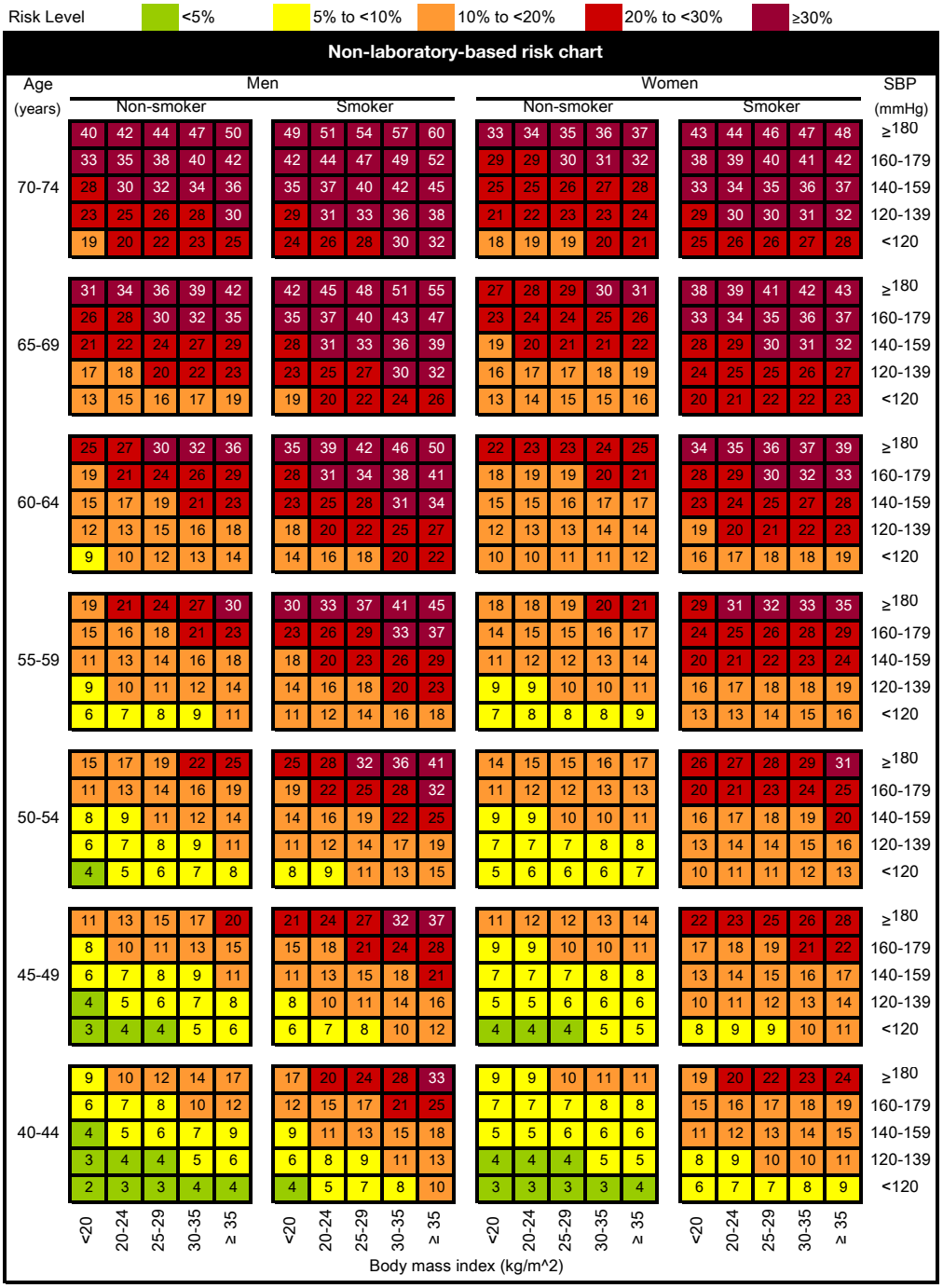


Eastern Europe

WHO cardiovascular disease risk non-laboratory-based charts

North Africa and Middle East

Afghanistan, Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, occupied Palestinian territory, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen

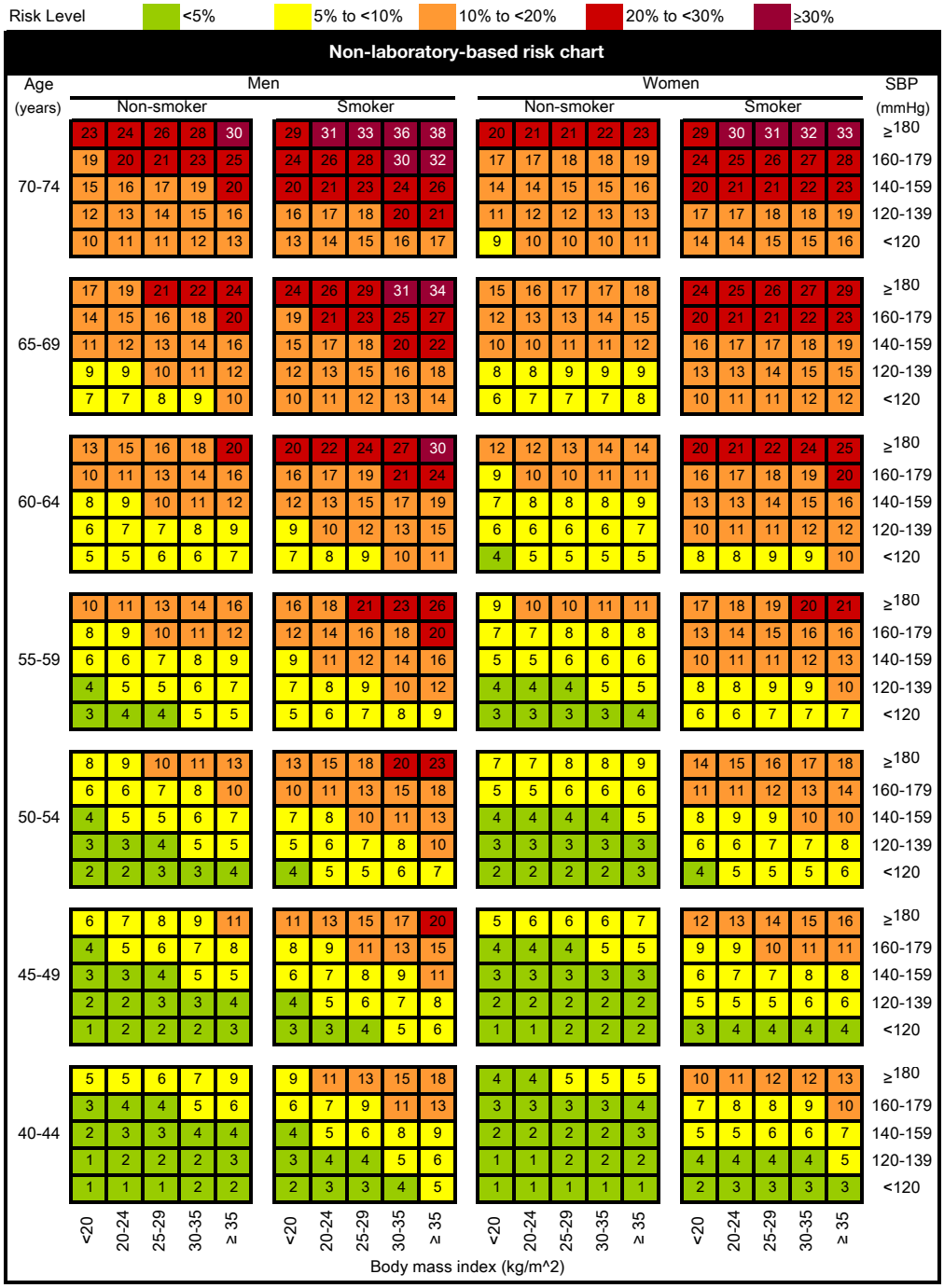


North Africa and Middle East

WHO cardiovascular disease risk non-laboratory-based charts

Western Sub-Saharan Africa

Benin, Burkina Faso, Cabo Verde, Cameroon, Chad, Cote d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo

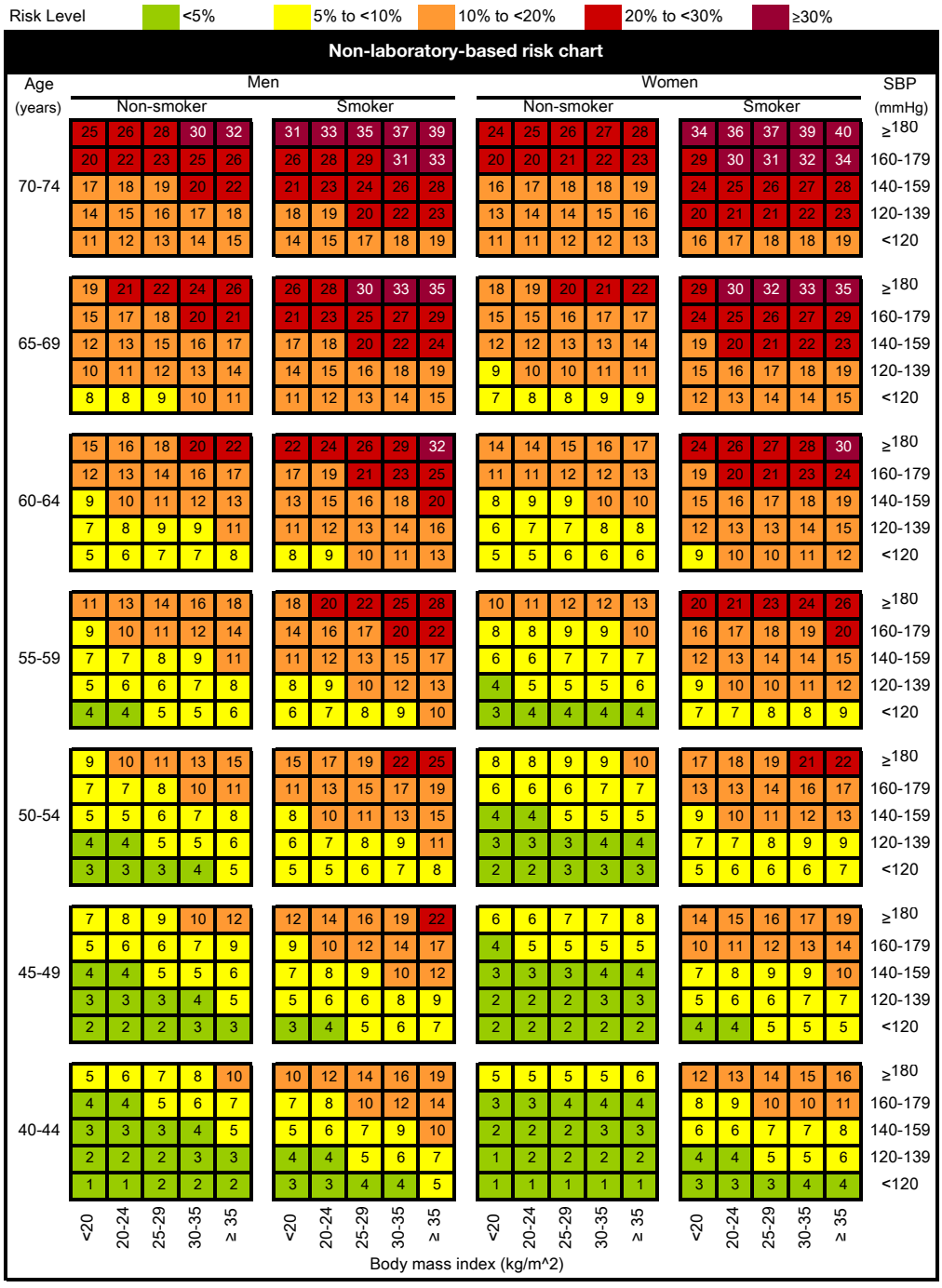


Western Sub-Saharan Africa

WHO cardiovascular disease risk non-laboratory-based charts

Central Sub-Saharan Africa

Angola, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon

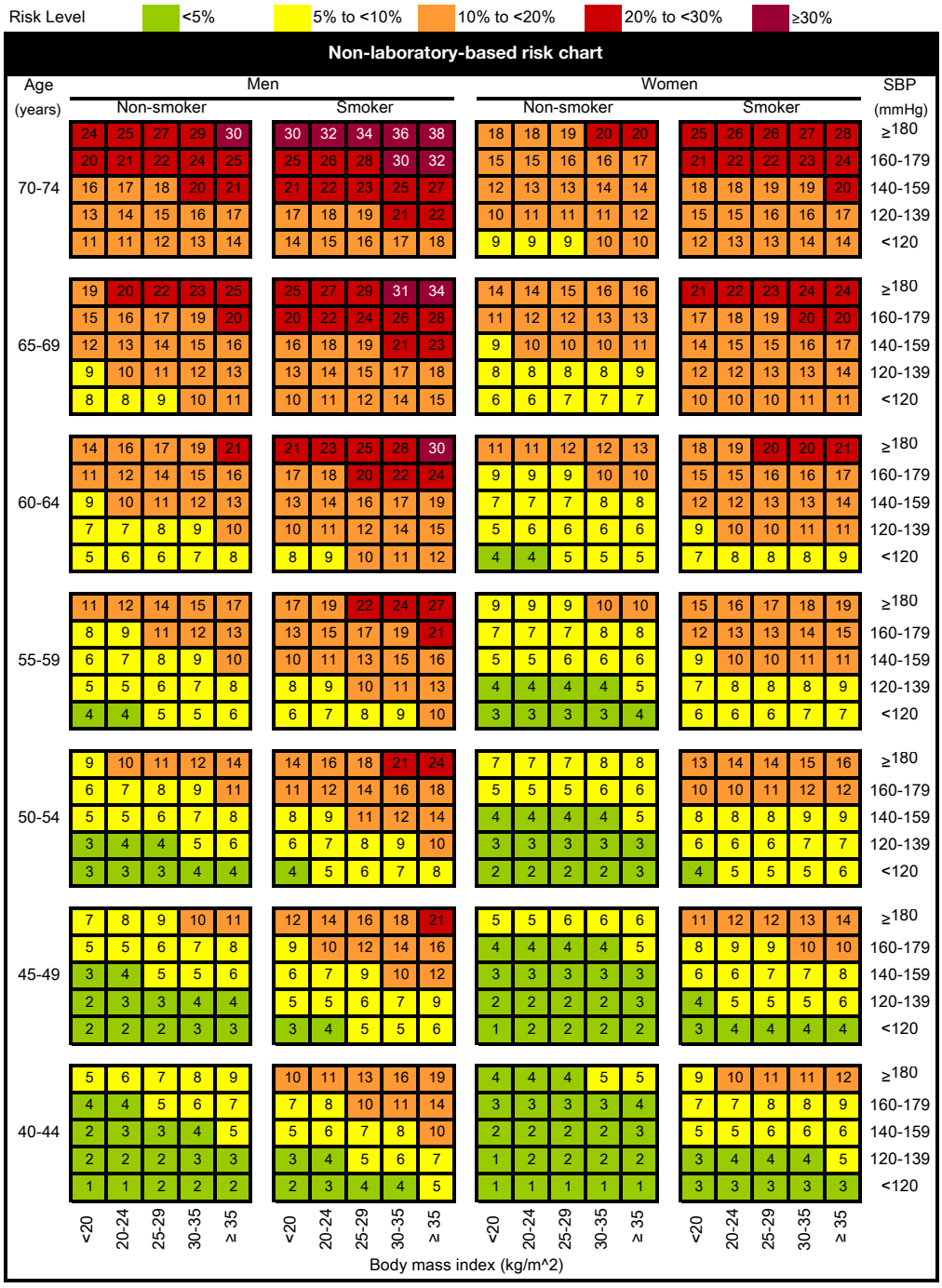


Central Sub-Saharan Africa

WHO cardiovascular disease risk non-laboratory-based charts

Eastern Sub-Saharan Africa

Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, Uganda, United Republic of Tanzania, Zambia

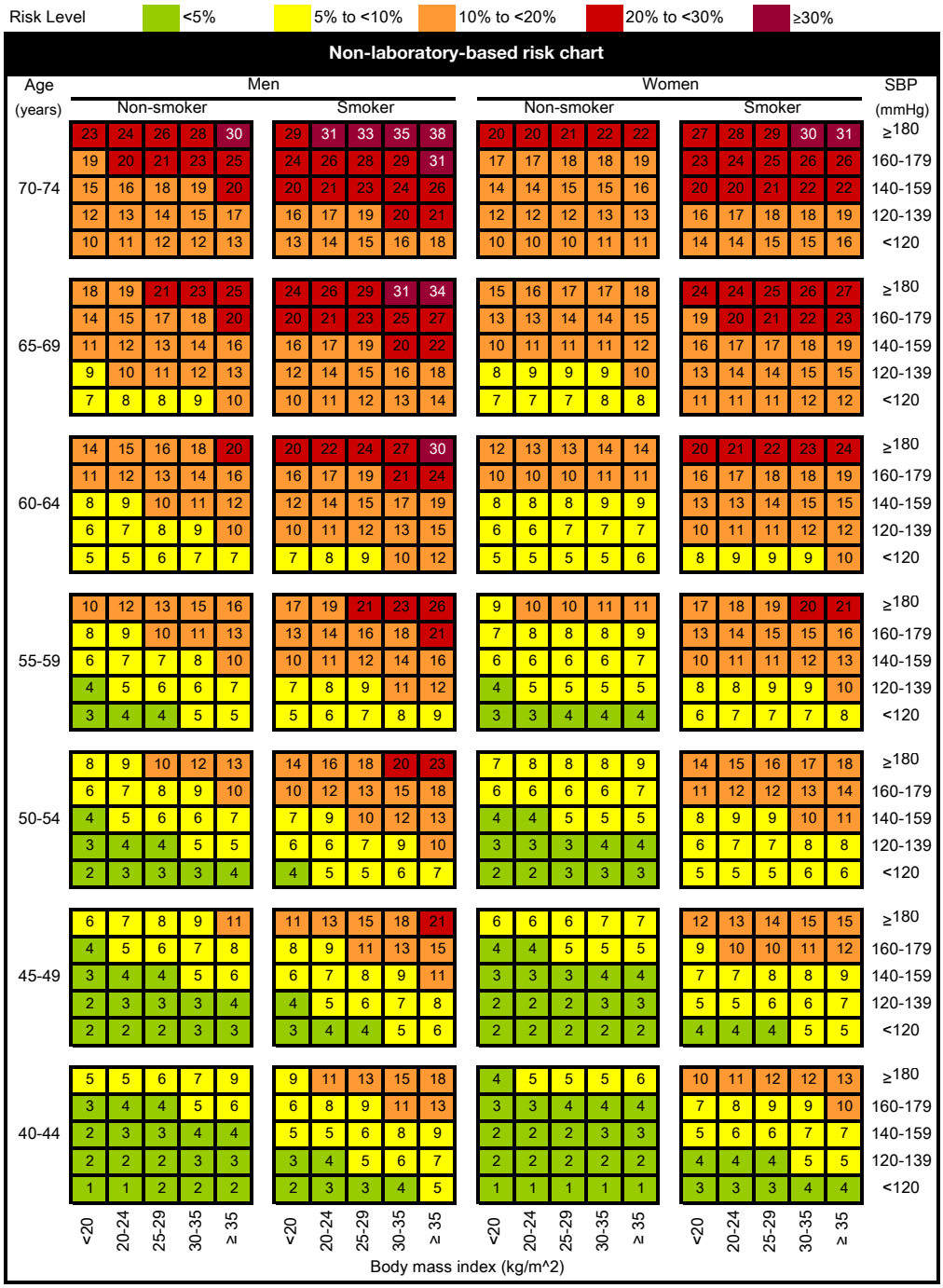


Eastern Sub-Saharan Africa

WHO cardiovascular disease risk non-laboratory-based charts

Southern Sub-Saharan Africa

Botswana, Eswatini, Lesotho, Namibia, South Africa, Zimbabwe

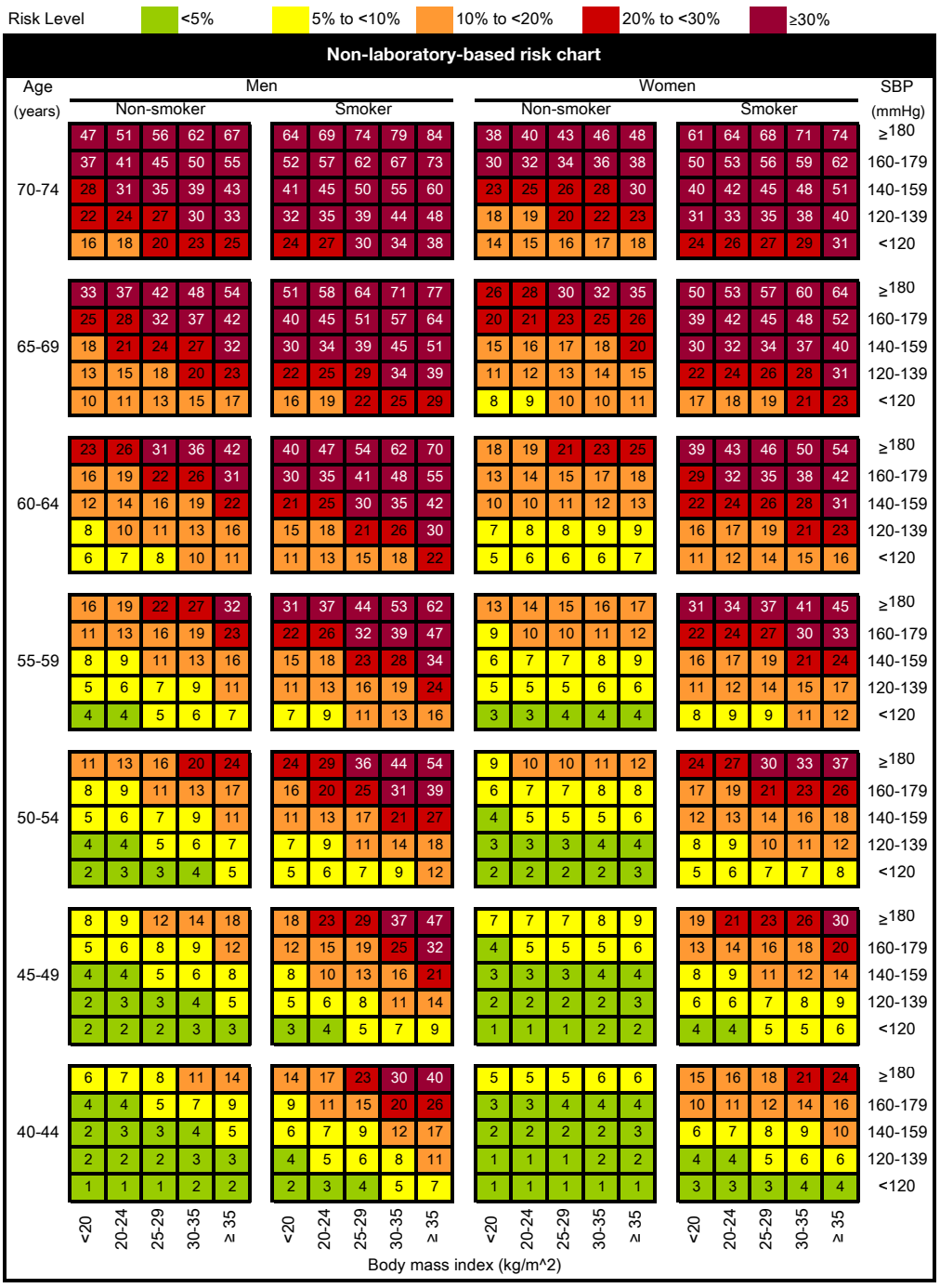


Southern Sub-Saharan Africa

WHO cardiovascular disease risk non-laboratory-based charts

Central Asia

Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan

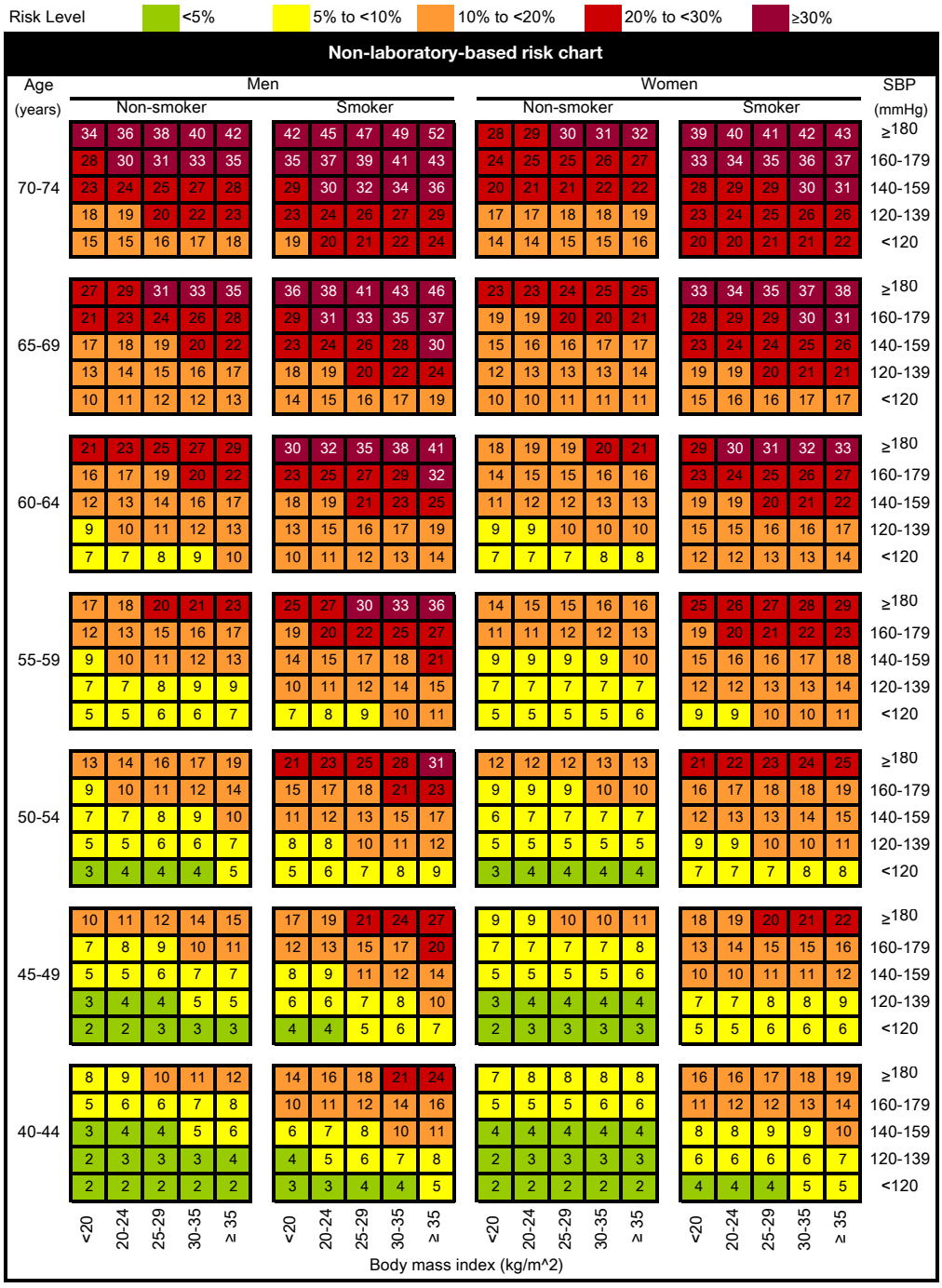


Central Asia

WHO cardiovascular disease risk non-laboratory-based charts

East Asia

China, Democratic People's Republic of Korea

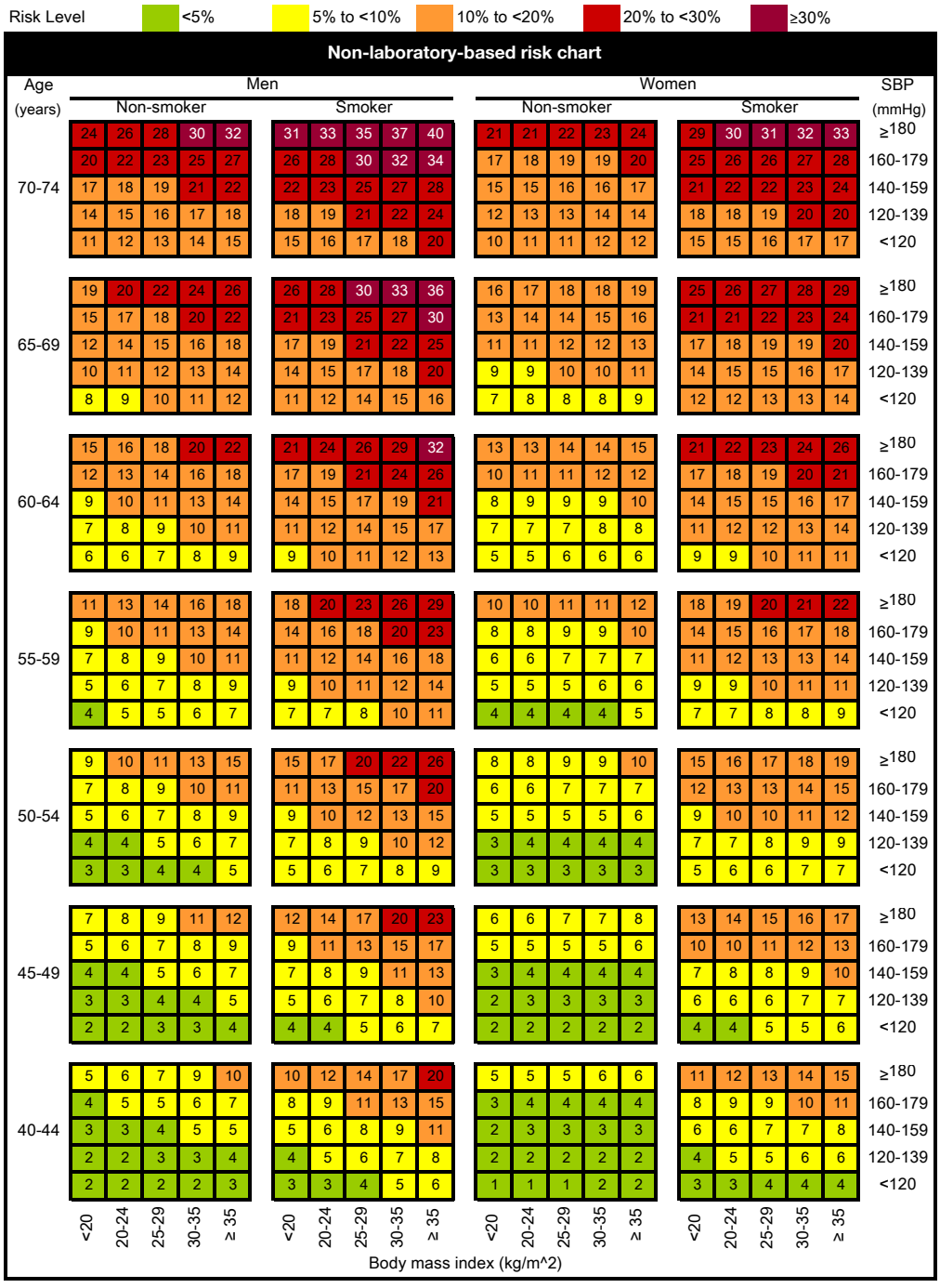


East Asia

WHO cardiovascular disease risk non-laboratory-based charts

South Asia

Bangladesh, Bhutan, India, Nepal, Pakistan

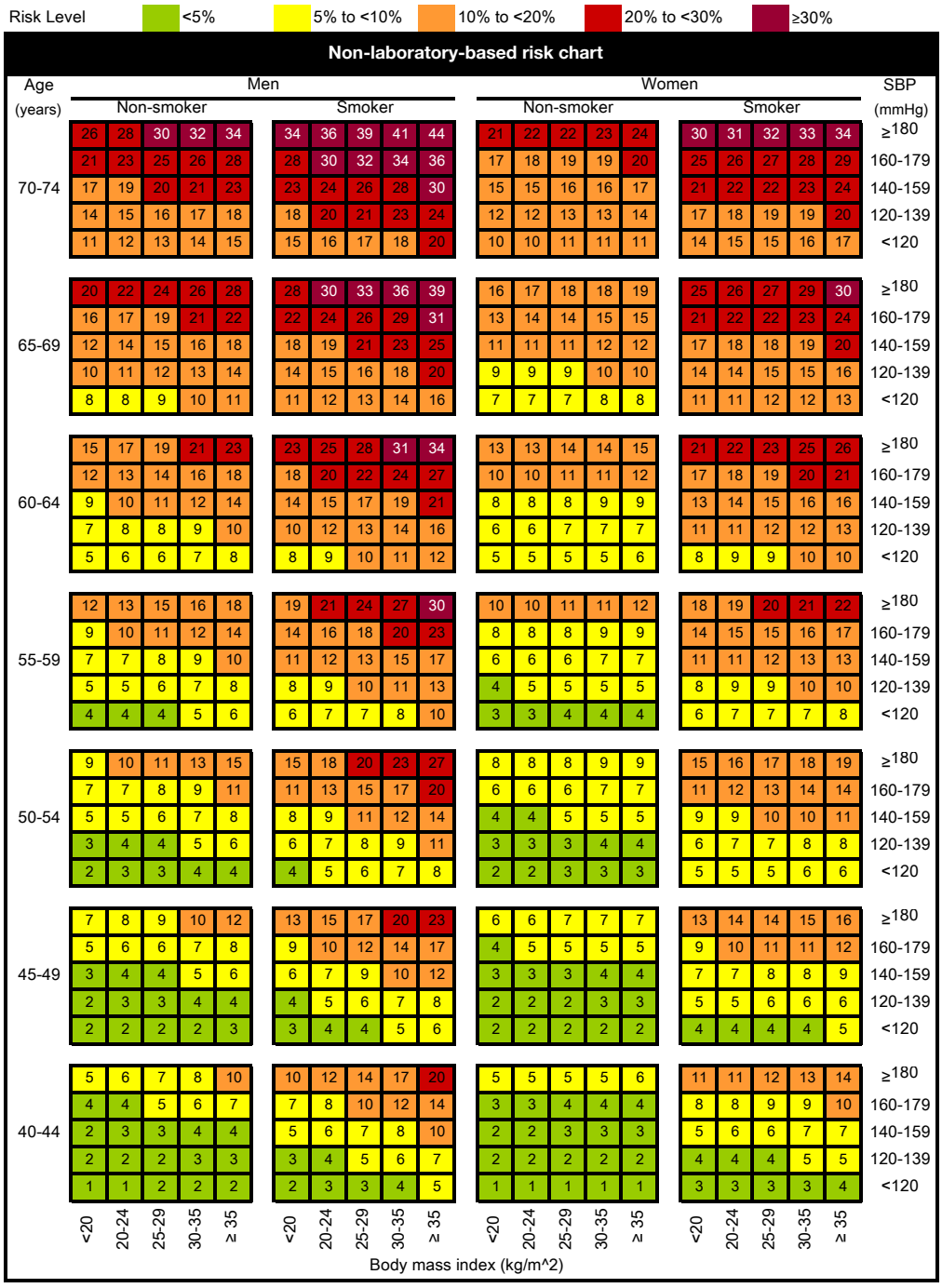


South Asia

WHO cardiovascular disease risk non-laboratory-based charts

South-East Asia

Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Maldives, Mauritius, Myanmar, Philippines, Seychelles, Sri Lanka, Thailand, Timor-Leste, Viet Nam

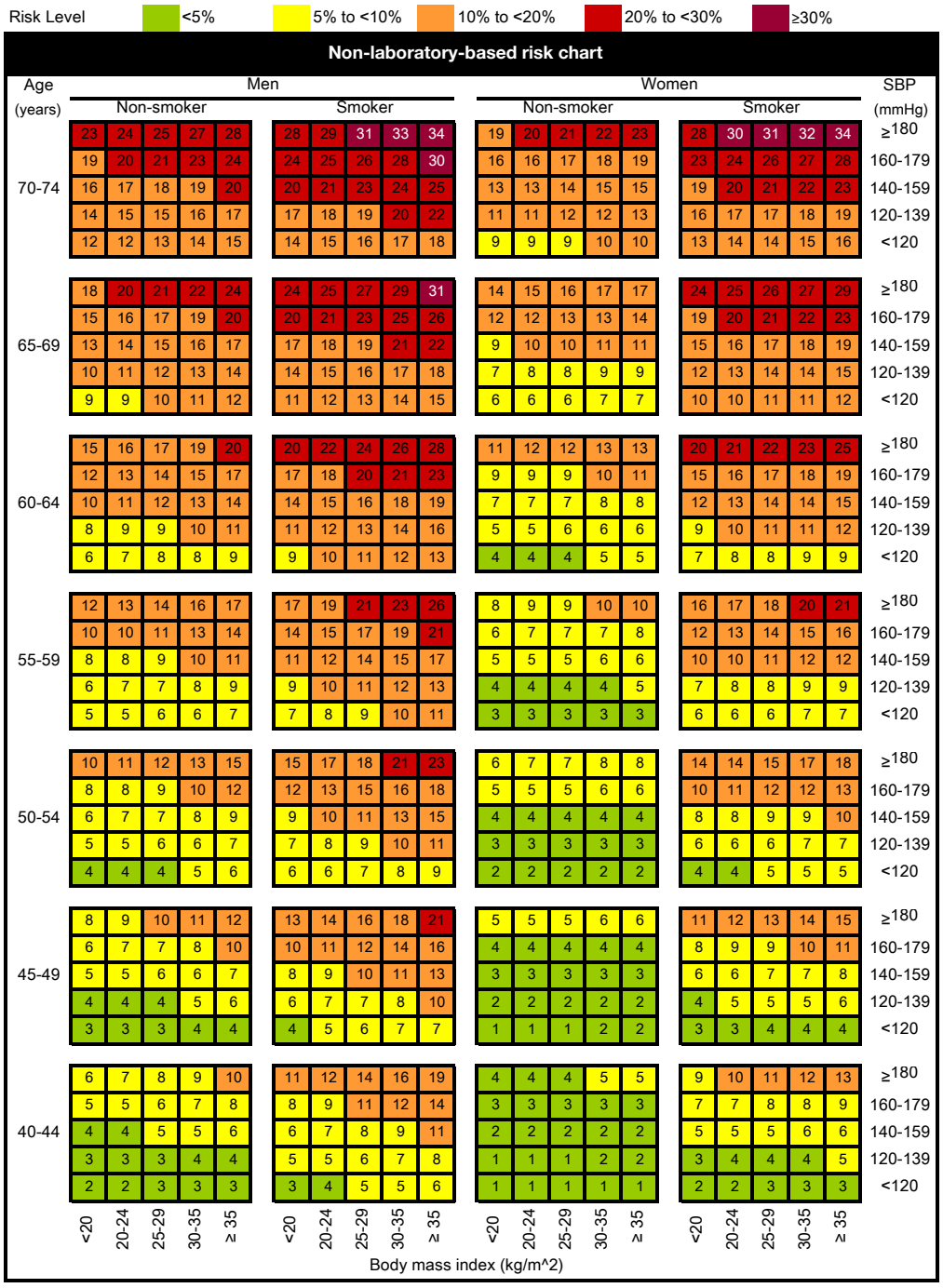


South-East Asia

WHO cardiovascular disease risk non-laboratory-based charts

High-income Asia Pacific

Brunei Darussalam, Japan, Republic of Korea, Singapore

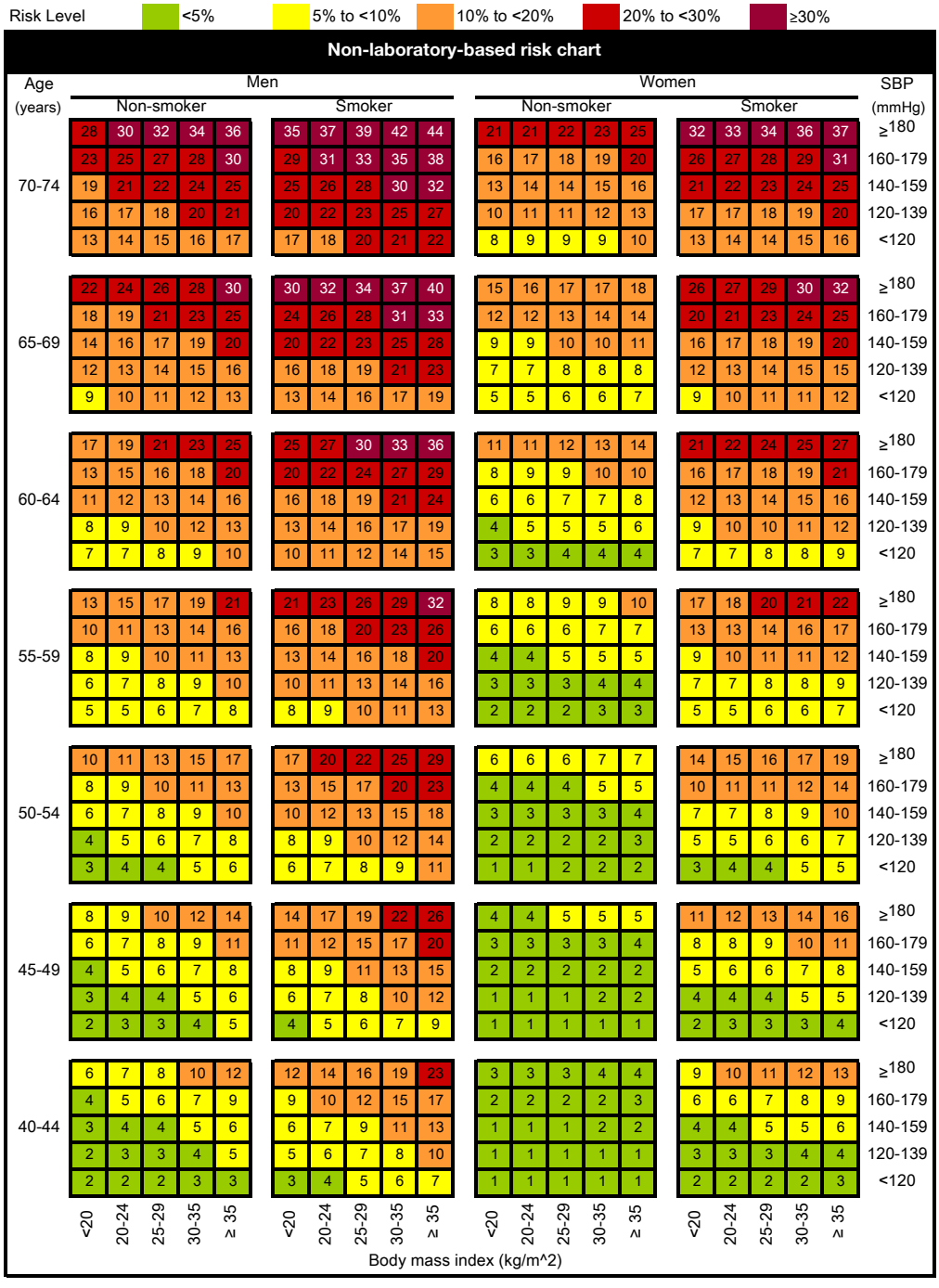


High-income Asia Pacific

WHO cardiovascular disease risk non-laboratory-based charts

Australasia

Australia, New Zealand

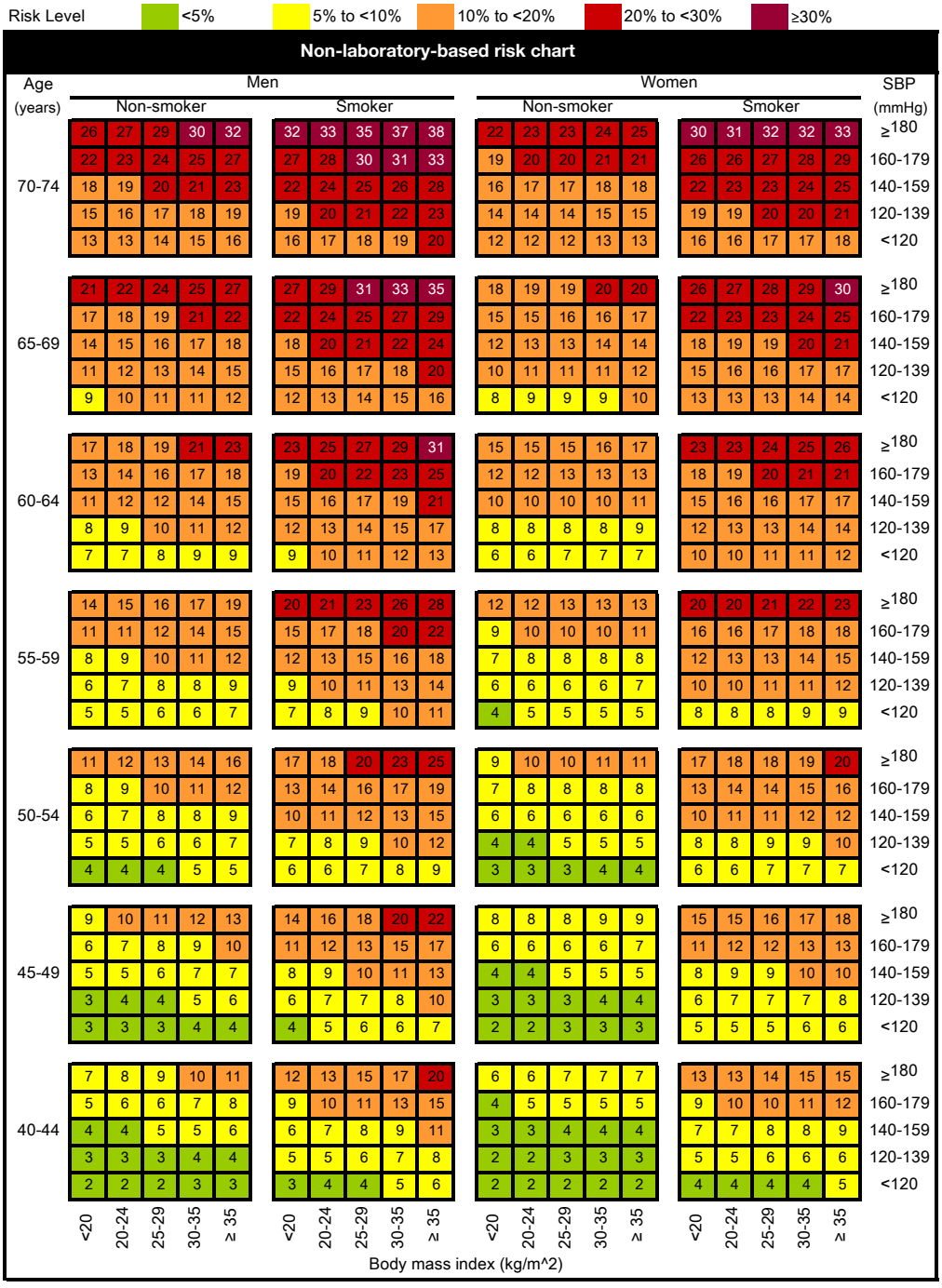


Australasia

WHO cardiovascular disease risk non-laboratory-based charts

Oceania

Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu



Oceania

Annex 4: Endpoint definitions used for incidence rates

Myocardial infarction

Case definition

Acute myocardial infarction (MI) – definite and possible MI according to the third universal definition of myocardial infarction:

- When there is clinical evidence of myocardial necrosis in a clinical setting consistent with myocardial ischaemia OR
- Detection of a rise and/or fall of cardiac biomarker values and with at least one of the following: i) symptoms of ischaemia, ii) new or presumed new ST-segment-T wave changes or new left bundle branch block, iii) development of pathological Q waves in the ECG, iv) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, or v) identification of an intracoronary thrombus by angiography or autopsy.
- Sudden (abrupt) unexplained cardiac death, involving cardiac arrest or no evidence of a noncoronary cause of death
- Prevalent MI is considered to last from the onset of the event to 28 days after the event and is divided into an acute phase (0–2 days) and subacute (3–28 days).

Stroke

Case definition

Stroke was defined according to WHO criteria – rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin *(20)*. Data on transient ischaemic attack (TIA) were not included.

- *Acute stroke:* stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event.
- *Ischaemic stroke:* an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.
- *Intracerebral haemorrhage:* a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.

Definitions are taken from GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, Supplement 1 *(20)*.

Annex 5a: Guide for comparison of CVD risk tools

Checklist: Cardiovascular disease risk prediction models in clinical practice		
From model derivation to implementation		**Considerations**
Derivation	Population	• Does the dataset used for model derivation contain information of a sufficient number of individuals (i.e. is the sample size large enough)? • Are the characteristics of individuals in the derivation sample sufficiently aligned with those of the target screening population to allow transferability of estimated risk ratios (e.g. age range, prior disease status)?
	Risk factors	• Are the relevant risk factors included? Note: main CVD risk factors (e.g. smoking, blood pressure) are key for risk prediction. • Are they accurately measured in sufficient numbers in the derivation sample? For example, use of sphygmomanometer for hypertension is more accurate than self-reported. • Can the risk factors be accurately measured in the target population?
	End points	• Does the model predict the relevant endpoint (e.g. overall CVD, stroke, CHD)? • Is endpoint collection in the derivation sample systematic and well-validated?
	Follow up	• Is the follow-up time in the derivation sample sufficient to allow risk estimation over the timeframe of interest (usually 10 years)?
	Statistical Model	• Are appropriate statistical models used for the type of risk estimation? • Are relevant assumptions tested (e.g. proportional hazards assumption)?
	Internal validation	• Discrimination – is the model able to predict order of CVD event among individuals? • Calibration – is there good agreement between predicted and observed incidence (absolute risk)? • Has the model been checked for overfitting (relevant for smaller sample sizes and can be checked by cross-validation)? • Reclassification – is there appropriate movement of individuals through relevant risk categories when comparing alternative risk models?

Checklist: Cardiovascular disease risk prediction models in clinical practice		
From model derivation to implementation		**Considerations**
Recalibration	Recalibrated	• Has the model been recalibrated for use in different populations?
	Recalibration data	• Are the data used for recalibration appropriate? For example, do the recalibration data share the same characteristics as the target population?
	Recalibration methods	• Is there a methodological framework proposed / provided for future recalibration in response to changing trends with time as well as divergent CVD rates across regions / populations? For example, is a guide or statistical code provided for recalibration?
		• What is the ease of recalibration? • Are additional data needed for recalibration and is this available?
External validation		• Is the model proven transferable to a new relevant setting / population other than used in the model derivation?
Usability	Format	• Is the format appropriate to be used in the population to which the model is applied (e.g. online risk calculator, colour-coded charts)?
	Risk-factor measurement	• Can all risk factors be feasibly measured and are alternative formats available for resource constraint settings (e.g. models using risk factors that don't require laboratory measurements)?
	Country settings	• Is the model available for different country settings?
Implementation	Guidelines	• Has the model been recommended for use by relevant guidelines?
	Health gains*	• Has the model been evaluated for health gains when used to assess total CVD risk and guide interventions (such as using statins) in high-risk populations? • Has use of the risk-prediction model resulted in significant health gains when used?
	Cost-effectiveness*	• Has use of the risk-prediction model been shown to be cost-effective?

* Cost-effectiveness and health gains of (different) CVD risk models in clinical practice are highly dependent on, for example, the target population and the clinical interventions for different thresholds (e.g. statin allocation).

Table based on Cooney et al. *(21)*, Rosello et al. *(22)*, 2016 European Guidelines on CVD *(23)* and the TRIPOD guidelines *(24)*. If of interest, the TRIPOD guidelines can be used for a more detailed checklist for statistical risk-prediction modelling *(24)*.

Annex 5b: Comparison of CVD risk charts

	WHO CVD risk 2019		WHO/ISH 2007	Globorisk 2015	IHMRS 2011	SCORE 2016
Derivation	Population	*Study design:* Prospective cohorts (85) with 376 177 individuals, 19 333 events *Age range:* 40–80 yrs Date of baseline survey: 1960–2013 *Location:* Europe, North America, Japan, Australia	*Study design:* No single derivation cohort. Risk-factor distribution, relative risks, CVD incidence from various sources combined. Date of baseline survey: Not applicable *Location:* Incidence, risk factors from 14 WHO regions	*Study design:* Prospective cohorts (8) with 50 129 individuals, 6042 events *Age range:* 40–84 yrs Date of baseline survey: 1948–1993 *Location:* North America	*Study design:* Case control study, 5349 cases 7423 controls *Median age:* 58 (49–67) yrs Date of baseline survey: 1999–2003 *Location:* 52 countries	*Study design:* Prospective cohorts *(12)* with 205 178 individuals, 7934 fatal events *Age range:* 40–65 yrs Date of baseline survey: 1967–1991 Location: Europe
	Risk factors (lab)	Age, sex, smoking, SBP, TC, DM	Age, sex, smoking, SBP, TC, DM	Age, sex, smoking, SBP, TC, DM	Age, sex, smoking, DM, HTN, Apolipoprotein B/A1 or TC/HDL-C ratios	Age, sex, smoking, SBP, TC or TC/HDL-C
	Risk factors (non-lab)	Age, sex, SBP, smoking, BMI	Sex, age, SBP, smoking, DM	Age, sex, smoking status, SBP, BMI	Age, sex, smoking, DM, HTN, family, diet, history, lifestyle, psychosocial factors	Not available
	Time horizon and outcomes	10-yr risk of fatal and nonfatal CVD (CHD or stroke)	10-yr risk of fatal and nonfatal CVD (CHD or stroke)	10-yr risk of fatal and nonfatal CVD (CHD or stroke)	Risk of fatal and nonfatal MI	10-yr risk of fatal CVD (CHD or stroke)
	Follow up	>10-yr follow-up in most cohorts	No actual follow-up, hypothetical 10-yr	>10-yr follow-up in 7 of 8 cohorts	No follow up, case-control design	>10-yr follow-up in all cohorts
	Statistical model	Cox survival models	Combination of several relative and absolute risks in 'Cox model type' structure	Cox survival model	Unconditional logistic regression	Weibull survival models
	Internal validation	Well-validated internally	Not applicable	Well-validated internally	Well-validated internally	Well-validated internally

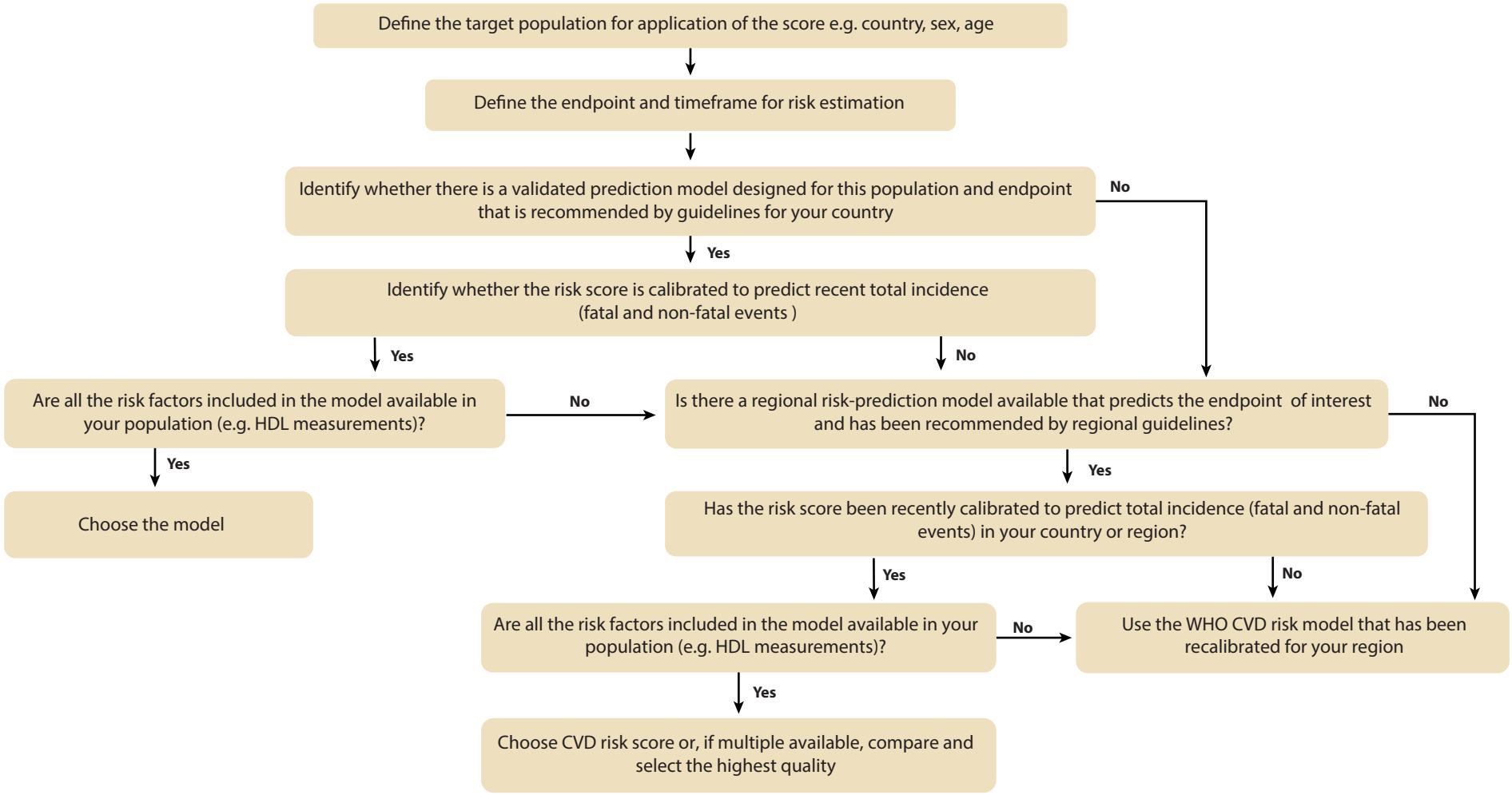
	WHO CVD risk 2019		WHO/ISH 2007	Globorisk 2015	IHMRS 2011	SCORE 2016
Recalibration	Recalibrated	Integral part of model development; calibrated to 21 global regions	Integral part of construction; calibrated for 14 global regions	Integral part model development; calibrated for 187 countries	Not recalibrated for different settings	High/low risk charts provided; recalibrated post hoc in several countries
	Recalibration data	Region-specific incidences from GBD and country-specific risk factors from NCD-RisC	Risk-factor distributions from WHO Comparative Risk Assessment study; Region-specific incidence from GBD	Used country-specific mortality rates and case-fatality to estimate incidence rates based on age trends in Swedish data; rates then modelled over past years and projected into future 10 years	Not applicable	Country-specific cohorts
	Recalibration methods	Simple framework and statistical code provided. Can be applied using routinely available data	No specific method provided	Intuitive framework provided. Can be applied with routinely available data. Requires modelling if future projections of rates desired as used in original score	Not applicable since model do not predict absolute risk	No standardized approach recommended
External validation	External validation	Well validated in several external cohorts	No adequate external validation	Well-validated in several external cohorts	Well-validated in several external cohorts	Well-validated in several external cohorts
Implementation	Format	Colour-coded charts and software code	Colour-coded charts	Colour-coded charts, online calculator	Calculation charts	Colour-coded charts and online calculator
	Low resource setting	Yes	Yes	Yes	Yes	No
	Website	WHO CVD risk	WHO/ISH	Globorisk		SCORE
	Country-specific versions available?	Different charts for 21 worldwide regions.	Different charts for 14 worldwide regions	Different charts available per country.	-	Low-risk charts and high-risk charts, for grouped European countries
	Guidelines	WHO on CVD prevention 2019	WHO guidelines for CVD prevention 2007	-	-	ESC Guidelines 2019

	WHO CVD risk 2019		WHO/ISH 2007	Globorisk 2015	IHMRS 2011	SCORE 2016
Advantages	Key advantages	Risk-prediction charts provided for different ethnic-geographic regions Simplicity of recalibration approach with code provided to allow efficient updating A non-laboratory variant is available Externally validated in numerous studies Risk distribution assessed in datasets representing 79 countries	Risk-prediction charts provided for different ethnic-geographic regions A non-laboratory variant is available	Risk-prediction charts provided for different ethnic-geographic regions Intuitive systematic recalibration approach A non-laboratory variant is available Externally validated in numerous studies	Included large number of women, youth and people from LMICs in derivation A non-laboratory variant is available Externally validated in numerous studies	Existence of low-risk and high-risk charts for European countries Externally validated in numerous studies
Limitations	Key limitations	Data used in model derivation were mostly from HICs	Absence of individual-level population data; models based on summary inputs No internal or external validation of the model in epidemiological cohorts	Rates used in recalibration rely on many modelling steps, assumptions and projections Only USA-based data in model derivation	Case-control rather than cohort design used; may induce bias in RR estimates, prevents estimation of absolute risk Not available for different settings	Only estimates risk of fatal CVD No non-laboratory variant available Model derived only in European cohorts

ESC: European Society of Cardiology; IHRMS; INTERHEART Modifiable Risk Score, WHO/ISH; World Health Organization / International Society of Hypertension; MI: myocardial infarction; TC: total cholesterol; SBP: systolic blood pressure; HTN: hypertension; DM: diabetes mellitus; BMI: body mass index; GBD study: Global Burden of Disease Study; CVD: cardiovascular disease; CAD: coronary artery disease; NCR-RisC: NCD Risk Factor Collaboration LMIC: Low and middle income countries

Based on: WHO, 2007 *(2)*, Cooney et al, 2009 *(21)*, Rossello et al, 2019 *(22)*, 2016 European Guidelines on CVD *(23)*, the TRIPOD guidelines *(24)*, Mendis et al, 2007 *(25)*, Hajifathalian et al, 2015 *(26)*, McGorrian et al, 2011 *(27)*, European Society of Cardiology, SCORE risk charts *(28)*.

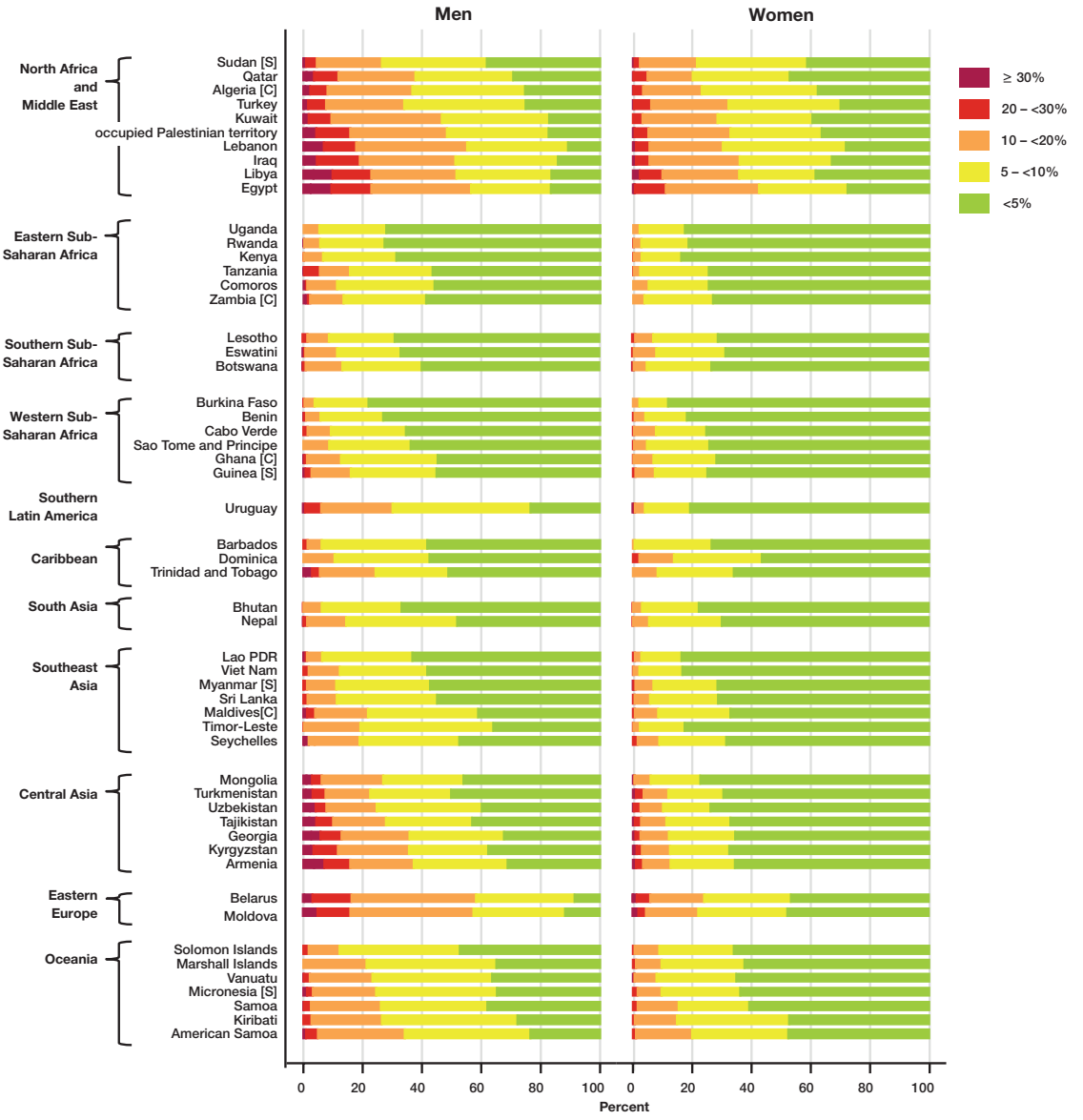
Annex 6: Identifying a CVD risk prediction model



Annex 7: Considerations for initiation of therapy

The appropriate threshold of an individual's total risk at which intensive lifestyle interventions and drug treatment are initiated depends on the availability of resources as well as the risk level. The percentage of patients from representative countries in each region who would be eligible for treatment based on each cut-off level is presented in Figure 5 *(3)*. As an example, <5% of the population of Uganda is at 10% or greater CVD risk, whereas approximately 50% of Egypt's population is above 10% CVD risk.

Figure 5: Distribution of 10-year CVD 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).

References

1. World health statistics 2009. Geneva: World Health Organization; 2009 (https://www.who.int/gho/publications/world_health_statistics/EN_WHS09_Full.pdf).
2. Prevention of cardiovascular diseases. Geneva: World Health Organization; 2007 (https://www.who.int/cardiovascular_diseases/publications/Prevention_of_Cardiovascular_Disease/en/).
3. The 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(10):E1332–45. https://doi.org/10.1016/S2214-109X(19)30318-3.
4. Lewington S, Clarke R. Combined effects of systolic blood pressure and total cholesterol on cardiovascular disease risk. Circulation. 2005;112(22):3373–74.
5. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. BMJ. 2003;326(7404):1419. Erratum in: BMJ. 2003;327(7415):586. BMJ. 2006;60(9):823.
6. Chow CK, Gupta R. Blood pressure control: a challenge to global health systems. Lancet. 2019;394(10199):613–15. doi.org/10.1016/S0140-6736(19)31293-0.
7. Lawes CM et al., Asia Pacific Cohort Studies Collaboration. Blood pressure and cardiovascular disease in the Asia Pacific region. J Hypertension. 2003;21(4):707–16.
8. MacMahon S, Rodgers A. The effects of blood pressure reduction in older patients: an overview of five randomized controlled trials in elderly hypertensives. Clin Exp Hypertens. 1993;15(6):967–78.
9. Integrated management of cardiovascular risk: report of a WHO meeting. Geneva, World Health Organization; 2002.
10. Gaziano TA. Cardiovascular disease in the developing world and its cost-effective management. Circulation. 2005;112(23):3547–3553.
11. “Best buys” and other recommended interventions for the prevention and control of non-communicable diseases. Geneva: World Health Organization; 2007 (https://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-eng.pdf?sequence=1).
12. Prevention of cardiovascular disease: guidelines for assessment and management of cardiovascular risk. Geneva: World Health Organization; 2007 (https://apps.who.int/iris/bitstream/handle/10665/43685/9789241547178_eng.pdf?sequence=1).
13. Package of essential noncommunicable (PEN) disease interventions for primary health care in low-resource settings. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/bitstream/handle/10665/133525/9789241506557_eng.pdf?sequence=1).

14. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Reference Life Table. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018 (http://ghdx.healthdata.org/gbd-2017).

15. NCD Risk Factor Collaboration (NCD-RisC) (http://ncdrisc.org/).

16. WHO PEN Protocol 1. Prevention of heart attacks, strokes and kidney disease through integrated management of diabetes and hypertension (https://www.who.int/ncds/management/Protocol1_HeartAttack_strokes_kidneyDisease.pdf?ua=1).

17. HEARTS technical package for cardiovascular disease management in primary health care: healthy-lifestyle counselling. Geneva: World Health Organization: 2018 (WHO/NMH/NVI/18.1). Licence: CC BY-NC-SA 3.0 IGO (https://apps.who.int/iris/bitstream/handle/10665/260422/WHO-NMH-NVI-18.1-eng.pdf?sequence=1).

18. HEARTS technical package for cardiovascular disease management in primary health care: evidence-based treatment protocols. Geneva: World Health Organization; 2018 (WHO/NMH/NVI/18.2). Licence: CC BY-NC-SA 3.0 IGO (https://apps.who.int/iris/bitstream/handle/10665/260421/WHO-NMH-NVI-18.2-eng.pdf?sequence=1).

19. HEARTS technical package for cardiovascular disease management in primary health care: diagnosis and management of diabetes. Geneva: World Health Organization: 2020 (WHO/UCN/NCD/20.1). Licence: CC BY-NC-SA 3.0 IGO (https://www.who.int/publications-detail/who-ucn-ncd-20.1).

20. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1789–858.

21. 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(14):1209–27. doi: 10.1016/j.jacc.2009.07.020.

22. Rossello X et al. Risk prediction tools in cardiovascular disease prevention: A report from the ESC Prevention of CVD Programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP). Eur Heart J Acute Cardiovasc Care. 2019;26(14):1534–44. doi:10.1177/2048872619858285.

23. Piepoli MF et al. Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). European guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2016;37(29):2315–81 (https://doi.org/10.1093/eurheartj/ehw106).

24. Collins GS, Reitsma JB, Altman DG, Moons K. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement. BMJ. 2015;350:g7594. doi: 10.1136/bmj.g7594.

25. Mendis S et al. World Health Organization (WHO) and International Society of Hypertension (ISH) risk prediction charts: assessment of cardiovascular risk

for prevention and control of cardiovascular disease in low and middle-income countries. J. Hypertens. 2007;25(8):1578–82.

26. Hajifathalian K et al. A novel risk score to predict cardiovascular disease risk in national populations (Globorisk): a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol. 2015;3(5):339–55. doi: 10.1016/S2213-8587(15)00081-9.
27. McGorrian C et al. Estimating modifiable coronary heart disease risk in multiple regions of the world: the INTERHEART modifiable risk score. Eur Heart J. 2011;32(5):581–89. doi: 10.1093/eurheartj/ehq448.
28. European Society of Cardiology. SCORE risk charts. The European cardiovascular disease risk assessment model (https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/SCORE-Risk-Charts).