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GLOBAL EFFECT OF CARDIOVASCULAR RISK FACTORS ON LIFETIME ESTIMATES

Deleted: The Global Cardiovascular Risk Consortium

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ABSTRACT

Background: Five risk factors account for approximately 50% of the global cardiovascular disease burden. We investigated the lifetime risk for cardiovascular disease and death and estimated the lifetime difference related to absence and variation of classical risk factors.

Methods: We harmonized individual-level data from 2,078,948 participants across 133 cohorts, 39 countries, and 6 continents. Lifetime risk and mean lifetime difference for cardiovascular disease and death from any cause associated with the absence of arterial hypertension, hyperlipidemia, underweight or overweight or obesity, diabetes, and smoking at age 50 were estimated up to age 90 by cause-specific Weibull models. Risk factor trajectories were analyzed to predict lifetime difference by risk factor variation.

Results: The lifetime risk for cardiovascular disease was 24% (95% confidence interval [CI], 21 to 30) in women and 38% (95% CI, 30 to 45) in men for whom all risk factors were present. Compared to those with none of the risk factors, the estimated lifetime difference for cardiovascular disease was 13.3 years (95% CI, 11.2 to 15.7) for women and 10.6 years (95% CI, 9.2 to 12.9) for men; for death the estimated lifetime difference was 14.5 years (95% CI, 9.1 to 15.3) for women and 11.8 years (95% CI, 10.1 to 13.6) for men. Compared to those with no changes in the presence of a risk factor, those who modified hypertension and smoking between 55 and 60 years of age was associated with the highest estimated additional life-years for cardiovascular disease and death, respectively.

Conclusion: The absence of five classical risk factors at age 50 was associated with over a decade greater life expectancy than those who had all five risk factors, in both sexes. Those who modified hypertension and smoking in midlife also had longer life expectancy than those who did not.

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INTRODUCTION

Cardiovascular diseases remain the leading cause of mortality worldwide, imposing substantial social, economic, and public health burden. Five modifiable risk factors account for approximately 50% of the global burden of cardiovascular disease, indicating that about half of all cases of cardiovascular disease could potentially be reduced through effective risk factor management.[1] Current estimates of lifetime risk for cardiovascular disease increase with accumulated risk factor load[2,3] and range from 5% to 50%, depending on the specific cardiovascular disease end point, follow-up duration, population risk factor profiles, and cardiovascular disease risk in different populations.[3-6,7] These estimates, however, fail to account for dynamic changes in individual risk profiles over time, which could affect long-term outcomes. Furthermore, the association between individual risk factors and differences in lifetime risk remains unclear.

Robust global, individual-level data on lifetime estimates are needed to guide preventive action worldwide. These analyses from the *Global Cardiovascular Risk Consortium* (GCVRC) aim to estimate the sex-specific lifetime risk for cardiovascular disease and death; provide the estimated mean lifetime difference between those with and without classical cardiovacular disease risk factors, and between those who did and did not modify certain risk factors; evaluate the lifetime difference related to risk factor modification during a predefined age decade; identify the most useful regional targets for effective primary prevention strategies.

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METHODS

Study Design and Oversight

The study was designed by the *Global Cardiovascular Risk Consortium* Management Group whose members are outlined in the **Supplementary Appendix** (available online at NEJM.org with the full text of this article). Data are available at the Hamburg Data Center. After approval of the statistical analysis plan by the *Global Cardiovascular Risk Consortium* Statistical Working Group (as shown in the Supplementary Appendix), analyses were performed by FO and again reviewed within the *Global Cardiovascular Risk Consortium* Statistical Working Group. The first version of the manuscript was drafted by CM, SB and FO and reviewed and edited by all authors. All authors jointly agreed to submit the manuscript for publication and vouch for the accuracy and completeness of the data. The study had no formal sponsor.

Study population

We pooled and harmonized individual-level data from 2,078,948 individuals, aged 18 or older, across 8 geographic regions (North America, Latin America, Western Europe, Eastern Europe and Russia, North Africa and the Middle East, sub-Saharan Africa, Asia and Australia) participating in the *GCVRC*. The process of data harmonization[1] is summarized in the **Supplementary Appendix**. Grouping of regions, selection of cohorts and data handling were described previously.[1] For the present analyses, 99,485 individuals with cardiovascular disease defined as a history of myocardial infarction, unstable angina, coronary revascularization, or ischemic or hemorrhagic stroke at baseline were excluded from analyses where incident cardiovascular disease was the outcome. Individuals with missing information on baseline cardiovascular disease (N=92,131, 4.3%) were retained and treated as having no cardiovascular disease at baseline. After further exclusion of individuals with missing follow-up information, 1,227,987 individuals remained available for analysis of incident cardiovascular disease and 2,042,815 for death. **Figure S1** displays the study flow in detail. A description of each cohort including Local Ethics Committee information is provided in the **Supplementary Appendix**.

Cardiovascular risk factors and outcome definition

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Information on systolic blood pressure, non-high-density lipoprotein cholesterol (non-HDL cholesterol), body-mass index, diabetes and current smoking was collected at baseline according to the protocols of the respective studies (available at nejm.org). Data were harmonized using the variable definitions of the MONICA cohorts.[8] For the main analyses, continuous risk factors were categorized using guideline-based targets: arterial hypertension was identified by a systolic blood pressure ≥130 mmHg; hyperlipidemia was determined by non-HDL cholesterol levels ≥130 mg/dL; and underweight or overweight or obesity was defined as a body-mass index <20 or ≥25 kg/m², respectively. Diabetes was defined by medical history, self-report, or newly diagnosed at baseline examination using measures of glycemia, depending on the standard operating procedures of the respective cohorts. Current smoking was defined as regularly (at least 1 cigarette daily) or occasionally (less than 1 cigarette per day) smoking cigarettes, cigars, cigarillos or pipes. Incident cardiovascular disease was defined as first fatal or non-fatal myocardial infarction, unstable angina, coronary revascularization, ischemic or hemorrhagic stroke, and cardiovascular or unclassifiable death. **Table S1** summarizes the variables of interest, **Table S2** presents the standardized definitions used for the coding system to classify cardiovascular disease events, **Table S3** provides the background information of the population studied, and **Table S4** details data availability. Information on cohorts with available repeated risk factor measurements is provided in **Table S5**.

Lifetime estimates

The estimated lifetime risk for cardiovascular disease and death is based on the estimated cumulative risk of developing the outcome of interest before age 90.[7] The mean estimated lifetime difference between those individuals with and without classical risk factors and between those who did and did not modify certain risk factors is based on cardiovascular disease-free life expectancy and overall life expectancy, respectively, and was estimated in terms of median survival time without a cardiovascular disease event or death (i.e. the age at which cumulative survival probability falls below 0.5).[7] In this analysis, the estimated lifetime difference represents the additional cardiovascular disease- or death-free life-years associated with the absence of risk factors at a given index age, e.g., 50 or 60 years, and is computed as the difference between the life expectancies of an individual without the risk factors and an individual with all five risk factors. Additionally, an analysis of single risk factors is provided.

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Lifetime difference according to risk factor modification is an estimate of the additional life-years associated with changes in risk factors (to levels below the above thresholds) and is computed similarly to estimated lifetime difference, using longitudinal risk factor information in a time interval (e.g., from 50 to 60 years) before estimating life expectancies beyond that interval. The estimated quantities represent differences between subpopulations having distinct risk factor profiles, and capture the degree to which variation in life expectancy is explained by these important factors in a large, global population. In the case of single risk factors, the effect is adjusted for the other four. They should be interpreted as observational, without implying causality. In other words, the models described below can be used to estimate differences between subpopulations of individuals who do and do not have one or more risk factors, or who do and do not modify a risk factor. Owing the possibility that those who have – or modify – one or more risk factors can differ in ways that are explained by unmeasured factors that also predict survival, the estimated effects may not fully capture the within-individual causal effect of modifying a risk factor.

Statistical analysis

Missing data were imputed using multiple imputation with chained equations or multilevel multiple imputation.[9,10] Age- and sex-standardized baseline characteristics were calculated according to geographic region with the use of direct standardization, using the age and sex distribution of the *GCVRC* data set as the standard. Sex-specific Weibull models, with age as time scale,[11] were estimated for each study and pooled across studies by region as well as globally using multivariate random effects meta-analysis[12,13] to allow for between-study heterogeneity. The Weibull models included the following covariates (risk factors): systolic blood pressure, non-HDL cholesterol, body-mass index, diabetes, and current smoking. Initially, systolic blood pressure, non-HDL cholesterol and body-mass index entered the models dichotomized using the thresholds described above. The distributional assumptions of the Weibull models were assessed graphically (**Figure S2**). Additional analyses were performed with various alternative cutoffs. On one such version, sex-specific regional standard deviation scores were derived for these three variables by subtracting region-specific means and dividing by region-specific standard deviations. One and two standard deviations were used as cutoff, effectively allowing for different cutoffs per region in the analyses. Based on these models, cumulative

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incidence rates were estimated. The regional standard deviation scores were used to account for heterogeneity in risk factor prevalence and distribution among cohorts from different geographic regions to improve comparability. Due to the age of some of the included datasets coupled with secular changes in cardiovascular disease and mortality, incidence rates estimated from these models were calibrated using WHO mortality and population data as previously described.[12,14] Calibrated incidence rates were used to estimate lifetime risk, life expectancies and lifetime differences.[7] More precisely, the calibrated incidences were used to obtain survival probabilities, which then were used to estimate life expectancies for selected combinations of risk factors. The difference of life expectancies for two risk factor profiles was used to calculate the lifetime difference. For a subset of the data, multiple examination rounds were available. This data was used to estimate life expectancies and lifetime difference according to risk factor variation, based on joint models for the longitudinal trajectories of the risk factors and time-to-event data.[7] Details of the statistical methods are provided in the **Supplementary Appendix**. Statistical analyses were performed in R statistical software, version 4.3.3.[15]

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RESULTS

Baseline characteristics

Among 2,078,948 individuals across 133 cohorts, 39 countries, and 6 continents, the median systolic blood pressure was 128.7 mmHg (interquartile range, 116.7 to 142.0), non-HDL cholesterol was 155.6 mg/dL (interquartile range, 127.7 to 186.8), and body-mass index was 25.7 kg/m^2 (interquartile range, 22.8 to 28.9). A total of 7.7% of individuals had diabetes and 22.3% were current smokers (**Table 1**). Baseline characteristics of the health examination surveys used for regional calibration are provided in **Tables S6a-b**.

Lifetime risk and difference by risk factor burden

The median follow-up of the cohort studies was 7.6 years (interquartile range, 5.9 to 15.1) for cardiovascular disease and 8.2 years (interquartile range, 6.7 to 15.5) for death. The maximum follow-up time for both outcomes was 47.3 years. At an index age of 50 years, among those who had none of the five classical risk factors, the estimated lifetime risk for cardiovascular disease before age 90 was 13% (95% confidence interval [CI], 12 to 16) for women and 21% (95% CI, 18 to 23) for men; for those who had all five risk factors, the estimated risk was 24% (95% CI, 21 to 30) for women and 38% (95% CI, 30 to 45) for men (**Figure 1A**). The estimated lifetime risk for death before age 90 was 53% (95% CI, 36 to 88) for women and 68% (95% CI, 57 to 77) for men with none of the risk factors and 88% (95% CI, 72 to 99) for women and 94% (95% CI, 87 to 97) for men having all five risk factors (**Figure 1B**). The estimated lifetime difference for cardiovascular disease between those individuals with and without classical risk factors was 13.3 years (95% CI, 11.2 to 15.7) for women and 10.6 years (95% CI, 9.2 to 12.9) for men (**Figure 1C** and **Figure 2A**); in the absence of all five risk factors, the estimated lifetime difference for death was 14.5 years (95% CI, 9.1 to 15.3) for women and 11.8 years (95% CI, 10.1 to 13.6) for men (**Figure 1D** and **Figure 2B**). The estimated lifetime risk and difference between those individuals with and without classical risk factors for both cardiovascular disease and death by geographic region at an index age of 50 years are presented in **Figures S3a-b** and **S4a-b**. Results on estimated lifetime risk and difference between those individuals with and without classical risk factors at an index age of 60 years are shown in **Figures S5a-b** and **S6a-b**.

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Lifetime difference between individuals with and without single risk factors

For cardiovascular disease, the absence of diabetes was associated with an estimated lifetime difference of 4.7 years (95% CI, 4.2 to 6.2) for women and 4.2 years (95% CI, 3.6 to 5.1) for men; the absence of smoking was 5.5 years (95% CI, 5.0 to 6.9) for women and 4.8 years (95% CI, 4.3 to 5.7) for men. (**Figure 2A, Table S7a**). Systolic blood pressure <130 mmHg was related to a lifetime difference of 1.3 years (95% CI, 1.1 to 2.1) for women and 1.8 years (95% CI, 1.4 to 2.4) for men, and increased up to 2.3 years (95% CI, 1.9 to 3.1) for women and 2.1 years (95% CI, 1.7 to 2.7) for men when comparing between regional standard deviation score of <2 vs. ≥2. Non-HDL cholesterol was associated with a lifetime difference of -0.4 years (95% CI, -0.8 to 0.1) for women and -1.1 years (95% CI, -1.5 to -0.5) for men if applying a strict limit of <130 mg/dL, but increased to 1.2 years (95% CI, 0.7 to 2.0) for women and 1.1 years (95% CI 0.7 to 1.6) for men if the regional standard deviation score was applied. Absence of underweight and overweight or obesity was associated with a lifetime difference of 0.6 years (95% CI, 0.4 to 1.1) for women and 0.1 years (95% CI, -0.2 to 0.5) for men and increased up to 2.6 years (95% CI, 2.2 to 3.3) for women and 1.9 years (95% CI, 1.7 to 2.3) for men when applying the regional standard deviation score. For death, absence of diabetes was associated with a lifetime difference of 6.4 years (95% CI, 4.4 to 7.9) for women and 5.8 years (95% CI, 4.9 to 6.8) for men and the absence of smoking with 5.6 years (95% CI, 3.9 to 7.0) for women and 5.1 years (95% CI, 4.3 to 5.9) for men, respectively (**Figure 2B, Table S7b**). The lifetime difference between individuals with and without elevated systolic blood pressure, non-HDL cholesterol and body-mass index increased, similarly to what was estimated for cardiovascular disease, when applying the regional standard deviation score. The lifetime differences between individuals with and without hypertension, hyperlipidemia, or underweight and overweight or obesity, employing a range of different cutoffs are shown in **Tables S8a-c**. Results did not substantially change in a 1-year landmark analysis excluding the first year of follow-up (**Tables S9a-b**). Information on the region-specific standard deviations is provided in **Table S10**.

The lifetime difference between individuals with and without hypertension for both outcomes and according to geographic region is displayed in **Figure 3**. Globally, the lifetime difference for cardiovascular disease for a standard deviation score of <2 was 2.3 years (95% CI, 1.9 to 3.1) for women

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and 2.1 years (95% CI, 1.7 to 2.7) for men; and for death 2.9 years (95% CI, 2.2 to 3.8) for women and 2.9 years (95% CI, 2.4 to 3.4) for men; corresponding to regional cutoffs ranging from 155.7 to 175.0 mmHg for women and from 156.9 to 173.2 mmHg for men. The lifetime difference between individuals with and without risk factors for both cardiovascular disease and death varied by geographic region; for cardiovascular disease up to 4.9 years (95% CI, 1.5 to 7.6) in Latin American women and for death up to 5.4 years (95% CI, 0.7 to 7.9) in North American women.

Lifetime difference by risk factor modification

When all risk factors were present between the ages of 50 and <55 years and the status of the individual risk factors was modified between the ages of 55 and <60 years, the difference in estimated life-years between those who did and did not make modifications are shown in **Table 2** and **Figures S7a-b**. Modification of hypertension was linked to the most additional life-years observed for cardiovascular disease, and modification of smoking or hypertension was linked to the most additional life-years for death. The number of additional life-years was higher for those who controlled a greater number of risk factors.

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DISCUSSION

Using harmonized individual-level data from 2,078,948 participants across 133 cohorts, 39 countries, and 6 continents, we analyzed the lifetime risk for cardiovascular disease and death and estimated the mean lifetime difference between those individuals with and without classical cardiovascular risk factors, and the effect of modifying certain risk factors. We report five key findings. First, even among those who had none of the classical risk factors, as defined here, the lifetime risk for cardiovascular disease remained substantial, estimated at 13% (95% CI, 12 to 16) in women and 21% (95% CI, 18 to 23) in men. Second, the absence of all five risk factors at 50 years of age was associated with a maximum lifetime difference of 13.3 years (95% CI, 11.2 to 15.7) in women and 10.6 years (95% CI, 9.2 to 12.9) in men compared to individuals who did have risk factors. Third, the extent of lifetime difference between those individuals with and without classical cardiovascular risk factors varied depending on which specific risk factor was absent. Fourth, regional heterogeneity was seen in the magnitude of lifetime difference as illustrated for hypertension, the leading global contributor to cardiovascular disease. Finally, using risk trajectory analyses, we found that among all the risk factors assessed, modifying the presence of hypertension was related to the most additional life-years for cardiovascular disease.

An individual's lifetime risk of cardiovascular disease has been associated with the accumulation of risk factors.[2] Prior studies have estimated lifetime risks exceeding 55%[3] using thresholds for blood pressure or cholesterol less stringent than those examined in our study. Existing estimates of an individual's lifetime risk of cardiovascular disease have largely been derived from data collected from U.S.[3] or European populations[14]. By leveraging a global dataset, our findings highlight that there is geographic variability in lifetime cardiovascular risk, extending previous observations that reported similar lifetime risk for cardiovascular disease across different ethnic groups with comparable risk factor profiles.[2] While only approximately 50% of cardiovascular disease events are attributable to five classical risk factors,[1] non-classical risk factors may account for residual cardiovascular disease risk.[16] This is consistent with prior evidence on the occurrence of myocardial infarction among individuals without standard modifiable cardiovascular risk factors.[17]

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Pooled data from five US population-based cohorts suggested that individuals with an optimal risk profile at age 45 had a 14-year difference in life expectancy compared to individuals with two or more traditional risk factors.[3] In our study, using contemporary definitions for cardiovascular disease risk factors, we associated a lifetime difference of more than a decade between individuals with and without risk factors. Notably, the association of non-HDL cholesterol and body-mass index with cardiovascular disease has a J- or U-shaped patterns,[1,18] which complicates direct estimates of their contribution. The interaction among obesity, diabetes, and hypertension[19] could have influenced results related to body-mass index. Our analyses also suggest that achieving optimal risk factor levels during midlife was associated with a higher probability of living more years free of cardiovascular disease.[3] When hypertension was present between age 50 to <55 years and absent between ages 55 to <60, this was associated with the greatest increase in life-years free from cardiovascular disease and death in our analysis. Smoking cessation was associated with similar differences in reducing mortality.

Existing risk prediction tools primarily rely on regionally focused studies, which may limit their broad applicability.[7,14] Some models offer static estimates over predefined time intervals, such as 10 years, and do not account for changes in risk factor burden over time. Our study contributes to current knowledge in several important ways. First, we improved the generalizability of findings beyond locally focused studies by presenting results from a large and diverse global dataset of individual-level, prospectively collected, harmonized data. Second, our comparative analysis of those who modified one or more risk factors during a critical midlife decade, compared to those who did not, suggests that modifying a risk factor could change the association with lifetime years in the presence or absence of a risk factor. Third, to improve self-empowerment of the individual, we extended traditional lifetime risk assessments by shifting the wording from simply acknowledging risk towards exploring the potential association between risk factor modification and additional healthy life-years.

This study has several limitations. The GCVRC data includes cohorts with varying representativity, data quality, and quantity, dates of baseline assessments, follow-up times, end point definitions, and use of clinical interventions. While the regression model quantifies important associations between risk factors and survival, the associations do not have a causal interpretation, and in particular, the

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estimated effects may be partially driven by unmeasured factors that are associated with both the risk factor and outcome. For example, we found that lower blood pressure is associated with additional life-years after controlling the other risk factors in the model: non-HDL cholesterol, body mass index, diabetes, and smoking. The overall effect could have been influenced by unmeasured factors that are associated with both lower blood pressure and overall survival, such as physical activity, nutrition, and access to health care. We cannot exclude the possibility that an entry age into the time-to-event analyses, which may differ from 50 years, could have introduced bias into the estimated incidences. Limited data density in few regions may influence the effect sizes of lifetime estimates at the regional level. However, structured harmonization was used to reduce variation, and sensitivity and additional analyses yielded results similar to those for the overall study population.

In conclusion, achieving optimal thresholds for key risk factors was associated with a lifetime difference between individuals with and without risk factors for cardiovascular disease and death on a global scale. Modification of arterial hypertension from present to absent during midlife was related to the most additional life-years for freedom from cardiovascular disease.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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Figure Legends

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Figure 1: Lifetime **risk** and **difference** for **cardiovascular disease** (A, C) and **death** (B, D) related to five modifiable risk factors. Shown are risk curves for individuals without the five risk factors (solid lines) compared to those individuals with all five risk factors (dashed lines) at an index age of 50 years. Cumulative incidence curves are shown for women (red) and men (blue). The curves were generated using recalibrated predictions from Weibull models.

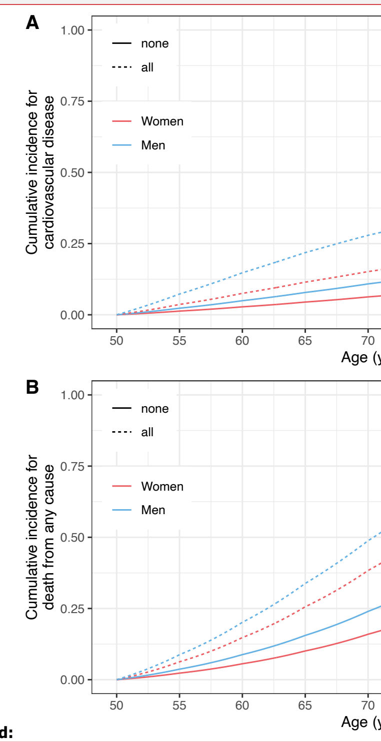

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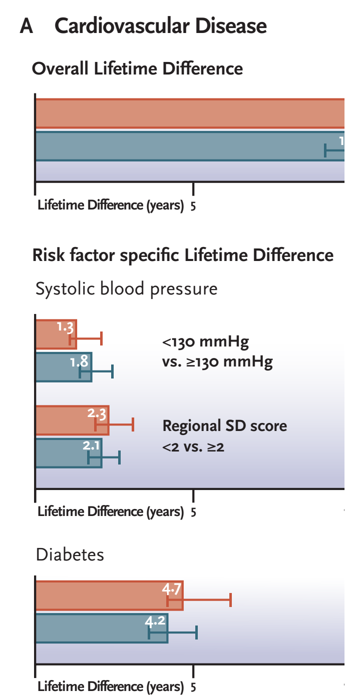
Figure 2: Estimated lifetime **difference** between individuals with and without risk factors for **cardiovascular disease** (A) and **death** (B) related to five modifiable risk factors. Lifetime difference is shown for 1) the absence vs. presence of **all five risk factors** at an index age of 50 years and 2) by the absence of **single risk factors** and presence of all other risk factors, and for women (red) and men (blue).



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The estimated lifetime difference for an individual with or without a risk factor was calculated as the difference between the predicted cardiovascular disease-free life expectancies with all and without any risk factors, respectively. Lifetime difference for systolic blood pressure, non-HDL cholesterol and body-mass index is presented for two scenarios. Estimates and 95% confidence intervals for overall lifetime difference, systolic blood pressure <130 mmHg vs. ≥130 mmHg, non-HDL cholesterol <130 mg/dL vs. ≥130 mg/dL, body-mass index ≥20 and <25kg/m^2 vs. <20 or ≥25 kg/m^2, diabetes, and smoking are based on recalibrated predictions from Weibull models including these variables as covariates. Estimates and 95% confidence intervals for regional standard deviation (SD) scores are based on recalibrated predictions from Weibull models including dichotomized regional SD scores (< 2 vs. ≥2) for systolic blood pressure, non-HDL cholesterol and body-mass index, and diabetes and smoking as covariates.

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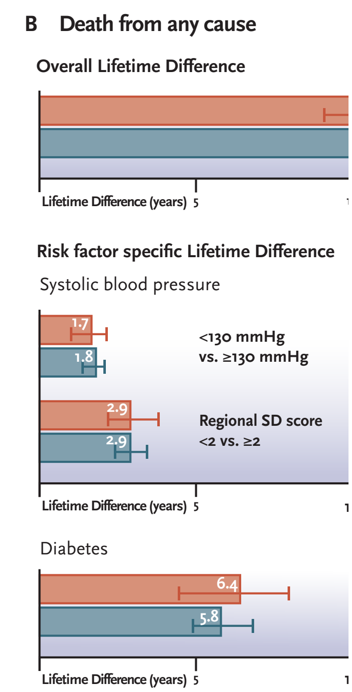

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Figure 3: Estimated lifetime **difference** between individuals with or without risk factors for **cardiovascular disease** and **death** by absence of **arterial hypertension** vs. presence of any risk factor according to different geographic regions. Hypertension was selected as the risk factor globally contributing the highest population-attributable fraction to cardiovascular disease development. Results are shown at an index age of 50 years and separately for women (red) and men (blue). Estimates and 95% confidence intervals presented are for a dichotomized region standard deviation score for systolic blood pressure (< 2 vs. ≥2) and are based on recalibrated predictions from Weibull models including dichotomized regional standard deviation scores for systolic blood pressure, non-HDL cholesterol and body-mass index (< 2 vs. ≥2), and diabetes and smoking as covariates. The use of regional standard deviation scores allows for different regional cutoffs. Clipped confidence intervals are indicated with arrows. cardiovascular disease denotes cardiovascular disease. Death denotes death from any cause. For sub-Saharan Africa, insufficient data were available for cardiovascular disease. For Asia, no lifetime difference is shown for cardiovascular disease in women as values could not be estimated due to high life expectancy.

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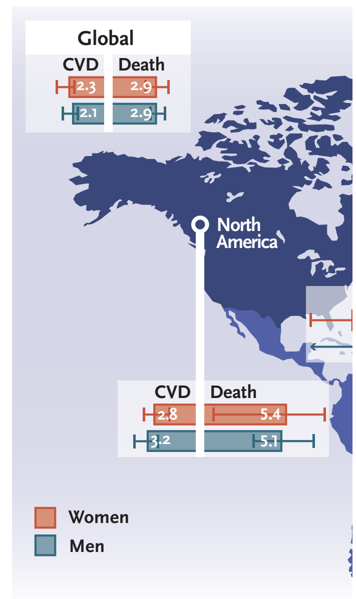

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Tables

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Table 1. Age- and sex standardized baseline characteristics by geographic region.									
	Geographic regions								
	Global	**North America**	**Latin America**	**Western Europe**	**Eastern Europe and Russia**	**North Africa and the Middle East**	**Sub-Saharan Africa**	**Asia**	**Australia**
Cohort studies									
Cohort studies — no.	133	11	11	66	16	6	5	12	6
Participants — no.	2,078,948	65,178	192,546	1,049,898	51,133	195,307	19,949	458,028	46,909
Range of survey years	1963-2021	1971-2011	1990-2013	1970-2021	1983-2014	1963-2020	1987-2017	1988-2018	1983-2007
Participants									
Median age (IQR) — yr	53.2 (44.4, 62.0)	54.0 (45.0, 63.0)	54.0 (45.0, 63.0)	53.0 (43.9, 61.9)	53.4 (44.4, 62.0)	53.8 (45.0, 62.0)	53.1 (44.0, 62.2)	54.0 (45.0, 62.7)	53.5 (44.1, 62.2)
Male sex — %	47.3	47.3	47.3	47.3	47.3	47.3	47.3	47.3	47.3
Median systolic blood pressure (IQR) — mm Hg	128.7 (116.7, 142.0)	122.0 (111.0, 135.0)	126.7 (118.0, 138.0)	132.0 (120.0, 146.5)	132.0 (120.0, 147.5)	116.0 (105.0, 130.0)	126.0 (114.0, 142.0)	125.0 (112.7, 140.0)	127.0 (116.0, 139.0)
Systolic blood pressure ≥ 130 mmHg — %	48.6	34.1	43.6	56.8	56.5	26.6	43.7	43.6	42.8
Median diastolic blood pressure (IQR) — mm Hg	80.0 (72.0, 88.0)	74.0 (67.0, 81.0)	82.7 (76.7, 90.0)	81.0 (74.0, 88.5)	82.0 (75.0, 90.0)	75.0 (68.0, 80.0)	76.0 (69.5, 85.0)	80.0 (71.0, 89.0)	72.5 (64.5, 80.7)

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Median non-HDL cholesterol (IQR) — mg/dL	155.6 (127.7, 186.8)	149.8 (123.0, 179.0)	156.2 (131.1, 186.0)	162.4 (133.8, 193.4)	161.6 (134.1, 191.1)	140.9 (116.0, 168.1)	138.8 (111.8, 175.8)	140.0 (116.0, 165.9)	151.6 (124.9, 181.4)
Non-HDL cholesterol ≥ 130 mg/dL — %	73.1	68.6	75.8	77.9	78.0	61.3	55.6	60.9	70.2
Median body-mass index (IQR)	25.7 (22.8, 28.9)	27.2 (24.1, 30.9)	28.2 (25.4, 31.4)	26.0 (23.5, 29.1)	27.1 (24.2, 30.5)	27.0 (24.0, 30.3)	22.3 (19.9, 25.7)	22.6 (20.1, 25.4)	26.3 (23.7, 29.5)
Body-mass index < 20kg/m² or ≥ 25kg/m² — %	63.9	71.3	79.6	63.7	71.8	72.9	55.4	51.8	66.5
Diabetes — %	7.7	12.9	15.1	4.8	8.7	17.5	12.9	5.2	4.6
Current smoking— %	22.3	22.7	31.3	20.9	29.9	14.8	25.1	24.7	15.0
Antihypertensive medications — %	17.2	27.2	18.9	17.0	27.9	22.9	15.6	8.6	12.8
Lipid-lowering medications — %	9.0	8.0	2.2	10.7	8.3	10.5	0	4.7	3.8
History of cardiovascular disease — %	4.9	7.4	3.6	5.1	11.0	5.7	2.2	3.6	6.8

Percentages, medians, and Interquartile Ranges (IQRs) per geographic region were computed with the use of direct standardization according to age (≤40 years, >40 to ≤45 years, >45 to ≤50 years, >50 to ≤55 years, >55 to ≤60 years, >60 to ≤65 years, >65 to ≤70 years, and >70 years) and sex distribution in the Global Cardiovascular Risk Consortium data set. To convert the values for non–high-density lipoprotein (non-HDL) cholesterol to millimoles per liter, multiply by 0.02586. cardiovascular disease denotes cardiovascular disease.

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Table 2. Life expectancy and lifetime **difference** allowing for variation in risk factors during 55 to <60 years of age. Individuals with all risk factors present between 50 to 60 years of age serve as reference. Lifetime difference according to risk factor variation is predicted up to age 90.

	Cardiovascular disease				**Death from any cause**			
	Life expectancy		**Lifetime difference**		**Life expectancy**		**Lifetime difference**	
	Women	Men	Women	Men	Women	Men	Women	Men
Variation in								
Hypertension	72.0 (69.7, 74.3) years	69.7 (69.0, 70.4) years	2.4 (1.3, 3.6) years	1.2 (0.8, 1.7) years	74.9 (72.8, 76.9) years	71.8 (70.6, 73.1) years	1.7 (1.1, 2.3) years	1.7 (0.8, 2.6) years
Hyperlipidemia	69.7 (67.3, 72.2) years	68.5 (67.7, 69.3) years	0.1 (- 0.7, 1.0) years	0.0 (- 0.7, 0.7) years	73.0 (71.3, 74.7) years)	69.9 (68.3, 71.5) years	- 0.2 (- 1.1, 0.7) years	- 0.3 (- 0.9, 0.2) years
Underweight or overweight/ obesity	69.9 (67.4, 72.4) years	68.5 (67.5, 69.4) years	0.3 (- 0.2, 0.8) years	0.0 (- 0.3, 0.3) years	73.2 (71.1, 75.2) years	70.1 (68.6, 71.7) years	0.0 (- 0.5, 0.5) years	- 0.1 (- 0.4, 0.2) years
Diabetes	70.7 (68.1, 73.4) years	69.0 (68.1, 69.8) years	1.1 (0.5, 1.8) years	0.5 (0.2, 0.8) years	74.7 (73.0, 76.3) years	71.4 (70.0, 72.8) years	1.5 (+ 0.8, 2.2) years	1.2 (0.6, 1.8) years
Smoking	71.3 (68.5, 74.1) years	69.5 (68.4, 70.6) years	1.7 (1.1, 2.3) years	1.0 (0.5, 1.6) years	75.2 (73.1, 77.3) years	72.6 (71.2, 74.0) years	2.1 (1.1, 3.0) years	2.4 (1.9, 2.9) years
Hypertension and hyperlipidemia	72.0 (69.7, 74.3) years	69.4 (68.6, 70.1) years	2.4 (0.9, 3.9) years	0.9 (- 0.0, 1.8) years	74.9 (72.9, 76.8) years	71.5 (70.3, 72.8) years	1.7 (0.9, 2.6) years	1.3 (0.7, 2.0) years
Hypertension, hyperlipidemia and diabetes	72.9 (71.0, 74.8) years	70.0 (69.2, 70.7) years	3.3 (1.9, 4.7) years	1.5 (0.4, 2.6) years	76.5 (74.8, 78.2) years)	72.7 (71.7, 73.6) years	3.3 (2.3, 4.4) years	2.5 (1.6, 3.4) years
Hypertension, hyperlipidemia, diabetes, and smoking	74.7 (72.6, 76.7) years	71.5 (70.8, 72.3) years	5.1 (3.7, 6.4) years	3.1 (2.1, 4.0) years	78.4 (76.8, 79.9) years	74.7 (73.8, 75.6) years	5.2 (4.1, 6.3) years	4.5 (3.5, 5.6) years

Life expectancy is estimated from survival curves obtained from recalibrated predictions based on joint models for longitudinal data (systolic blood pressure ≥130 mmHg, non-HDL cholesterol levels ≥130 mg/dL, body-mass index <20 kg/m^2 or ≥25 kg/m^2, diabetes, and smoking) and time-to-event (cardiovascular disease or death; death from any cause). Life expectancy and lifetime difference with 95% confidence intervals are provided.