Web appendix

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Detailed statistical methods

Model estimation

We used sex- and cohort-stratified Cox proportional hazards regression to estimate the coefficients of the risk function, similar to previous cohort pooling projects.[1-5] The risk predictors (smoking, diabetes, serum total cholesterol and systolic blood pressure) were measured at baseline. Participants' age was used as the time scale,[6] which allows age-specific cardiovascular disease (CVD) rates to vary across cohorts, and hence across populations to which the risk score is applied. This parameterization allows the risk equation to be recalibrated to each country, and each sex and age group within it, by replacing the age-sex-specific CVD rates from the pooled cohorts with those from the application country. We included interaction terms between all risk factors and age and, as described in the main paper, between sex and diabetes, and sex and smoking based on previous evidence.

The Cox model is given as:

$$\lambda_i(t) = \lambda_{0,k}(t)\exp\left(\sum_{l=1}^{4}\beta_l X_{i,l} + \sum_{l=1}^{4}\delta_l t X_{i,l} + \sum_{l=3}^{4}\gamma_l sex_i X_{i,l}\right) \qquad (1)$$

where subscript i denotes individual participants in the cohorts; k denotes sex-cohort combination; l denotes risk factors in the risk prediction equation (1: systolic blood pressure, 2: total cholesterol, 3: diabetes, and 4: smoking); t denotes age in years; $X_{i,l}$ is the level of the risk factor l for individual i at baseline; β_l is the log hazard ratio (HR) for the main effect of each risk factor, δ_l is the coefficient for linear interaction between risk factor l and age, and γ_l is the coefficient for interaction between diabetes and smoking, and sex; and $\lambda_{0,k}(t)$ is the age-specific

hazard of CVD at the average level of risk factors for participants of sex-cohort *k*. $\lambda_{0,k}(t)$ is conceptually equivalent to an age-specific version of the *S0(t)* parameter in the specification used by D'Agostino and colleagues in the Framingham Risk Score.[7] This formulation of the risk prediction equation does not need a coefficient for age although it includes interaction terms between age and other risk factors as described below.

Risk prediction

The first step in recalibrating the risk score for a country (and age and sex), is to calculate the CVD rate for each year of follow-up in the 10-year period of risk prediction using the coefficients of the proportional hazards model. For an individual who is aged *t* years (e.g. 60 years in the worked out example of Figure 2), this is given by the equation below:

$$\varphi_i(t) = \varphi_{0,k}(t)\exp[\sum_{l=1}^{4}\beta_l(X_{i,l} - \overline{X}_{l,k,t}) + \sum_{l=1}^{4}\delta_l t(X_{i,l} - \overline{X}_{l,k,t}) + \sum_{l=3}^{4}\gamma_l sex_i(X_{i,l} - \overline{X}_{l,k,t})] \qquad (2)$$

where $\varphi_{0,k}(t)$ is the age-specific average CVD rate for country-sex *k* at age *t* (current age and the subsequent 9 years of life) and $\overline{X}_{l,k,t}$ is the country-sex-specific mean level of risk factor *l* at age *t*, i.e. at the time of risk prediction (analogous to the baseline in the cohorts that were used for estimating the coefficients). In practice, event rates and risk factor levels are often available in 5-year age groups in national populations.

The estimated 10-year risk of CVD for an individual aged *t* years at the time of risk prediction is:

$$P_i(CVD) = 1 - \prod_{j=t}^{t+9}(\exp(-\varphi_i(j)) \quad (3)$$

where j denotes the age for individual i at the time of risk prediction and in the 9 subsequent years of their life, and $\varphi_i(j)$ is the estimated CVD hazard from the above equation for each of those 10 years of age.

Appendix Table 1: Information about cohorts used in estimating the coefficients of the risk score

Cohort name*	Baseline date	Median follow up (years)	Number of participants	Percent female	Age range at baseline	Mean (SD) age at baseline	Number of fatal plus non-fatal CVD events (% stroke)	Number of fatal CVD (% stroke)	Mean (SD) total cholesterol (mmol/L)	Mean (SD) systolic blood pressure (mmHg)	Current smoking prevalence (%)	Diabetes prevalence (%)
ARIC	1987-89	15	13,405	56	44-66	54.1 (5.8)	2,164 (28)	368 (17)	5.6 (1.1)	121 (19)	25.9	10.4
CHS	1989-93	13	4,364	60	66-90	72.6 (5.5)	1,064 (57)	526 (20)	5.5 (1.0)	137 (22)	12.5	14.7
FHS	1948-51	15	3,027	55	40-65	50.2 (6.6)	412 (31)	185 (16)	6.1 (1.2)	137 (24)	54.6	1.6
FHS-OFF	1971	15	1,822	49	40-62	46.9 (5.1)	183 (21)	67 (10)	5.5 (1.0)	128 (18)	42.7	3.9
HHP	1965-68	15	7,572	0	45-68	54.4 (5.6)	810 (33)	359 (37)	5.6 (1.0)	135 (21)	44.1	6.1
MRFIT	1973-76	11	10,481	0	40-57	48.0 (4.7)	938 (10)	418 (8)	6.6 (0.9)	148 (16)	57.3	3.8
PRHHP	1965	12	5,416	0	42-77	54.4 (6.5)	292 (36)	296 (34)	5.2 (1.1)	133 (23)	41.4	7.3
WHICT	1993	8	4,042	100	50-79	62.1 (7.0)	179 (45)	46 (20)	5.8 (1.0)	128 (18)	8.9	10.0

* ARIC: atherosclerosis risk in communities; CHS: cardiovascular health study; FHS: Framingham heart study original cohort; FHS-OFF: Framingham heart study offspring cohort; HHP: Honolulu heart program; MRFIT: multiple risk factor intervention trial; PRHHP: Puerto Rico heart health program; WHICT: women's health initiative clinical trial. Detailed information on these cohorts are provided elsewhere. [8-16] WHICT was stratified on type of intervention.

Appendix Table 2: Characteristics and summary statistics for health examination surveys used in the analysis

Country	Survey name	Survey Year	Number of participants used in the analysis †	Mean systolic blood pressure (mmHg)	Mean total cholesterol (mmol/L)	Diabetes prevalence (%)	Current smoking prevalence (%)
China	CHNS	2009	6,346	128	5.0	10	28
Czech Republic	Post-MONICA	2007	2,478	131	5.5	15	30
Denmark	DANHES*	2008	13,787	131	5.5	4	16
England	HSE*	2011	1,569	129	5.5	12	30
Iran	NCDSS	2007	8,642	131	5.1	14	23
Japan	NHNS	2012	11,174	133	5.3	12	15
Malawi	STEPS	2009	1,045	140	4.5	2	14
Mexico	ENSANUT	2006	4,061	129	5.3	27	16
South Korea	KNHANES	2011	3,940	122	5.0	13	22
Spain	ENRICA	2008-10	7,822	133	5.3	14	23
United States	NHANES	2011-12	1,764	125	5.2	18	19

*Hb1Ac ≥6.5% was used for diabetes diagnosis as fasting glucose was not available.

† Number of participants 40-84 years of age who had data on sex, systolic blood pressure, total cholesterol, diabetes, and smoking.

Appendix Table 3: Characteristics of the cohort studies used for external validation

Cohort* characteristics	**SHHEC**	**TLGS**	**AusDiab**
Baseline date	1984-1992	1999-2001	1999-2000
Median follow up (years)	10	10	10
Number of subjects† (% female)	12,579 (51)	4,097 (57)	8,230 (54)
Age range at baseline	40-75	40-80	40-80
Mean (SD) age at baseline	51 (7)	54 (10)	56 (11)
Number of fatal CVD (% stroke)	346 (25)	111 (23)	166 (37)
Mean (SD) total cholesterol (mmol/L)	6.4 (1.2)	5.8 (1.2)	5.8 (1.1)
Mean (SD) systolic blood pressure (mmHg)	133 (20)	127 (21)	132 (19)
Current smoking prevalence (%)	46	14	14
Diabetes prevalence (%)	15	19	10

*SHHEC: Scottish Heart Health Extended Cohort; TLGS: Tehran Lipid and Glucose Study; AusDiab: Australian Diabetes, Obesity and Lifestyle study

†Participants between 40 and 80 years of age; with no missing risk factor data; and with no history of coronary heart disease or stroke at baseline were included. Detailed information on SHHEC, TLGS and AusDiab have been reported elsewhere.[17-20]

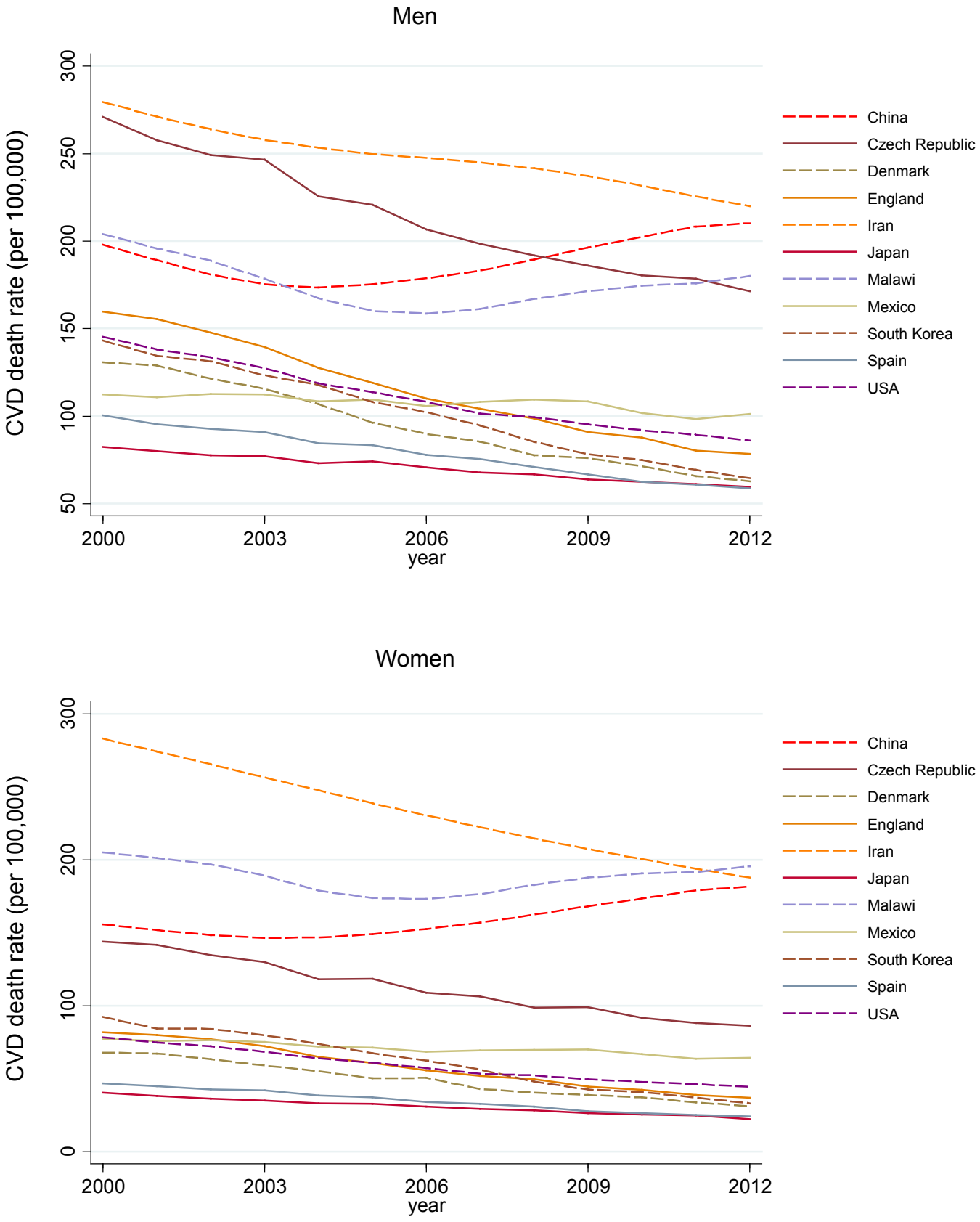
Appendix Table 4: Results of validation of the fatal CVD model

		Discrimination	**Calibration**
	Cohort name	**C statistic (95% CI)**	**Hosmer-Lemeshow Chi-square (p) df=8**
Internal validation	Total	71 (70-73)	15.5 (0.051)
	Men	70 (68-72)	20.2 (0.010)
	Women	80 (76-84)	9.8 (0.28)
Validation in each of the cohorts iteratively excluded when estimating coefficients	ARIC	78 (74-82)	33.3 (<0.0001)
	CHS	67 (62-71)	39.4 (<0.0001)
	FHS	74 (69-80)	7.7 (0.46)
	FHS-OFF	70 (59-81)	8.1 (0.42)
	HHP	73 (69-77)	18.4 (0.018)
	MRFIT	60 (57-63)	26.8 (<0.0001)
	PRHHP	77 (73-80)	11.4 (0.18)
	WHICT	76 (66-85)	11.1 (0.20)
External validation	SHHEC	74 (71-77)	12.0 (0.15)
	TLGS	83 (79-86)	12.9 (0.12)
	AusDiab	84 (82-87)	44.3 (<0.0001)

Appendix Table 5: Population in risk category (%) of 10 year fatal CVD by country, sex, and age group.

	Men: 40-64 years					**Women: 40-64years**				
	<3%	**3-6%**	**7-9%**	**10-14%**	**≥15%**	**<3%**	**3-6%**	**7-9%**	**10-14%**	**≥15%**
China	48.3	27.8	11.1	7.3	5.4	55.3	28.8	6.8	4.1	4.9
Czech Republic	40.5	35.9	10.2	8.4	5.0	82.5	13.8	2.0	1.0	0.6
Denmark	86.7	12.4	0.7	0.2	0.0	97.9	2.0	0.1	0.1	0.0
England	85.8	11.9	1.6	0.4	0.2	96.4	2.7	0.7	0.2	0.0
Iran	38.9	38.1	9.8	7.7	5.5	59.6	23.9	6.6	4.5	5.4
Japan	78.6	19.2	1.5	0.8	0.0	98.3	1.5	0.2	0.0	0.0
Malawi	57.4	27.6	9.8	3.2	2.1	64.3	22.3	5.9	4.9	2.7
Mexico	68.1	24.5	3.8	3.0	0.6	84.3	12.4	2.2	1.0	0.0
South Korea	92.8	6.1	0.2	0.1	0.7	99.0	0.8	0.0	0.1	0.1
Spain	88.2	10.6	0.4	0.5	0.2	99.0	1.0	0.1	0.0	0.0
USA	73.8	21.9	2.8	0.4	1.0	92.6	6.8	0.3	0.2	0.1
	Men: 65-84 years					**Women: 65-84 years**				
	<3%	**3-6%**	**7-9%**	**10-14%**	**≥15%**	**<3%**	**3-6%**	**7-9%**	**10-14%**	**≥15%**
China	0.0	0.7	5.8	12.6	81.0	0.0	1.1	8.7	18.6	71.5
Denmark	5.2	45.4	18.7	14.9	15.8	35.1	37.7	10.9	7.7	8.6
England	4.2	35.7	19.5	14.9	25.8	29.9	24.9	11.0	11.5	22.7
Japan	8.4	44.9	18.4	12.9	15.4	47.3	27.6	8.5	4.1	12.5
Mexico	0.0	21.5	14.4	15.1	49.0	4.4	31.3	10.1	19.3	34.9
South Korea	7.0	42.2	15.0	18.0	17.8	29.6	30.9	12.1	10.2	17.2
Spain	11.7	43.4	15.5	14.9	14.5	44.2	31.0	8.2	5.4	11.2
USA	2.9	33.2	21.7	16.2	26.0	22.7	30.6	7.8	19.4	19.5
	Men: 40-84 years					**Women: 40-84 years**				
	<3%	**3-6%**	**7-9%**	**10-14%**	**≥15%**	**<3%**	**3-6%**	**7-9%**	**10-14%**	**≥15%**
China	36.5	21.2	9.8	8.6	23.9	42.2	22.3	7.3	7.5	20.7
Denmark	61.9	22.5	6.2	4.7	4.8	78.7	12.9	3.4	2.4	2.6
England	60.7	19.2	7.1	4.8	8.1	77.1	9.2	3.7	3.5	6.6
Japan	43.5	32.0	9.9	6.8	7.7	74.9	13.5	4.0	1.9	5.7
Mexico	54.6	23.9	5.9	5.4	10.2	69.0	16.0	3.8	4.5	6.7
South Korea	76.8	12.8	3.0	3.4	3.9	82.4	8.0	2.9	2.5	4.2
Spain	66.8	19.8	4.7	4.6	4.2	80.2	11.3	2.9	1.8	3.8
USA	54.8	24.9	7.8	4.7	7.7	72.6	13.6	2.4	5.7	5.7

Appendix Figure 1: Age-standardised CVD death rates per 100,000 people by country and year. The WHO standard population was used for age-standardisation.



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