Supplemental Material

Supplemental Methods:

Cause of Death Ensemble Model (CODEm) methods.

Here we summarize ensemble modeling and CODEm methods; interested readers can access more detailed information about the CODEm method and ensemble modeling elsewhere.[1]

In brief, ensemble models combine predictions of multiple individual models. Ensemble models estimated in a variety of fields have demonstrated smaller prediction error than the best individual model. Another advantage of ensemble models is that they capture not only input parameter uncertainty, but also uncertainty stemming from model specification. In order to combine predictions from multiple models (varying in model form, outcome definition, and covariate selection), individual model results are usually weighted before averaging to produce ensemble estimates.

CODEm worked with two main model forms: linear mixed effects models and spatial-temporal models. Linear mixed effects models assumed fixed effects of covariates, and hierarchical random effects by super-region, region, country, and age. Spatial-temporal models begin with the mixed effects models, but remove the random country effect, instead calculating residuals (predicted – observed estimate) and performing local regressions on nearby data (in the dimensions of country ("space") and time (year). Gaussian Process Regression was used to carry forward sampling and non-sampling variance in the source data. Two types of dependent cause of death variables were used: mortality rates and "cause fraction" (e.g., proportion of IHD mortality in all-cardiovascular disease mortality or all-cause mortality). The two model forms (mixed effects linear models and spatial-temporal models) and two outcome definitions (rate and cause fraction) led to four model "families" (four combinations of form and outcome) contributing to ensemble models.

Covariates were added stepwise to models, in order of a prior literature-based assumptions about causal association and strength of association, and kept in models if the covariate showed estimated direction of association and if the multivariate covariate coefficient was significant at the <0.05 level. Biological/physiological covariates (e.g., country mean blood pressure or cholesterol), behavioral covariates (country mean dietary consumption and physical activity level) and contextual covariates (e.g., mean education level, per capita income, and health system access) were examined.[2] A complete list of covariates contributing to the IHD mortality models is available elsewhere.[3] Multiple models were developed from combinations of covariate sets in all four model families. We decided to apply more

weight to predictions from models that performed better out-of-sample, using monotonically declining weights based on the model's performance rank.

Supplemental References

1. Foreman KJ, Lozano R, Lopez AD, Murray CJ. Modeling causes of death: An integrated approach using codem. *Population health metrics*. 2012;10:1
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3. Forouzanfar MH, Moran AE, Flaxman AD, Roth G, Mensah GA, Ezzati M, Naghavi M, Murray CJ. Assessing the global burden of ischemic heart disease, part 2: Analytic methods and estimates of the global epidemiology of ischemic heart disease in 2010. *Glob Heart*. 2012;7:331-342

Supplemental Table 1: Site-years by decade and source type for the GBD 2010 Study IHD mortality analysis.

Source Type	1980-1989	1990-1999	2000-2011
Surveillance	0	27	24
Verbal autopsy	14	23	40
Vital Registration	808	966	940

Supplemental Table 2: Site-years by GBD 2010 region for the IHD mortality analysis.

GBD Super Region	GBD Region	Site-years of IHD mortality data
High Income		
	Asia Pacific, High Income	**92**
	Europe, Western	**605**
	Australasia	**56**
	North America, High Income	**60**
	Latin America, Southern	**87**
Eastern Europe/Central Asia		
	Europe, Central	**274**
	Europe, Eastern	**194**
	Asia, Central	**186**
Latin America/Caribbean		
	Latin America, Tropical	**59**
	Latin America, Central	**218**
	Latin America, Andean	**56**
	Caribbean	**409**
East Asia/Pacific		
	Asia, Southeast	**144**
	Asia, East	**71**
	Oceania	**15**
North Africa / Middle East		**136**
South Asia		**54**
Sub-Saharan Africa		
	Sub-Saharan Africa, Southern	**102**
	Sub-Saharan Africa, East	**18**
	Sub-Saharan Africa, Central	**0**
	Sub-Saharan Africa, West	**8**

Supplemental Table 3: Increase in IHD deaths due to allocation of specific ill-defined or "undefined-coded" deaths to IHD, and proportion of deaths coded to specific codes assigned to IHD.

Disease/ICD code pertinent to undefined code	Percent increase in IHD death due to assignment of each undefined code (21.5% total increase)	Percent proportion of each of undefined codes assigned to IHD
Some ill-defined from R00-R99	3.4%	13.8%
Hypertension	3.1%	47.2%
R54: Senility	2.9%	20.6%
All cardiac conduction disorders	2.4%	89.9%
Atherosclerosis	2.4%	40.0%
All ill-def. descriptions of heart disease	1.8%	47.3%
DIC, Cardiac arrest ,Acute respiratory failure and Coma	1.7%	25.6%
I50: Heart failure	1.5%	76.9%
J81: Pulmonary oedema	0.5%	76.3%
All encephalopathy and Cerebral oedema	0.5%	66.8%
Embolism & thrombosis	0.3%	40.1%
Cardiogenic shock and other Shock	0.3%	55.2%
All disorders of electrolyte & fluid balance	0.2%	13.0%
I99:Oth. & unspec. disorders of circulatory system	0.2%	48.2%
Ill-defined (result of age and sex restriction)	0.1%	13.6%
Ill-defined: from M09-M99	0.1%	19.0%
Pneumonitis	0.1%	2.7%
Ill-defined: from N39.3-N97.8	0.1%	21.9%
Renal failure	0.1%	0.8%
Fever ,Malasia, Febrile and convulsions unknown origin	<0.5%	8.2%
Ill-defined: from F32-F99	<0.5%	16.3%
Cardiac sign and symptom	<0.5%	70.7%
Ill-defined: from D10-D36.9	<0.5%	16.1%
Ill-defined: from G43-G58.9	<0.5%	14.6%
Different Paralytic syndrome and palsy syndrome	<0.5%	2.2%

Ill-defined: from L01-L98.9	<0.5%	15.9%
Unspecified liver disease	<0.5%	0.9%
Ill-defined: from H00-H99	<0.5%	14.4%
Ill-defined: from K00-k14.9	<0.5%	17.9%
Ill-defined: from A00-B99	<0.5%	14.2%
Ill-defined: from Q10-Q84.9	<0.5%	4.7%
Ill-defined: from J30-J35.9	<0.5%	11.2%
Undefined ICD code	<0.5%	31.6%
All unspecified parasitic diseases	<0.5%	0.1%

Supplemental Table 4: Global Burden of Disease, Injuries and Risk Factors 2010 Study Region and Country List.

Super Region	Region	Country
East Asia/Pacific		
	Asia, East	China
		Korea, Democratic People's Republic of
		Taiwan
	Asia, Southeast	Cambodia
		Indonesia
		Lao People's Democratic Republic
		Malaysia
		Maldives
		Myanmar
		Philippines
		Sri Lanka
		Thailand
		Timor-Leste

		Viet Nam
	Oceania	Fiji
		Kiribati
		Marshall Islands
		Micronesia, Federated States of
		Papua New Guinea
		Samoa
		Solomon Islands
		Tonga
		Vanuatu

Eastern Europe/Central Asia

	Asia, Central	Armenia
		Azerbaijan
		Georgia
		Kazakhstan
		Kyrgyzstan
		Mongolia
		Tajikistan
		Turkmenistan
		Uzbekistan
		Albania
	Europe, Central	Bosnia and Herzegovina
		Bulgaria
		Croatia
		Czech Republic
		Hungary
		Macedonia, the Former Yugoslav
		Republic of
		Montenegro
		Poland
		Romania

		Serbia
		Slovakia
		Slovenia
	Europe, Eastern	Belarus
		Estonia
		Latvia
		Lithuania
		Moldova
		Russian Federation
		Ukraine

High Income

	Asia Pacific, High Income	Brunei Darussalam
		Japan
		Korea, Republic of
		Singapore
	Australasia	Australia
		New Zealand
	Europe, Western	Andorra
		Austria
		Belgium
		Cyprus
		Denmark
		Finland
		France
		Germany
		Greece
		Iceland
		Ireland
		Israel
		Italy
		Luxembourg
		Malta

		Netherlands
		Norway
		Portugal
		Spain
		Sweden
		Switzerland
		United Kingdom
	Latin America, Southern	Argentina
		Chile
		Uruguay
	North America, High Income	Canada
		United States

Latin America/Caribbean

	Caribbean	Antigua and Barbuda
		Bahamas
		Barbados
		Belize
		Cuba
		Dominica
		Dominican Republic
		Grenada
		Guyana
		Haiti
		Jamaica
		Saint Lucia
		Saint Vincent and the Grenadines
		Suriname
		Trinidad and Tobago
	Latin America, Andean	Bolivia
		Ecuador

	Peru
Latin America, Central	Colombia
	Costa Rica
	El Salvador
	Guatemala
	Honduras
	Mexico
	Nicaragua
	Panama
	Venezuela
Latin America, Tropical	Brazil
	Paraguay

North Africa / Middle East

North Africa / Middle East	Algeria
	Bahrain
	Egypt
	Iran, Islamic Republic of
	Iraq
	Jordan
	Kuwait
	Lebanon
	Libyan Arab Jamahiriya
	Morocco
	Occupied Palestinian Territory
	Oman
	Qatar
	Saudi Arabia
	Syrian Arab Republic
	Tunisia
	Turkey
	United Arab Emirates
	Yemen

South Asia

	Asia, South	Afghanistan
		Bangladesh
		Bhutan
		India
		Nepal
		Pakistan

Sub-Saharan Africa

	Sub-Saharan Africa, Central	Angola
		Central African Republic
		Congo
		Congo, the Democratic Republic of the
		Equatorial Guinea
		Gabon
	Sub-Saharan Africa, East	Burundi
		Comoros
		Djibouti
		Eritrea
		Ethiopia
		Kenya
		Madagascar
		Malawi
		Mauritius
		Mozambique
		Rwanda
		Seychelles
		Somalia
		Sudan
		Tanzania, United Republic of
		Uganda
		Zambia
	Sub-Saharan Africa, Southern	Botswana

	Lesotho
	Namibia
	South Africa
	Swaziland
	Zimbabwe
Sub-Saharan Africa, West	Benin
	Burkina Faso
	Cameroon
	Cape Verde
	Chad
	Cote d'Ivoire
	Gambia
	Ghana
	Guinea
	Guinea-Bissau
	Liberia
	Mali
	Mauritania
	Niger
	Nigeria
	Sao Tome and Principe
	Senegal
	Sierra Leone
	Togo

Supplemental Table 5: Annual IHD deaths, males and females, by region, 1980-2010, the Global Burden of Disease 2010 Study

Year	1980	1985	1990	1995	2000	2005	2010
Asia Pacific, High Income	102,725	109,964	113,347	119,074	127,826	142,299	166,853
Europe, Western	970,818	970,646	929,366	885,249	831,709	745,285	745,590
Australasia	41,780	43,058	42,128	40,280	36,551	34,436	37,738
North America, High Income	726,848	739,737	703,057	685,624	655,069	613,831	619,377
Europe, Central	281,482	309,389	331,497	346,890	334,231	340,145	344,139
Latin America, Southern	55,206	55,958	56,753	55,837	60,488	61,990	65,106
Europe, Eastern	741,533	800,386	834,783	1,079,003	1,125,919	1,219,386	1,115,213
Asia, East	359,016	416,822	472,158	604,981	787,789	873,827	992,163
Latin America, Tropical	94,861	106,649	111,338	125,006	134,071	146,546	166,596
Latin America, Central	68,099	75,836	91,521	106,884	121,056	137,658	166,532
Asia, Southeast	140,306	166,005	215,719	262,910	292,138	325,325	383,323
Asia, Central	119,401	125,561	138,157	168,986	167,981	179,638	184,167
Latin America, Andean	11,409	13,599	15,575	16,870	19,425	21,917	24,350
North Africa / Middle East	205,187	226,276	263,978	307,579	336,802	371,325	418,019
Caribbean	29,407	34,962	40,315	46,384	47,019	49,183	54,576
Asia, South	433,832	500,273	704,833	915,207	1,090,272	1,186,987	1,323,551

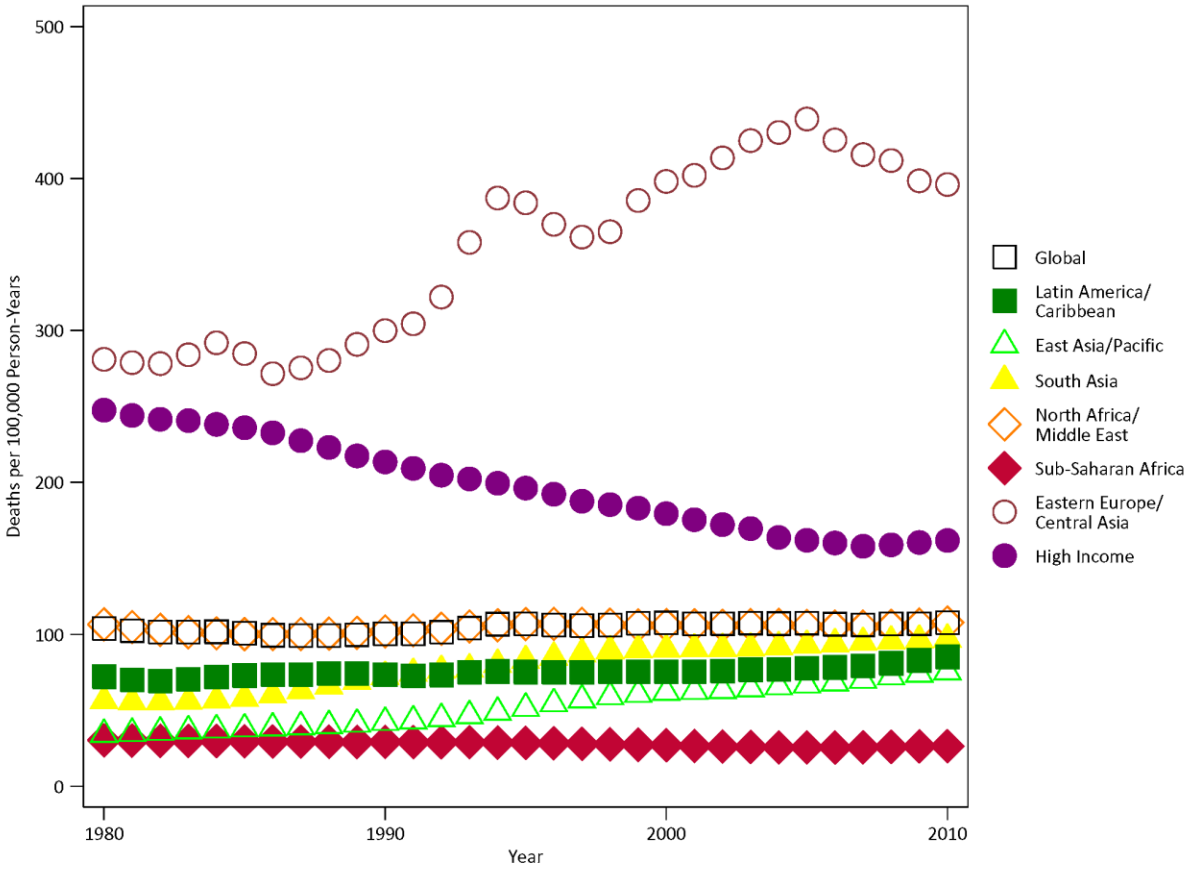
Oceania	1,604	1,980	2,552	3,027	3,377	3,949	4,581
Sub-Saharan Africa, Southern	16,883	18,131	20,094	22,420	22,275	22,721	24,103
Sub-Saharan Africa, East	42,241	47,965	54,706	59,459	60,780	66,701	75,673
Sub-Saharan Africa, Central	15,508	17,923	20,272	22,699	24,269	27,481	33,306
Sub-Saharan Africa, West	37,140	42,668	49,641	56,603	66,515	72,152	84,315

Supplemental Table 6: Years of life lost (YLL) due to IHD, males and females, by region, 1980-2010, the Global Burden of Disease 2010 Study

Year	1980	1985	1990	1995	2000	2005	2010
Asia Pacific, High Income	1,878,938	1,917,315	1,798,146	1,737,100	1,762,044	1,812,636	1,920,451
Europe, Western	14,926,890	14,170,528	12,860,688	11,636,179	10,352,545	8,807,634	8,428,017
Australasia	702,407	676,014	615,515	542,832	461,622	405,899	419,557
North America, High Income	11,282,204	10,796,930	9,769,603	9,285,417	8,665,142	8,060,007	7,825,615
Europe, Central	4,825,839	5,233,820	5,597,369	5,724,146	5,306,431	5,089,778	4,835,548
Latin America, Southern	1,045,640	984,106	952,977	918,531	965,586	933,315	945,652
Europe, Eastern	12,195,199	12,864,701	13,363,422	19,080,796	19,691,217	21,395,103	17,671,525
Asia, East	7,514,092	8,485,632	9,449,260	11,905,005	14,940,087	15,493,412	16,795,598
Latin America, Tropical	2,148,570	2,308,880	2,341,808	2,542,240	2,669,026	2,779,536	3,015,732
Latin America, Central	1,440,409	1,546,425	1,762,410	2,025,428	2,188,620	2,366,529	2,827,557
Asia, Southeast	3,194,862	3,774,990	4,818,933	5,720,044	6,153,507	6,704,804	7,765,379
Asia, Central	2,038,453	2,110,414	2,434,441	3,126,687	3,140,725	3,358,046	3,344,003
Latin America, Andean	244,027	283,086	312,129	328,017	386,016	426,970	437,785
North Africa / Middle East	5,254,483	5,639,548	6,521,855	7,338,169	7,613,176	7,995,777	8,822,768
Caribbean	561,395	639,033	694,309	741,590	737,508	759,499	839,991
Asia, South	10,961,439	12,583,981	17,300,420	21,750,749	25,316,742	27,628,587	29,759,902

Oceania	45,732	55,796	71,723	85,162	93,788	107,351	122,337
Sub-Saharan Africa, Southern	380,082	402,485	439,982	501,979	525,788	531,476	514,823
Sub-Saharan Africa, East	1,095,487	1,239,823	1,414,599	1,551,138	1,554,534	1,628,544	1,781,311
Sub-Saharan Africa, Central	395,017	450,581	508,418	560,763	597,068	666,283	805,163
Sub-Saharan Africa, West	1,138,204	1,293,544	1,492,723	1,723,077	1,858,139	1,890,019	2,146,457
Totals	83,269,368	87,457,630	94,520,731	108,825,050	114,979,311	118,841,204	121,025,168

Supplemental Figure 1a. Males: Crude Ischemic Heart Disease Mortality Rate per 100,000 persons by Super Region and Globally, 1980-2010, the Global Burden of Disease 2010 Study.



Supplemental Figure 1b. Females: Crude Ischemic Heart Disease Mortality Rate per 100,000 persons by Super Region and Globally, 1980-2010, the Global Burden of Disease 2010 Study.