Endemic Cardiovascular Diseases of the Poorest Billion

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Abstract—The poorest billion people are distributed throughout the world, though most are concentrated in rural sub-Saharan Africa and South Asia. Cardiovascular disease (CVD) data can be sparse in low- and middle-income countries beyond urban centers. Despite this urban bias, CVD registries from the poorest countries have long revealed a predominance of nonatherosclerotic stroke, hypertensive heart disease, nonischemic and Chagas cardiomyopathies, rheumatic heart disease, and congenital heart anomalies, among others. Ischemic heart disease has been relatively uncommon. Here, we summarize what is known about the epidemiology of CVDs among the world's poorest people and evaluate the relevance of global targets for CVD control in this population. We assessed both primary data sources, and the 2013 Global Burden of Disease Study modeled estimates in the world's 16 poorest countries where 62% of the population are among the poorest billion. We found that ischemic heart disease accounted for only 12% of the combined CVD and congenital heart anomaly disability-adjusted life years (DALYs) in the poorest countries, compared with 51% of DALYs in high-income countries. We found that as little as 53% of the combined CVD and congenital heart anomaly burden (1629/3049 DALYs per 100 000) was attributed to behavioral or metabolic risk factors in the poorest countries (eg, in Niger, 82% of the population among the poorest billion) compared with 85% of the combined CVD and congenital heart anomaly burden (4439/5199 DALYs) in high-income countries. Further, of the combined CVD and congenital heart anomaly burden, 34% was accrued in people under age 30 years in the poorest countries, while only 3% is accrued under age 30 years in high-income countries. We conclude although the current global targets for noncommunicable disease and CVD control will help diminish premature CVD death in the poorest populations, they are not sufficient. Specifically, the current framework (1) excludes deaths of people <30 years of age and deaths attributable to congenital heart anomalies, and (2) emphasizes interventions to prevent and treat conditions attributed to behavioral and metabolic risks factors. We recommend a complementary strategy for the poorest populations that targets premature death at younger ages, addresses environmental and infectious risks, and introduces broader integrated health system interventions, including cardiac surgery for congenital and rheumatic heart disease. **(*Circulation*. 2016;133:2561-2575. DOI: 10.1161/CIRCULATIONAHA.116.008731.)**

Key Words: cardiomyopathies ■ cardiovascular diseases ■ congenital heart disease ■ epidemiology ■ global health ■ health equity ■ poverty ■ rheumatic heart disease

Worldwide, the burden of cardiovascular disease (CVD), and some of their behavioral and metabolic risk factors, have taken center stage in noncommunicable disease (NCD) policy.[1,2] The endemic burden of CVD among the world's poorest billion people, however, has been overlooked in global discussions. Epidemiological transition models based on the profiled causes of deaths related to CVD describe a progression from diseases of pestilence and famine to delayed degenerative diseases as countries develop economically.[3] Here we focus specifically on what is known about the endemic CVDs of pestilence and famine that are still part of the unfinished agenda for people living in extreme poverty. A systematic review of all available data on cardiovascular health among the poorest billion is beyond the scope of our article. We conclude with a series of research and policy recommendations to improve cardiovascular health among the poorest people.

Who Are the Poorest Billion?

The 2 most commonly used approaches for measuring poverty are (1) 1-dimensional approaches focused on income or

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wealth and (2) multidimensional approaches that attempt to provide a fuller picture by integrating information including education, health, and assets. Both approaches suggest that, in absolute numbers, the world's poorest billion are concentrated largely in rural sub-Saharan Africa and South Asia – though there are differences.[4,5] In 2012, there were ≈1 billion individuals worldwide living an income of < US$2.05 per day adjusted for 2011 purchasing power parity. By this income measure, around 41% of the poorest billion lived in sub-Saharan Africa; and another 37% lived in South Asia in 2012; and another 18% lived in East Asia, mainly in the rural Western China. About 4% of the poorest billion lived in Latin America and the Caribbean (Table I in the online-only Data Supplement).[4]

The Multidimensional Poverty Index, the most commonly used multidimensional method, integrates poverty measures from 10 indicators in 3 major dimensions: education, health, and living standards.[6] Multidimensional poverty measures allow assessment of both monetary and nonmonetary poverty. In rural China, for example, ≈40% of households were poor by Multidimensional Poverty Index, but not poor by income thresholds.[7] People with a weighted deprivation score of ≥44.4% comprise the poorest billion population across the globe. The location of the poorest billion using national-level (Figure 1, Table I in the online-only Data Supplement), and regional-level (Figure 2) data are shown. Subnational disaggregation shows the heterogeneous distribution of the poor. Further disaggregation of multidimensional poverty at the individual level (Table II in the online-only Data Supplement) shows that 54% of the poorest billion are concentrated in South Asia, whereas another 38% reside in sub-Saharan Africa. The remaining 8% are spread throughout East Asia and the Pacific (5%), the Arab States (1%), and Latin America and the Caribbean (1%). Niger is the country with the highest proportion of its population (82%) included within the poorest billion. Although the Multidimensional Poverty Index is comprehensive of three-quarters of the world's population, there are important limitations to its representativeness.[8] Countries without recent population surveys (since 2004) are excluded from analysis. Most significantly, Western China was excluded from subnational analysis because of lack of large representative recent surveys. A more detailed discussion is in the online-only Data Supplement.

Primary Data on the CVDs of the Poorest Billion

There are 3 main sources of primary information about CVD and its risk factors among the world's poorest billion people: (1) cardiovascular registries from facilities serving populations living in extreme poverty; (2) verbal autopsy studies of deaths in the poorest populations; and (3) population-based risk-factor surveys. The primary sources frequently lack individual socioeconomic information. In addition, there are few population health examination surveys in low-income populations that go beyond traditional CVD risk factors.

Facility-Based CVD Registries

Evidence from hospital registries in regions with a high concentration of the poor reveals a CVD epidemiology that is different from high-income settings. For comparison, in the First National Health and Nutrition Examination Survey in the United States, >60% of the population attributable risk for congestive heart failure was attributable to coronary heart disease.[9] In contrast, Table 1 shows the findings from heart failure registries from facilities likely to include a significant proportion of patients living in extreme poverty. We found registries from 12 countries in sub-Saharan Africa in addition to Haiti since 1996.[10–27] Even the registries share an urban or referral bias (only Rwanda had echocardiographic data from a secondary [district] hospital in a rural area).[12] Within a previous systematic review of heart failure studies, there were no published registries from geographic areas with high concentrations of extreme poverty within South Asia and Western China.[28]

Several patterns emerge from the African and Haitian registries. First, the causes of heart failure in the series are much more diverse than in high-income settings. The causes include hypertensive heart disease, cardiomyopathies, rheumatic heart disease, pericardial disease, and congenital heart anomalies.

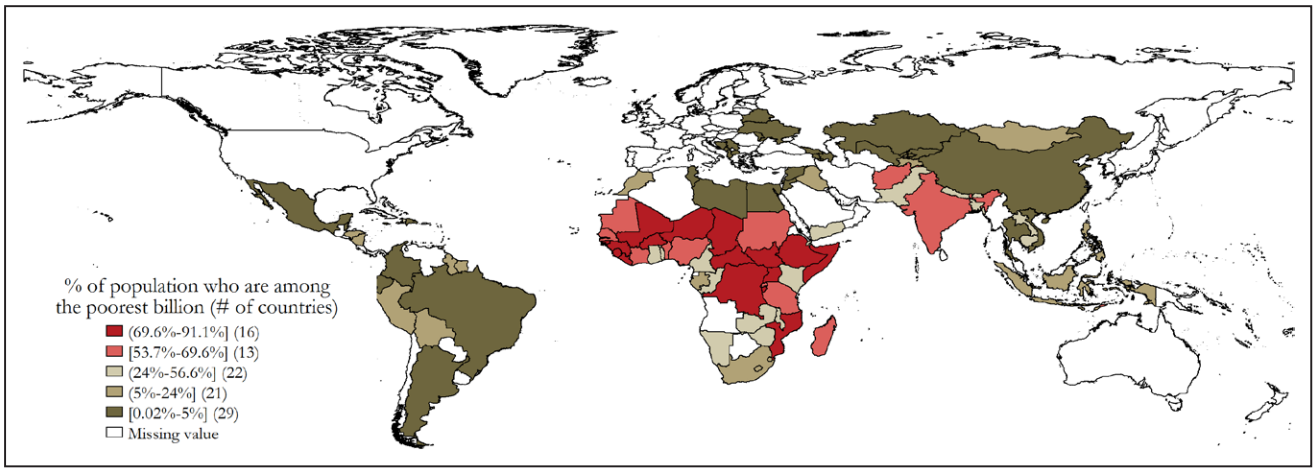

Figure 1. Poorest billion people identified at country level: Winter 2015.[8] The map shows the 29 poorest countries identified by the Winter 2015 Global Multidimensional Poverty Index (MPI ≥0.283). The countries were home to 1.1 billion people, using 2011 population figures. The red colors indicate the percentage of a country's population who are poor (individual MPI-weighted deprivation score ≥33.3%). The darkest red indicates the 16 poorest countries, each with ≥69.6% of population who are multidimensionally poor. Data for Algeria and Myanmar are older than 2004 and not included.

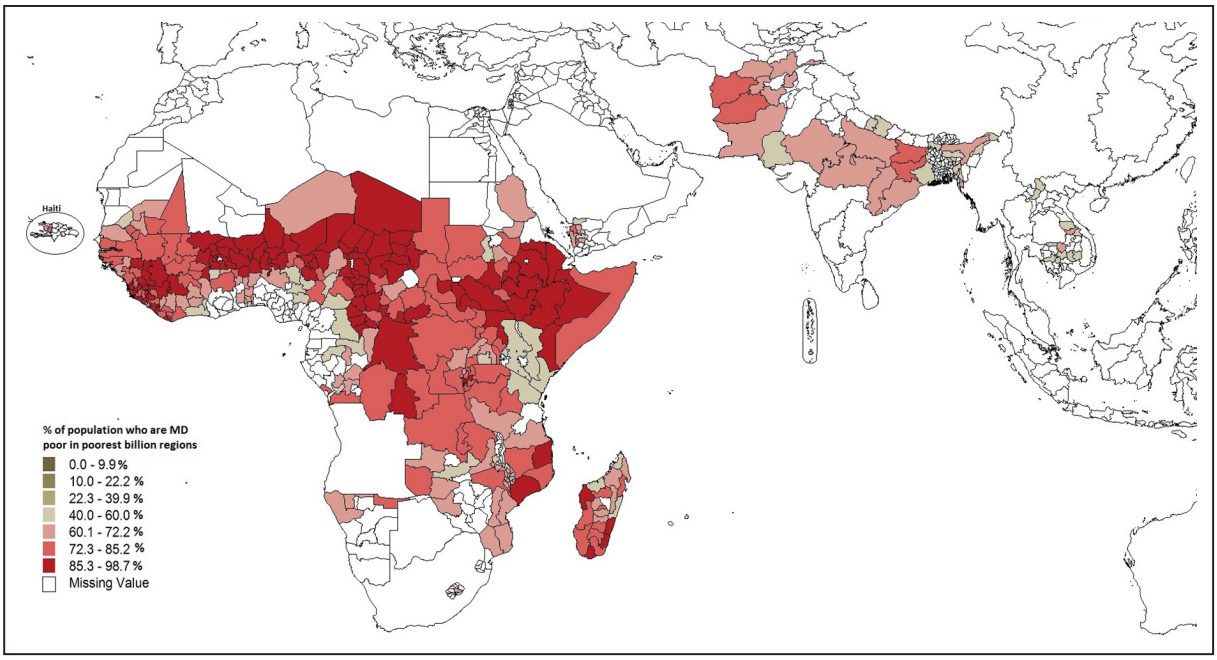

Figure 2. Poorest billion people identified at subnational level: Winter 2015.[8] The map colors shows the percentage of people in a subnational region who are multidimensionally poor (individual MPI-weighted deprivation score ≥33.3%). Haiti and the Dominican Republic are shown in the Inset. Countries and regions for which subnational data are not available or whose data are older than 2005 are not included in the analysis. MPI indicates multidimensional poverty index.

Second, ischemic heart disease (IHD) is relatively infrequent. For example, of 3908 cases of CVD in Malawi, only 3 patients had myocardial infarction.[19] Third, rural regions tend to have higher frequency of nonischemic cardiomyopathies and rheumatic heart disease relative to urban centers.

Of the recent anatomic autopsy series published from sub-Saharan Africa, IHD is generally infrequent at 3% to 6%.[29–31] In 1 series in Nairobi, IHD was found in 25% of patients whose family requested an autopsy, primarily to settle medical insurance claims, and is likely not representative of the poor.[32]

Verbal Autopsy Studies

In settings where most people die at home without clinical evaluation, verbal autopsy is a widely used tool to estimate cause of death based on interviews with caretakers and family members. The current 2014 World Health Organization Verbal Autopsy Standards include the following broad CVD categories: (1) acute (ischemic) cardiac disease, (2) cerebrovascular disease, and (3) other and unspecified cardiac disease.[33] There is potential for wide uncertainty and misclassification because the accuracy for verbal autopsy in comparison with clinical diagnosis may be <50%.[34,35] The INDEPTH network recently reviewed the results of verbal autopsy studies from 22 Health and Demographic Surveillance sites in predominantly rural, low-income settings.[36] The review shows that verbal autopsy studies report substantial variation in the ratio of estimated age-standardized nonischemic to ischemic cardiovascular mortality. The proportion of cardiac deaths due to IHD – as opposed to nonischemic causes – ranged widely from 7% to 85% across the verbal autopsy studies (Table III in the online-only Data Supplement). Nonetheless, despite the limitations in identifying CVD cause of death, verbal autopsy remains a valuable tool for population-based assessment in many regions.

Population-Based Risk-Factor Surveys

One of the greatest drivers of IHD risk is age.[36] Populations living in extreme poverty appear to be quite young because of high fertility rates. For example, in the poorest 16 countries in 2012, 84% of the population was <40 years of age.[37] For comparison, in more developed regions only ≈50% of the population was <40 years of age.[37] IHD risk typically rises exponentially only after 40 years of age.[38]

Population health surveys measuring CVD risk factors often include some form of socioeconomic information, allowing CVD risk data to be disaggregated by some measure poverty.[39,40] The complex patterns by geographic region are also instructive. Total tobacco exposure is relatively low in sub-Saharan Africa and poor regions of South America. However, even in sub-Saharan Africa, current smoking appears to be more prevalent among the poor and less educated than among wealthier populations.[41] However, the number of cigarettes consumed per smoker is lower in rural than in urban areas.[42] In South Asia, cigarette use is relatively low, particularly among women, although alternative forms of tobacco (bidis and oral tobacco) are more common.[41,43] In China, smoking prevalence is very high among men: higher in rural (56%) than urban (49%) settings, and higher in western China (59%) than other regions.[44]

Age-standardized mean systolic blood pressures in sub-Saharan Africa, particularly Central and Southern Africa, is among highest in the world, and has been rising.[45] Blood pressure as assessed in multinational community-based surveys is generally lower in rural regions than in urban regions.[39] The Prospective Urban Rural Epidemiology (PURE) study is a 17-country cohort including countries across the income spectrum. In low-income countries, prevalence of hypertension is high in rural settings (31.5%), although it is higher in urban areas (44.4%).[46] Awareness, treatment, and control of

Table 1. Heart Failure Registries in Sub-Saharan Africa and Haiti Since 1996. Percent of Diagnosed Heart Failure Cases by Category for Each

Author	Country	Year	Setting	N	Age*	HTN HD, %	CMP, %	RHD, %	IHD, %	Peric, %	CHA, %	Right HF, %	EMF, %	Other, %
Rural														
Tantchou Tchoumi et al[10]	Cameroon	2011	Rural	462	43	15	32	34	–	7	3	8	–	–
Kwan et al[11]	Haiti	2016	Rural	81	50	7	64	5	1	2	1	–	–	20
Kwan et al[12]	Rwanda	2013	Rural	192	35	6	41	32	–	5	15	–	1	–
Total (rural)†			Rural	735		12	38	30	0.1	6	6	5	0.3	2
Urban														
Jingi et al[13]	Cameroon	2013	Urban	1252	N/A	42	31	3	2	7	2	–	–	13
Damasceno et al. (THESUS-HF)[14]	Cameroon Ethiopia Kenya Mozambique Nigeria Senegal South Africa Sudan Uganda	2012	Urban	1006	52	45	29	14	8	7	–	–	1	7
Kingue et al[15]	Cameroon	2005	Urban	167	57	54	26	25	2	2	1	8	3	1
Amoah et al[16]	Ghana	2000	Urban	572	42	21	11	20	10	–	10	–	4	–
Bloomfield et al[17]	Kenya	2016	Urban	125	61	12	28	18	18	–	–	8	–	16
Oyoo et al[18]	Kenya	1999	Urban	91	55	18	25	32	2	13	2	8	–	–
Soliman et al[19]	Malawi	2008	Urban	3908	40	24	19	30	<1	14	4			8
Ojji et al[20]	Nigeria	2009	Urban	340	51	63	19	7	–	2	–	2	1	6
Ojji et al[21]	Nigeria	2013	Urban	475	N/A	61	24	9	–	–	–	3	–	3
Onwuchekwa et al[22]	Nigeria	2009	Urban	423	54	56	12	4	–	–	–	2	–	13
Ansa et al[23]	Nigeria	2008	Urban	245	N/A	37	34	13	–	–	–	–	–	16
Thiam et al[24]	Senegal	2003	Urban	170	50	34	7	45	18	–	–	–	–	–
Stewart et al[25]	South Africa	2008	Urban	844	55	33	28	8	9	–	–	14	–	–
Makubi et al[26]	Tanzania	2014	Urban	427	55	45	28	12	9	–	–	–	–	6
Freers et al[27]	Uganda	1996	Urban	406	N/A	9	10	14	1	–	18	–	24	–
Total (urban)†			Urban	10 360		34	22	18	3	7	3	2	1	7

CHA indicates congenital heart anomalies; CMP, cardiomyopathy; EMF, endomyocardial fibrosis; HF, heart failure; HTN HD, hypertensive heart disease; IHD, ischemic heart disease; N/A, not available; Peric, pericardial disease; and RHD, rheumatic heart disease.

*Age reported as mean or median.

†Totals are mean percentage weighted by study size.

hypertension were lower in low-income countries than in middle-income countries, and lower in rural than in urban areas.

Age-standardized rates for overweight and obesity are the lowest in the world in South Asia and Central and Eastern sub-Saharan Africa, whereas underweight is most prevalent.[47] However, there is notably high obesity prevalence in Southern and Western Africa, particularly among women.[47] Low physical activity is overall least prevalent in sub-Saharan Africa and South Asia in comparison with worldwide estimates.[48] However, there is regional variation with relatively higher rates of low physical activity in West Africa. Furthermore, people throughout sub-Saharan Africa generally experience heavy occupational physical activity, which may not be as cardioprotective as recreational activity.[49]

Diabetes mellitus currently has low prevalence throughout sub-Saharan Africa, although relatively high prevalence in South Asia; though it is rising in both regions at rates that are higher than what would be expected based on trends in obesity.[50] Within Malawi, for example, there is no substantial difference in diabetes

prevalence with education level.[51] Likewise, cholesterol levels in sub-Saharan Africa are among the lowest in the world, and do not seem to be rising as they have in East Asia.[52] In South Asia, mean cholesterol has been stable and slightly less than global averages.[52]

Heavy episodic alcohol consumption is associated with increased IHD, stroke, and atrial fibrillation.[53] Episodic drinking is second highest in sub-Saharan Africa and in Latin America and the Caribbean, after Eastern Europe.[54] Fruit and vegetable intake is another exception, with low consumption in the world's poorest regions.[55] Availability and cost of a healthy diet may be prohibitive for the poorest populations who consume less healthy processed carbohydrates and lower quality fats, such as palm oil.[55]

Environmental, Infectious, and Early Life Nutritional Risk Factors

The poorest billion are disproportionately exposed to air pollution and infectious risk factors for CVD. Persistent biomass fuel use among the poor is well documented in censuses and demographic and health surveys. Approximately 3 billion people living in low- and middle-income countries are exposed to household air pollution from the use of biomass fuel.[56] Exposure to small particulate matter, and other components of biomass smoke, as well, are thought to contribute to hypertension.[57] Biomass smoke exposure may also contribute to right heart failure, potentiating the effect of other endemic causes of pulmonary hypertension including infectious lung diseases.[58] Women, who perform a majority of the cooking, often in poorly ventilated kitchens, endure the greatest exposure.[59] However, a direct link between household air pollution and CVDs has not yet been demonstrated. The associations between higher ambient fine-particle concentration and increased risk of IHD, stroke, and heart failure are more clear.[60] Important sources of ambient fine-particle pollution include road dust and vehicle/industrial emissions, residential biomass and coal burning, road dust, and dust blown from deserts. Solid-waste burning was also a significant contributor to pollution in poor neighborhoods in Ghana, but not more wealthy neighborhood.[61] South Asia has some of the highest ambient particulate matter levels worldwide and increasingly many African cities have levels higher than high-income cities.[62]

Long-term exposure to lead is associated with high blood pressure and clinical CVD. Populations in Central and Southern Africa and South Asia have some of the highest bone lead concentrations in the world.[63] Phasing out of leaded fuel and has begun only lately in low- and middle-income countries.[63]

Infectious risk factors are an underappreciated cause of CVD among the poor. Infectious drivers of CVD include Chagas disease, enteroviruses, schistosomiasis, tuberculosis, streptococcal pharyngitis, human immunodeficiency virus, rubella, and other causes of inflammation.[64] There is substantial geographic variation in exposure to pathogens related to CVD even among the poor. We discuss the endemic CVDs associated with infectious diseases in more detail in the online-only Data Supplement, but there is a need to better quantify their contribution to the cardiovascular burden.

Fetal and early childhood undernutrition is also related to CVD later in life. Genetically determined short stature is associated with increased risk of CVD death in adulthood.[65] Early childhood undernourishment has been associated with elevated cholesterol, elevated fasting plasma glucose, and increased IHD risk.[66] The highest stunting rates in the world are in sub-Saharan Africa and South Asia.[67]

Global Burden of Disease Study

The Global Burden of Disease (GBD) study uses statistical models to estimate worldwide disease burden based on systematic reviews of primary data.[68] Available data sources, including vital registration and verbal autopsy data, are combined in the GBD study with Bayesian methods to generate estimates of death and disability attributable to CVD.

As a first approximation of the CVD burden among the poorest, we have analyzed GBD 2013 study data by World Bank country income classification. In addition, we have also analyzed GBD data for the 16 countries in which ≥70% of the population was living in multidimensional poverty (≥33.3% weighted deprivation), and in which ≥50% were among the poorest billion (≥44.4% of weighted deprivations). The 16 poorest countries have a combined population of ≈330000 people, and are all in sub-Saharan Africa (Niger, Ethiopia, South Sudan, Chad, Burkina Faso, Somalia, Sierra Leone, Guinea-Bissau, Guinea, Mali, Burundi, Central African Republic, the Democratic Republic of Congo, Mozambique, Liberia, and Uganda). Subnational disease burden and risk assessment in the GBD study is currently limited to Mexico and China and is not linked to socioeconomic measures. As a result, we were not able to include subnational regions with high poverty prevalence in middle-income countries in our analysis.

We should note here several ways in which we part with some common conventions in analysis of CVD in the GBD study. First, we describe "combined CVDs" to include both GBD categories of "congenital heart anomalies" and "cardiovascular diseases". We also use crude rates, rather than age-standardized rates given the younger age distribution of poorer populations (age-standardized rates are presented in figures in the online-only Data Supplement). We also focus on disability-adjusted life-years (DALYs) rather than on deaths to account for the importance of death at younger ages.

Estimated CVD Burden Among the Poorest in the GBD Study

We find that, although NCDs as a whole are a significant fraction of the disease burden in the poorest countries, CVD alone, and more specifically IHD, is not (Figure 3). We find that NCDs, CVD, and IHD become progressively less important relative to total burden and to each other in lower-income groups. In the poorest 16 countries, CVD (5.5% of DALYs and 3% of deaths) and IHD (1% of DALYs and 3% of deaths) have an overall small contribution to total disease burden. In contrast, in high-income countries, CVD (18% of DALYs and 38% of deaths) and IHD (9% of DALYs and 20% of deaths) have greater contributions where deaths occur at older ages.

Among the poorest 16 countries, the leading causes of combined CVD DALYs are congenital heart anomalies (19.5%), IHD (18.8%), and hemorrhagic stroke (18.3%; Table 2).[69] However, the leading causes of CVD deaths are estimated to be IHD (26%) and hemorrhagic (23%) and ischemic stroke (19%). The relative prominence of congenital heart anomaly DALY burden in comparison with mortality reflects disease onset at earlier ages. Although still relatively low, the proportion of GBD-estimated IHD deaths as a fraction of total

Table 2. Estimated Crude DALYs and Deaths From CVD Including Congenital Heart Anomalies in the 16 Poorest Countries With ≥70% of the Population Living in Multidimensional Poverty, and ≥44.4 of Weighted Deprivations* Both Sexes, GBD 2013 Study[69]

CVD Category	DALYs per 100 000		% of CVD DALYs	Total Deaths		Deaths per 100 000		% of CVD Deaths
	Rate	95% Uncertainty Interval		Number	95% Uncertainty Interval	Rate	95% Uncertainty Interval	
Congenital heart anomalies	694	(291–1504)	19.5	28 708	(12 185–61 888)	8.2	(3.5–17.7)	6.9
Ischemic heart disease	669	(523–837)	18.8	101 480	(79 356–127 513)	29.1	(22.7–36.5)	24.5
Hemorrhagic stroke	650	(476–880)	18.3	89 538	(62 453–127 470)	25.6	(17.9–36.5)	21.6
Other cardiovascular and circulatory diseases	448	(297–700)	12.6	45 449	(29 401–74 956)	13.0	(8.4–21.5)	11.0
Ischemic stroke	382	(180–537)	10.8	73 813	(34 993–102 649)	21.1	(10.0–29.4)	17.8
Cardiomyopathy and myocarditis	223	(142–313)	6.3	18 723	(12 472–26 327)	5.4	(3.6–7.5)	4.5
Hypertensive heart disease	211	(140–309)	5.9	33 290	(21 375–51 642)	9.5	(6.1–14.8)	8.0
Rheumatic heart disease	187	(134–292)	5.3	13 707	(9174–23 753)	3.9	(2.6–6.8)	3.3
Endocarditis	60.0	(38.9–87.7)	1.7	5858	(3976–8606)	1.7	(1.1–2.5)	1.4
Aortic aneurysm	25.4	(15.3–39.9)	0.7	3794	(2341–5954)	1.1	(0.7–1.7)	0.9
Atrial fibrillation and flutter	5.2	(3.4–7.4)	0.15	117	(56–201)	0.03	(0.02–0.06)	0.03
Peripheral vascular disease	1.6	(0.9–2.5)	0.04	175	(108–271)	0.05	(0.03–0.08)	0.04
Combined CVD	3557	(2242–5509)	100	414 651	(398 128–447 831)	118.7	(114.0–128.2)	100
Combined CVDs as a proportion of total burden			5.5					12.4

CVD indicates cardiovascular disease; DALY, disability-adjusted life-year; and GBD, Global Burden of Disease.

*Sixteen poorest countries by multidimensional poverty index (% of population with ≥ 44.4% of weighted deprivations): Niger (82%), Ethiopia (79%), South Sudan (82%), Chad (78%), Burkina Faso (71%), Somalia (72%), Sierra Leone (65%), Guinea-Bissau (64%), Guinea (61%), Mali (64%), Burundi (65%), Central African Republic (63%), Democratic Republic of the Congo (63%), Mozambique (57%), Liberia (51%), and Uganda (52%).

CVD deaths (15%) in the poorest countries contrasts with the general absence of IHD as a cause of heart failure in the low-income country CVD registries previously described.

Risk-Factor Attribution for CVD in the GBD Study

The GBD study attributes a select group of underlying risks in 3 overlapping major categories – behavior, metabolic, and environmental/occupational – to the mortality and morbidity estimates. The behavioral risks that impact CVD are tobacco, alcohol and drug use, low physical activity, and selected dietary risks. The metabolic risks are systolic high blood pressure (≥115 mm Hg), high body mass index, high fasting plasma glucose, high total cholesterol, and low glomerular filtration rate. The environmental risks that impact CVD are household and ambient

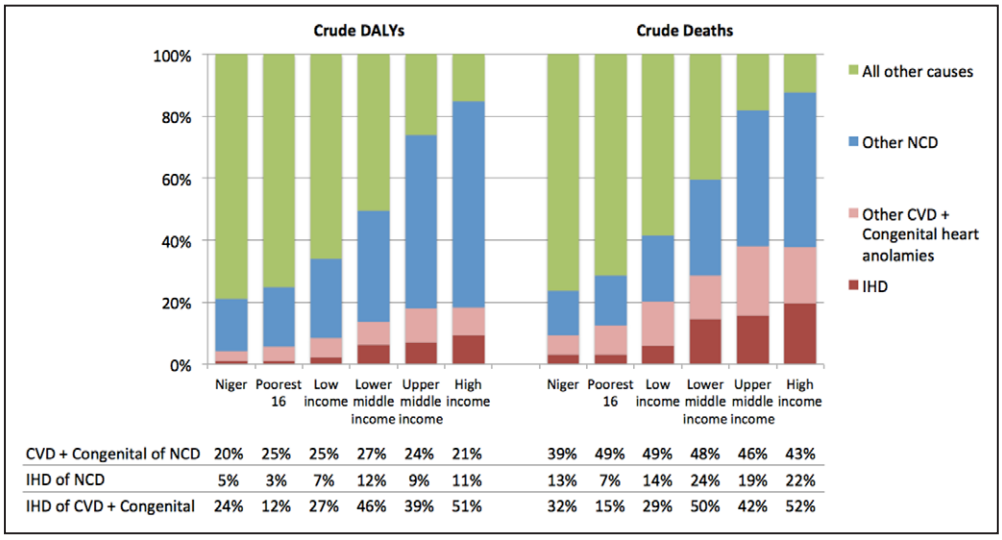

Figure 3. Proportion of crude DALYs from IHD, CVD (including congenital heart anomalies), and NCDs by World Bank income grouping and for the 16 countries with ≥70% of the population living in multidimensional poverty.[67] CVD indicates cardiovascular disease; DALY, disability-adjusted life-year; IHD, ischemic heart disease; and NCD, noncommunicable disease.

Table 3. Crude DALYs per 100 000 Population (%) by Risk Factor Category and Country Income Grouping, GBD Study 2013

Risk Factor Category*	Niger†	Poorest 16 Countries	Low Income	Lower Middle Income	Upper Middle Income	High Income	Global
Congenital heart anomalies							
Behavioral and metabolic risk factors	–	–	–	–	–	–	–
Environmental/occupational risk factors	–	–	–	–	–	–	–
Unattributed	672 (100)	694 (100)	597 (100)	475 (100)	310 (100)	105 (100)	366 (100)
Total	672 (100)	694 (100)	597 (100)	475 (100)	310 (100)	105 (100)	366 (100)
CVDs							
Behavioral and metabolic risk factors	1629 (69)	2039 (71)	2849 (79)	4152 (85)	3910 (89)	4439 (87)	3966 (86)
Environmental/occupational risk factors	728 (31)	916 (32)	1283 (36)	1408 (29)	1166 (27)	472 (9)	1141 (25)
Unattributed	695 (29)	736 (26)	661 (18)	661 (14)	417 (10)	623 (12)	571 (12)
Total	2378	2863	3609	4883	4386	5094	4599
Combined CVD and congenital heart anomalies							
Behavioral and metabolic risk factors	1629 (53)	2039 (57)	2849 (68)	4152 (77)	3910 (83)	4439 (85)	3966 (80)
Environmental/occupational risk factors	728 (24)	916 (26)	1283 (30)	1408 (26)	1166 (25)	472 (9)	1141 (23)
Unattributed	1367 (45)	1430 (40)	1258 (30)	1137 (21)	727 (15)	728 (14)	937 (19)
Total	3049	3557	4206	5358	4696	5199	4965

CVD indicates cardiovascular disease; and DALY, disability-adjusted life-year.

*The behavioral and metabolic category includes any overlap with environmental/occupational. The environmental/occupational category includes any overlap with behavioral and metabolic. Because of multicausality and the resulting overlap, the sum of the DALY rates in a given column will be greater than the total and greater than 100%.

†Niger is the country with the largest proportion of its population (82%) within the world's poorest billion people.

air pollution and lead exposure. No early childhood risk factor for CVDs is quantified. The burden not attributed to any modeled risk factor is also reported.

To better understand the disease burden attributable to traditional CVD risks factors, we analyzed the proportion of CVD DALYs that are explained by (1) behavioral and metabolic risk factors; (2) environmental risk factors; and (3) burden not attributed to any modeled risk for each of the country groups described above (Figure 4, Table 3).[69] Our presentation accounts for multicausality within the disease burden. For example, high sodium intake (a behavioral risk factor) and lead exposure (an environmental risk factor) both contribute to the hypertensive heart disease burden, with all or some of their burden mediated by high blood pressure. We describe the proportion of the burden attributable to both of behavioral/metabolic and environmental risk factors as an overlap. The

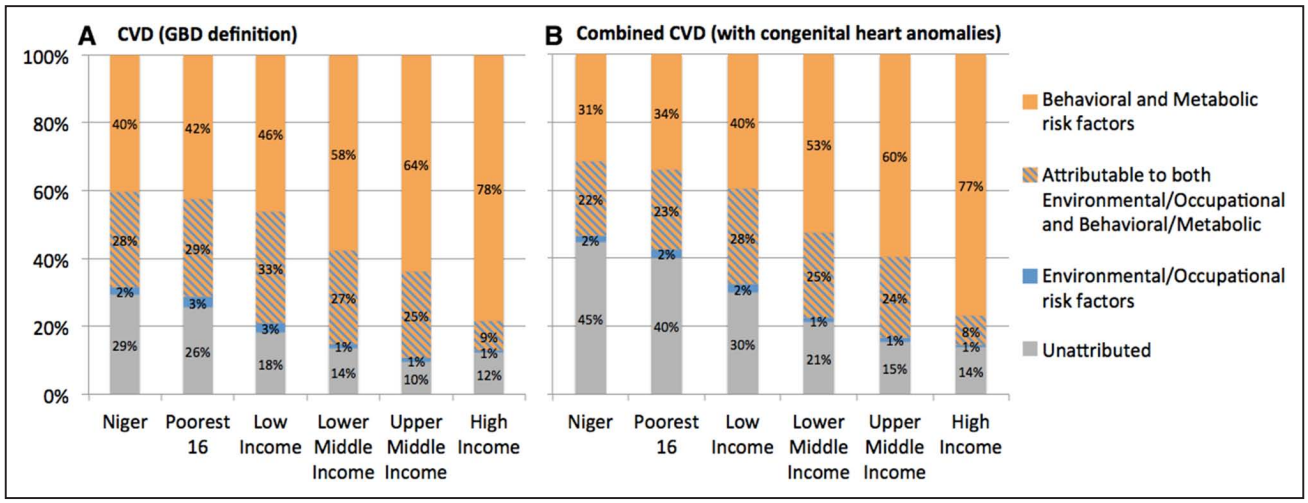

Figure 4. The proportion of crude DALYs attributable to risk-factor categories for CVD (excluding congenital heart anomalies; **Left**) and combined CVD and congenital heart anomalies by World Bank income category, the GBD study (**Right**). The risk factor categories include environmental/occupational, and unattributed risk factors (green), behavior and metabolic risk factors excluding overlap with environmental/occupational (orange) environmental/occupational excluding overlap with behavior and metabolic (blue), both environmental/occupational and behavioral/metabolic (orange and blue stripe), and unattributed risk factors (grey). All congenital heart anomaly DALYs are unattributed to any quantified risk.

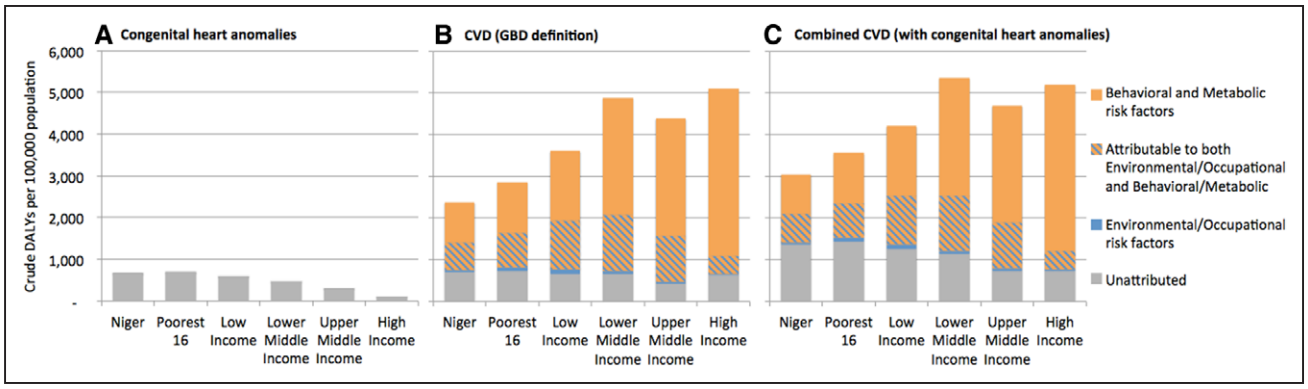

Figure 5. Crude DALYs per 100 000 population attributable to risk factor categories for congenital heart anomalies (**Left**), CVD (as defined in the GBD study; **Center**), and combined CVD including congenital heart anomalies by World Bank income category, the GBD study (**Right**). The risk factor categories include behavior and metabolic risk factors excluding overlap with environmental/occupational (orange) environmental/occupational excluding overlap with behavior and metabolic (blue), both environmental/occupational and behavioral/metabolic (orange and blue stripe), and unattributed risk factors (grey).

behavioral/metabolic category includes the overlap between the individual component risk categories.

We found that the fraction of CVD risk attributable to behavioral and metabolic risks was inversely related to income level. For the poorest countries, the proportion of CVD DALYs attributable to selected behavior/metabolic risk factors (including the overlap with environmental risk factors) was 71%; it declined to 57% when congenital heart anomalies – which are unattributed to any of the quantified risks – was included. With increasing income, the proportion of behavioral and metabolic risk factors rises to 87% for CVDs in high-income countries, and 85% when congenital heart anomalies are included. Twenty-three percent of the burden is estimated to be attributable to overlapping risks in the poorest countries. For the poorest billion, the burden due to behavioral and metabolic risk factors may be as low as 53%, as it is in Niger. The high burden of congenital heart anomalies for the poorest populations stems from greater exposure to infectious risk factors and lack of access to surgical care.[70] With access to appropriate medical and surgical care in developed countries, more than 90% of patient with congenital heart anomalies survive to adulthood.[71]

In addition, we analyzed the crude DALY rates and their risk factor attribution for (1) congenital heart anomalies, (2) CVD, and (3) combined CVD including congenital heart anomalies (Figure 5, Table 3). We found that congenital heart anomalies DALY rates (unattributed to any modeled risk factor) are much higher in the poorest 16 countries (694 DALYs per 100 000) compared with high-income countries (105 DALYs per 100 000). The burden of CVDs is lower in the poorest 16 countries (2863 DALYs per 100 000) compared with high-income countries (5094 DALYs per 100 000). The rate of combined CVDs including congenital heart anomalies is lower in the poorest 16 countries (3557 DALYs per 100 000) than high-income countries (5199 DALYs per 100 000). For CVDs (excluding congenital heart anomalies), the crude burden attributable to behavioral and metabolic risk factors rises from 2039 DALYs per 100 000 (poorest countries) to 4439 DALYs per 100 000 (high-income countries). When including congenital heart anomalies within combined CVDs, the burden attributable to behavioral and metabolic risk factors is much lower in the poorest countries (2039 per 100 000) than in high-income countries (4439 per 100 000). Conversely, DALY rates not ue to behavior or metabolic risks (unattributed burden and the portion of environmental burden which does not overlap behavior/metabolic) is higher in the poorest 16 countries (1518 DALYs per 100 000) than in high-income countries (760 DALYs per 100 000).

The crude burden reported is particularly relevant for establishing priorities within countries with a large proportion of the poor. Age-standardized estimates account for varying age distributions between countries and show there remains a gradient of inequity across countries by income category, though the magnitude is attenuated (Figures I and II and Table V in the online-only Data Supplement). For CVDs, behavior and metabolic risk factors account for 80% of the burden in the poorest countries and 87% in high-income countries. For combined CVDs including congenital heart anomalies, behavior and metabolic risk factors account for 75% of DALYs in the poorest countries and 84% in high-income countries.

Finally, we analyzed the crude DALY rate for CVD attributed to high systolic blood pressure (Figure 6). We found that,

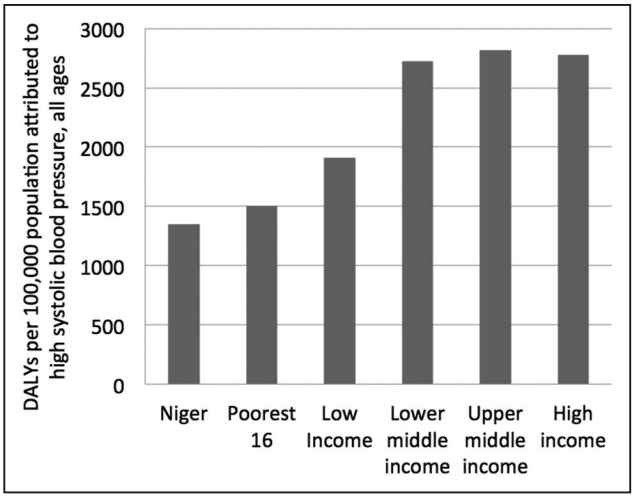

Figure 6. DALYs per 100 000 population attributable to systolic blood pressure (SBP) ≥115 mm Hg by World Bank income category, all ages, the GBD study. DALY indicates disability-adjusted life-year; and GBD, Global Burden of Disease.

because of the older age structure of high-income populations, the crude DALY rate for high blood pressure increases with increasing income. At the same time, high systolic blood pressure accounts for 42% of the combined CVD (including congenital heart anomalies) DALY rate (1500/3557 DALYs per 100 000) in the poorest countries, versus 53% (2776/5199 DALYs per 100 000) in high-income countries.

Challenges in Describing the CVD Burden of the Poorest

As we have discussed, facility-based cardiovascular registries appear to suggest lower burden of IHD in low-income countries than those estimated in the GBD study. Here we speculate why the GBD study may tend to overestimate the importance of IHD among the poor relative to other causes of cardiovascular mortality such as RHD.

For its cause of death and mortality estimates, GBD relies on vital registration systems and verbal autopsy studies. Vital registration data come primarily from high- and middle-income countries. In sub-Saharan Africa, for example, <5% of deaths, mostly concentrated in urban areas, are recorded.[72] In fact, the entire region of central sub-Saharan Africa has no vital registration or verbal autopsy data. Only a handful of sub-Saharan African countries contributed cause of death data to the GBD 2013 study: verbal autopsy data are available from Burkina Faso, Ethiopia, Mozambique, South Africa, and Tanzania; vital registration sources include Mauritius, Seychelles, and South Africa, with limited data from Mali, Mozambique, and Zimbabwe.[73] Where data are lacking, cause-of-death assignments are modeled starting with data from neighboring countries and adjusted for country-level covariates such as education, income, and blood pressure levels. Data inputs such as other risk factor prevalence and health facility registries are difficult to incorporate into the GBD modeled cause-of-death estimates. Furthermore, heart failure is not considered an underlying cause of death or disability in the *International Classification of Diseases* system.[74] Thus, the apparent heart failure burden is distributed among the underlying root CVD causes.[74] For sub-Saharan Africa, heart failure is attributed to hypertension (≈30%), cardiomyopathy (≈25%), valvular disease (≈15%), and IHD (≈5%).[26] Although the resultant modeled estimates for sub-Saharan Africa have wide uncertainty, they likely represent the best available population-based regional estimates.

Angina is the main source of IHD disability apart from heart failure. The Rose angina questionnaire is the most commonly used survey tool to assess angina. However, the questionnaire overestimates angina prevalence in settings where IHD is uncommon.[74]

The Endemic CVDs of Poverty

The findings from both the primary data and our analysis of the GBD study are consistent with a CVD distribution among the poor that is substantially less dominated by IHD and includes a broader range of conditions associated with infectious, environmental, and as-yet-unquantified early childhood risk factors.[75] Summarized in Table 4, they principally include hemorrhagic and ischemic stroke and heart failure from various causes, including hypertensive heart disease, nonischemic cardiomyopathies, rheumatic heart disease, congenital heart anomalies, right heart failure, and endomyocardial fibrosis. Further discussion can be found in the online-only Data Supplement.

The pattern of behavioral risks among the poor is distinct compared to more affluent populations. Generally, the poorest billion people lack the choice to live in healthier environments, access basic health systems, or to choose healthy foods and behaviors.[55,86] Despite the fact that the largest number of people living under multidimensional poverty are in Africa and South Asia, a distinct pattern of CVD risk factors is present in rural areas of Latin America.[87] For example, in rural Peru, 76% of people in a community-based sample did not have any of the 6 most common CVD risk factors.[87] Our summary supports a predominance of cardiovascular conditions that have long been endemic among the poorest populations.[88]

Appropriate Targets and Interventions for CVD Control Among the Poorest

The 9 targets of the global monitoring framework for NCD control have focused on the reduction of behavioral risks (salt, tobacco, alcohol, physical inactivity) and metabolic risks (high blood pressure, diabetes mellitus, and obesity), and on multidrug therapy for treatment of individuals at high risk of heart attack and stroke based on these risks.[89] Achieving the behavioral and metabolic risk targets is expected to contribute toward a 25% mortality reduction between the ages of 30 and 70 years for CVD, cancer, diabetes mellitus, and chronic lung disease by 2025. Several studies have modeled the 10-year effects of achieving the risk factor targets on age 30 to 70 year cardiovascular mortality in different regions of the world.[80,81] There is regional variation in the degree of CVD mortality reduction. Kontis et al[90] evaluated sub-Saharan Africa as a macro-region and found that achieving the risk-factor targets will contribute to but not achieve a 25% reduction in CVD by 2025, largely because some of the leading causes of premature NCD mortality, like cervical cancer and RHD, have no or limited association with the targets. Roth et al,[91] using GBD study data, projected that the goal will be achieved in Eastern and Southern sub-Saharan Africa, but not in the more impoverished Central or Western sub-Saharan Africa regions. Both studies suggest achieving the targets would result in large reductions of CVD deaths.[90,91] Lowering blood pressure is the main driver of overall CVD improvements, while the other behavioral and metabolic risk factors had much smaller contributions.[90,91]

Although we agree that the current global targets for NCD and CVD control will result in reductions in CVD burden, the results above indicate that the global targets are insufficient for the world's poorest populations because of the differences in CVD epidemiology. Specifically for CVD, the greatest deficiencies of the global target are the exclusion of deaths from congenital heart anomalies and deaths at <30 years of age from the analytic frame, and the absence of focus on infectious causes of CVDs.

In the poorest countries, up to 75% of the population is <30 years of age, whereas in high-income countries ≈70% of the population is >30 years of age.[37] Furthermore, many of the CVDs associated with risk factors of material poverty, such as rheumatic heart disease and some cardiomyopathies, strike at young ages. Finally, congenital heart anomalies go virtually

Table 4. Endemic CVDs of the Poor and Risk Factors

CVD Type	Poverty-Related Risk Factors for Premature Death (Including Lack of Awareness and Treatment of Underlying Conditions)	Estimated Burden	Source
Hemorrhagic stroke	High blood pressure Low fruit and vegetable intake	905 DALYs/100 000 people in low-income countries	GBD 2013[69]
Ischemic stroke	High blood pressure Cardioembolic causes: RHD, endocarditis, peripartum cardiomyopathy HIV Hemoglobinopathies	521 DALYs/100 000 people in low-income countries	GBD 2013[69]
Hypertensive heart disease	High blood pressure	255 DALYs/100 000 people in low-income countries	GBD 2013[69]
Cardiomyopathies	Chagas disease HIV Other viruses Severe anemia Micronutrient deficiencies	175 DALYs/100 000 people in low-income countries	GBD 2013[69]
Peripartum cardiomyopathy	Multiple gestation Malnutrition Lack of access to birth control	1 in 300 live births (Haiti) 1 in 1000 (South Africa) 1 in 1000–4000 (United States)	Single-center case series[76]
Chagas disease	*Trypanosoma cruzi* Living in homes with mud walls or thatched roofs Lack of parasite control Lack of medical insurance Low education Overcrowding	37 000 cases/y	[77–79]
Rheumatic heart disease	Recurrent group A streptococcal pharyngitis Crowded housing Lack of access to penicillin	183 DALYs/100 000 people in low-income countries Prevalence may be 36 million	GBD 2013[69,80]
Pericardial disease	Tuberculosis	≈7% of all TB cases: 700 000 people worldwide.	
Congenital heart anomalies	Maternal rubella Maternal diabetes mellitus Micronutrient deficiencies (folate) Herbicides and pesticides	8–9/1000 live births ≈190 000 deaths/y	[70, 81, 82]
Right heart failure	Acute respiratory infections Ambient air pollution Tuberculosis Schistosomiasis	20–25 million	[83]
Endomyocardial fibrosis	Unknown	Not well estimated, but sporadically significant in, eg, southern Uganda, parts of Mozambique	[84,85]

CVD indicates cardiovascular disease; DALY, disability-adjusted life-year; GBD Global Burden of Disease; HIV, Human immunodeficiency virus; and RHD, rheumatic heart disease.

untreated in the poorest populations in comparison with high-income populations. Consequently, about 34% of DALYs due to CVD (including congenital heart anomalies) are accrued before of 30 years of age in the poorest 16 countries (Table VII of the online-only data supplement). Meanwhile, only 3% of combined CVD DALYs (including congenital heart anomalies) are accrued before 30 years of age in high-income countries.

The limited framing of the global NCD and CVD mortality reduction target has been accompanied by a similarly

Table 5. Gaps/Challenges and Future Directions for Research and Policy

Gap/Challenge	Potential Solution/Future Direction
Improved disease surveillance data for decision making.	
Aggregated data hide the specific diseases of the poor.	Data sources must include people from all socioeconomic strata and all regions within a country, particularly rural. Include further subnational estimates within the Global Burden of Disease Study
Vital registration systems have incomplete coverage in LMICs.	Encourage low-cost vital registration techniques that include cause of death determination. Expand the Data for Health initiative to support LMICs to integrate mobile technologies in strengthening vital registration systems.
Verbal autopsy may not be accurate for endemic CVDs and may bias toward ischemic heart disease.	Further validation studies of verbal autopsy specifically assessing heart failure accuracy.
Lack of access to diagnostic tools for CVD in rural LMICs.	Expand availability or portable and handheld echocardiography using task shifting/sharing and telemedicine.
Within the International Classification of Diseases structure, heart failure burden is ascribed to the underlying preventable root cause, deemphasizing heart failure as a major cause of morbidity and mortality.	Reclassify heart failure as a cause of morbidity and mortality to better estimate its public health importance.
Identifying the poorest billion for data disaggregation	
Assessment of socioeconomic status and wealth are absent from most disease surveillance systems.	Integrate assessment of socioeconomic status or wealth into vital registration and disease surveillance systems.
Standard questionnaires to measure wealth, income, or expenses are long and cumbersome.	Use simplified asset indices for many LMICs derived from existing Demographic and Health Survey data, which are easy to use, have good agreement, and are freely available at www.equitytool.org.
Using income alone to define poverty is too narrow.	Use multidimensional poverty assessments to more accurately describe the simultaneous deprivations of the poor.
Equity-based CVD reduction targets	
Current UN targets exclude premature morbidity from children and young adults who have endemic CVDs.	Expand the age ranges for premature CVD reduction goals to include people <30 y.
Current CVD mortality reduction goals use deaths, which hide the burden of disease in the relatively young populations of the poor, and do not weight premature deaths among the young.	Express a CVD mortality in terms of reducing the rate of years of life lost. Mortality targets could explicitly include deaths at young ages, such as <40 y.
Current CVD reduction goals and targets exclude risks from infections, early childhood, and the environment, which affect the poor.	Include additional targets promoting the strengthening of integrated health systems and environmental and infectious risk factors, which are more pertinent to endemic CVDs.
Current health system targets exclude infectious risks and are not tailored for heart failure.	Expand multidrug therapy targets to include heart failure, in addition to stroke and ischemic heart disease.
Public health policies promoting health equity	
Poverty is the root cause of many endemic CVDs.	Multisector approach to addressing health, education, finance, labor, infrastructure, and agriculture for primordial prevention. Equity audits of interventions to ensure the most vulnerable people will realize the benefit. Improve fetal and early childhood nutrition.
Current cost-effectiveness analyses focus only on health gains or losses.	Further research using extended cost-effectiveness analysis of interventions evaluating additional outcomes such as poverty alleviation.
Current hospital-based health care in LMICs does not reach the poor.	Decentralized health systems including primary care clinics and community-based care need strengthening.
Catastrophic health-related expenses exacerbate the diseases of poverty.	Aspire toward universal health coverage to support financial risk protection.
Healthcare workforce in rural LMICs is sparse.	Further research evaluating the effectiveness of task shifting/sharing and community health workers for endemic CVD prevention and management. Incorporate endemic CVD care training into local medical and nursing schools and postgraduate programs
Lack of locally adapted and appropriate clinical guidelines and protocols.	Development of locally endorsed and contextually appropriate evidence-based protocols.

CVD indicates cardiovascular disease; GBD Global Burden of Disease LMIC, low- and middle-income countries; and UN, United Nations.

limited focus on behavioral and metabolic risk factors and their associated diseases. In addition, the 2 health system targets primarily also address metabolic risks: (1) available and affordable medicines for NCDs, and (2) preventive medicines for people at high risk of heart attack and stroke. Our analysis of GBD study data including death and disability at <30 years of age (eg, attributable to congenital heart anomalies and RHD), and focusing on DALYs rather than deaths, suggests that there is a significant opportunity to reduce the CVD burden in the poorest populations through a broader set of interventions; this analysis is summarized in Table 5. These finding are also supported by our review of primary data.

A CVD mortality target appropriate for the world's poorest could be expressed in terms of reductions in the crude rate of years of life lost as suggested recently in the context of the Sustainable Development Goals.[92] Or alternatively, mortality targets could explicitly prioritize deaths at younger ages, as affirmed by NCD divisions in several Eastern and Southern African countries calling for an 80% reduction in mortality from NCDs and injuries before 40 years of age.[93] The World Heart Federation has also endorsed a goal of reducing cardiovascular mortality <25 years of age in the context of its rheumatic heart disease control strategy.[94]

Strategies to achieve such broader mortality targets in the poorest populations would likely include attention to environmental risks, and broader healthcare interventions to address structural heart disease, as well.[95,96] Critical healthcare interventions include cardiac surgery at referral centers for congenital heart anomalies and advanced RHD.[97] In addition, integrated delivery models are needed to decentralize initial echocardiographic diagnosis and management of heart failure and RHD (including anticoagulation) to district hospitals.[12,98,99] Health centers need to be equipped to both identify and manage suspected streptococcal pharyngitis, rheumatic fever, hypertension, and stable RHD as part of primary care.[100–102] Community health workers need to be equipped to both offer adherence support and refer sick individuals to higher levels when necessary. Interventions to address mental health among those with established cardiac disease need to be introduced as part of a process of chronic care integration and decentralization.[103]

The World Health Organization's 2011 investment case to achieve global targets for NCD control called for ≈US$11.4 billion per year.[104] Approximately 75% of the investment was directed toward multidrug therapy for individuals at high CVD risk. Ninety-five percent of proposed funds were directed toward middle-income countries.

To rebalance and reinvigorate the global conversation on NCDs in the interest of those living in extreme poverty, *The Lancet* has convened a Commission on "Reframing NCDs and Injuries for the Poorest Billion."[105] The Commission will provide the analytic basis for integrated country-level investment prioritizing the specific needs of the world's poorest people. The Commission's report in 2017 will catalyze progress toward global health equity and poverty eradication. This publication is part of a contribution to that effort.

Conclusion

The poorest billion people are spread throughout the world. Estimating the CVD epidemiology of the poor is challenging – primarily due to the urban bias of data on CVD mortality and morbidity. Despite limitations, CVD registries from the poorest countries have consistently shown a low prevalence IHD and predominance of other endemic CVDs. Analysis of data from the GBD Study shows that metabolic and behavioral risk factors only contribute to about 53% of the combined CVD (including congenital heart anomalies) burden in the poorest country. Thus, current global NCD and CVD disease control targets will likely help reduce the premature CVD burden, but are not sufficient. Expanded targets focusing on infectious and environmental risks, as well integrated health system interventions that address CVD in people < 30 years of age due to RHD and congenital heart anomalies are needed.

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Disclosures

None.

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Endemic Cardiovascular Diseases of the Poorest Billion

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SUPPLEMENTAL MATERIAL

Title: The Endemic Cardiovascular Diseases of the Poorest Billion

The limitations of the Multi-dimensional Poverty Index (MPI)

The MPI incorporates data from about 75% of the world's population. However, there are areas with no available data. The survey sources have missing data on Western China, Northern Mali, Western Sahara, Vakaga in Central African Republic, the Federally Administered Tribal Areas of Pakistan, and North and South Sinai in Egypt. These regions could not be surveyed due to on-going conflict, territorial dispute, or because they are sparsely populated. Seventeen countries with MPI data older than 2005 are excluded for comparability purposes. Most of the countries with old data are in Eastern Europe, Myanmar, and Angola. The Oxford Poverty and Human Development Initiative has not become acquainted with any national or internationally comparable survey for Algeria, Botswana, Cape Verde, Eritrea, Equatorial Guinea, Seychelles in Africa; Chile, Costa Rica, Cuba, El Salvador, Panama, Paraguay, Venezuela in Latin America; Iran, Lebanon, Israel, Oman and Saudi Arabia in the Middle East; or Papua New Guinea and Taiwan in the East Pacific, among other countries. Developed countries are not part of the analysis as many of the indicators are less relevant in a developed context.

The endemic CVDs of poverty

Here, we briefly summarize the epidemiology of stroke and endemic causes of heart failure in low-income countries and the poverty-related risk factors. Summarized in **table 4**, they principally include hemorrhagic and ischemic stroke and heart failure from various causes.

Stroke

Hemorrhagic stroke occurs more frequently than ischemic strokes in low-income countries. From the GBD 2013 study, hemorrhagic stroke causes 905 DALYs/100,000 people while ischemic stroke causes 521 DALYs/100,000 people in LMICs.[1] The proportion of strokes due to hemorrhage is 63% in low-income countries and 38% in high-income countries. Further, age-standardized stroke mortality and morbidity are twice as high in LMICs as in high-income countries, driven mainly by difference in hemorrhagic stroke.

Elevated blood pressure is the principal risk factor for stroke among the poor. High prevalence of hypertension and low awareness and treatment rates are major contributors to the high burden of stroke in LMICs.[2] The Prospective Urban Rural Epidemiology (PURE) study is a 17-country cohort including countries across the income spectrum. In low-income countries, prevalence of hypertension is high in rural settings (31.5%), though higher in urban areas (44.4%).[3] Awareness, treatment, and control of hypertension were lower in low-income countries than middle-income countries, and lower in rural than urban areas. The findings suggest there is overall lack of access to basic hypertension care, particularly in rural regions where health systems may be weakest. Atherosclerosis is rare as shown in a study of 56 stroke patients in rural Tanzania where only one patient was found to have any carotid artery stenosis.[4] Additionally, human immunodeficiency virus (HIV) was also a risk factor for stroke in urban and rural Tanzania.[5]

Hypertensive Heart Disease

Heart failure is one end-organ complication of untreated hypertension. Hypertension prevalence is highest among patients with heart failure in sub-Saharan Africa.[6] The diagnosis is generally made among patients with a history of hypertension, particularly those people with preserved left ventricular systolic function. However, as awareness for hypertension is low in LMICs, and patients may no longer have elevated blood pressure as heart failure progresses, there may be misclassification.

Cardiomyopathies

Prior to the introduction of basic cardiac diagnostics in sub-Saharan Africa, the term "tropical cardiomyopathies" described the high prevalence of heart failure from undefined causes. [7,8] The underlying causes among the rural poor globally include uncontrolled HIV[9] and other viruses, American trypanosomiasis (Chagas' disease),[10] micronutrient deficiencies,[11] and severe chronic anemia. The vast majority of cardiomyopathies remain idiopathic.

Primary idiopathic dilated cardiomyopathies cause 20-50% of heart failure among hospitalized people in sub-Saharan Africa and Haiti (**Table 1**). Specific diagnostic studies including stress testing and coronary angiography are not generally available in rural LMICs, limiting the capacity to diagnose IHD. Nonetheless, the lack of atherosclerotic risk factors among people with cardiomyopathy suggests non-ischemic etiologies as patients with cardiomyopathies are generally young, physically active, predominantly women, thin, and non-smokers.[12]

Peripartum cardiomyopathy is a frequent cause of cardiomyopathy in populations of African descent – with hot spots in Haiti and Nigeria where the incidence is nearly 10-fold higher than in the United States.[13] Patients with peripartum cardiomyopathy are at high risk of death in the peripartum period, leading to disruptions to family life.[14] Though there is a genetic predisposition, mediating risk factors disproportionately affecting people in poverty also include multiple gestations, older age, and lack of access to birth control.

Chagas' disease one of the most common causes of non-ischemic cardiomyopathy in Latin America with about 37,000 incident cases annually.[10] Chagas' disease predominantly affects the rural poor and had been characterized as a Neglected Tropical Disease.[15] The protozoa which causes Chagas' disease is transmitted via insects which live in the cracks of mud huts and thatched roofs.[10] Socioeconomic conditions, particularly long duration of residence in endemic regions, overcrowding, lack of medical insurance, and low education are associated with poor seroconversion and more rapid cardiomyopathy progression.[16,17] Multinational parasite

control initiatives have reduced incidence by 70% and are cost saving.[18] However, rural regions where the disease is still endemic require further population-wide strategies such as the hyperendemic Gran Chaco region shared between rural Bolivia, Paraguay, and Argentina.[10]

Treatment of patients with cardiomyopathies in LMICs is generally suboptimal. Few patients take the evidence-based combination of diuretic, beta-blocker, and angiotensin converting enzyme inhibitor.[12,19,20] Subsequently, mortality is high for patients with heart failure. [12,20,21] Delayed access to care, poorly equipped health centers, and poorly trained healthcare staff may contribute to the high mortality in rural LMICs.

Rheumatic Heart Disease

RHD is the long-term consequence of recurrent episodes of untreated acute rheumatic fever and disproportionately affects people living in poverty. Global estimates are based on several school-based surveys. A conservative estimate suggests that 36 million people worldwide have RHD—mostly living in impoverished settings.[22]

Poverty remains one of the leading causes of RHD. In sub-Saharan Africa, children with RHD are more likely to attend lower socioeconomic schools,[23] have low formal education, and have no formal employment.[24] In Australia's Northern Territory, the incidence of acute rheumatic fever and RHD were more than 60-times higher among poor indigenous people than non-indigenous.[25] Countries with higher degrees of social inequality have higher RHD prevalence.[26] Observational studies starting in the 1860s have shown reductions of RHD in Denmark and the United States prior to antibiotics – thought to reflect improved housing and school standards resulting in decreased crowding.[27,28] In fact, the economic decline of former Soviet states has been associated with a concurrent rise in RHD prevalence.[29]

Pericardial disease

Tuberculosis and untreated malignancies cause the majority of pericardial effusions in low-income countries. There are about 11 million people with tuberculosis worldwide,[30] and pericarditis is found on autopsy in about 1% of all tuberculosis cases.[31] Mortality among patients with tuberculosis pericarditis is high – 26% at 6 months – which may represent the severity of the underlying illness.[32] Other than treatment of the underlying condition, pericardiocentesis, and pericardiectomy, treatment options are limited. Neither reducing inflammation through glucocorticoids nor immune stimulation with heat-killed Mycobacterium were effective in randomized clinical trials.[33]

Congenital Heart anomalies (CHA)

CHA accounts for nearly a third of major congenital abnormalities and is prevalent in about 8-9/1000 births.[34] In a multinational systematic review of patients with CHA, 34% had ventricular septal defect, 13% atrial septal defect, 10% patent ductus arteriosus, 8% pulmonic stenosis, and 5% tetralogy of Fallot.[34] CHA leads to more than 200,000 deaths worldwide with over 95% of the CHA deaths occur in LMICs.[35] Children with CHA may be more affected by lack of access to surgery and poverty. Survival among the poor is limited by delayed diagnosis and malnutrition.[36] More than half of the deaths can be avoided with surgical correction.[37] With access to appropriate medical and surgical care in developed countries, more than 90% of patient with CHA survive to adulthood.[38]

Right heart failure

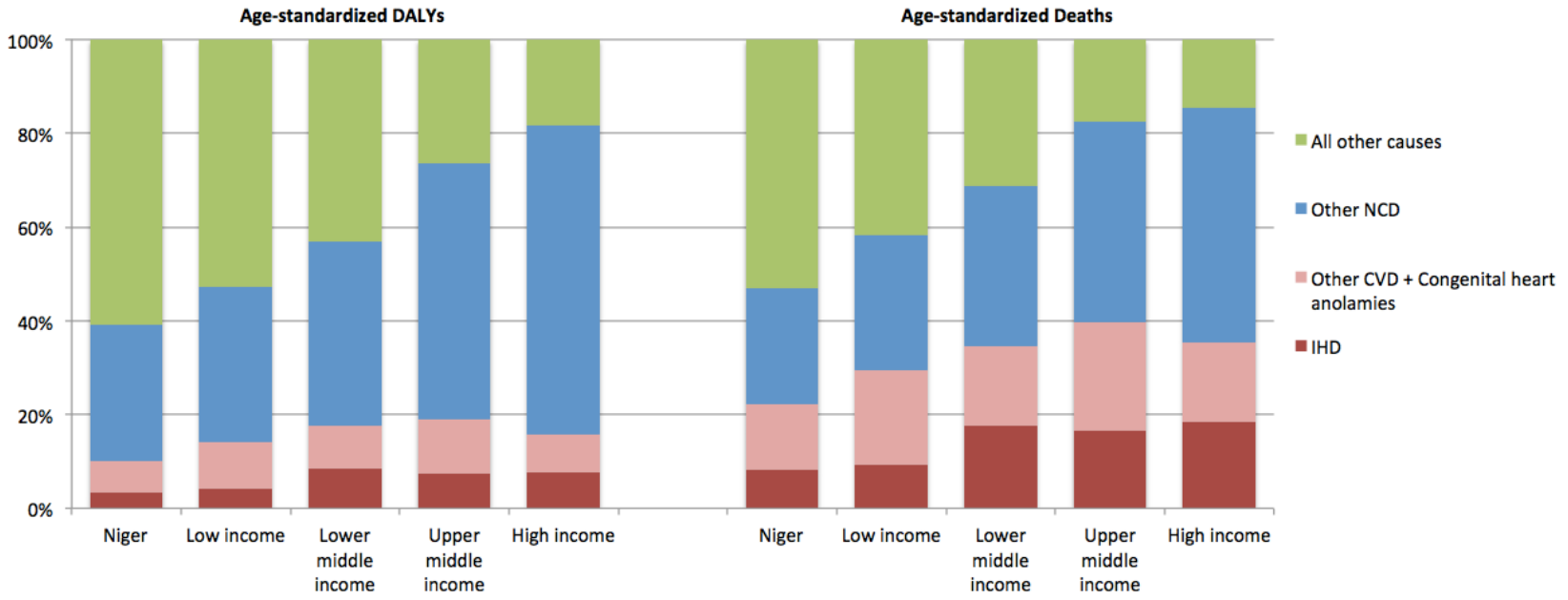
Pulmonary hypertension resulting in right heart failure (cor pulmonale) particularly affects people in LMICs. Similar to other cardiovascular conditions, available data comes from heart failure registries where 2-14% have right heart failure (**Table 1**). An estimated 20-25 million people in LMICs suffer from pulmonary hypertension.[39]

Several pulmonary hypertension etiologies specifically affect the poor in LMICs including schistosomiasis, HIV, hemoglobinopathies such as sickle cell disease and beta thalassemia, prior pulmonary tuberculosis infection, and high altitude, and household air pollution.[40] Additionally, around 3 billion people living in LMICs are exposed to household air pollution from the use of biomass fuel and inefficient cook stoves.[41] Exposure to household air pollution potentiates the effect of other endemic causes of pulmonary hypertension in LMICs.[42] Women, who perform a majority of the cooking in poorly ventilated kitchens, endure the greatest exposure.[43] Improved cookstove technology can reduce exposure to air pollution in laboratory-based settings. However, distribution programs in rural LMICs have largely been ineffective primarily due to low adoption and adherence.[44]

Endomyocardial Fibrosis (EMF)

EMF is a common cause of restrictive cardiomyopathy causing impaired filling of one or both ventricles. Described in 1948 in Uganda,[45] the majority of EMF cases arise in low-lying humid tropical regions including Nigeria, Ivory Coast, southern India, and Brazil.[46,47] Though global prevalence is difficult to estimate, a community-based echocardiographic study in rural Mozambique found a population prevalence of nearly 20%, with only a quarter of cases being symptomatic.[48] The etiology of EMF remains poorly understood, though evidence points towards eosinophillic inflammation and fibrosis possibly related to parasitic infections.[47]

Figure S1. Proportion of age-standardized DALYs for IHD, CVD (including congenital heart anomalies), and NCDs by World Bank income grouping and Niger.[69]



	Niger	Low income	Lower middle income	Upper middle income	High income	Niger	Low income	Lower middle income	Upper middle income	High income
CVD + Congenital of NCD	26%	30%	31%	26%	19%	47%	51%	50%	48%	42%
IHD of NCD	9%	9%	15%	10%	9%	18%	16%	25%	20%	22%
IHD of CVD + Congenital	33%	30%	48%	38%	48%	37%	31%	51%	42%	52%

Figure S2. Proportion of DALYs per 100,000 population attributable to risk factor categories for (A) CVD (as defined in the GBD study), and (B) all CVD including congenital heart anomalies, age-standardized, by World Bank income category, the GBD study. In the GBD study, congenital heart anomalies are not included within the CVD cause of death category, and are unattributed to any modeled risk factor.

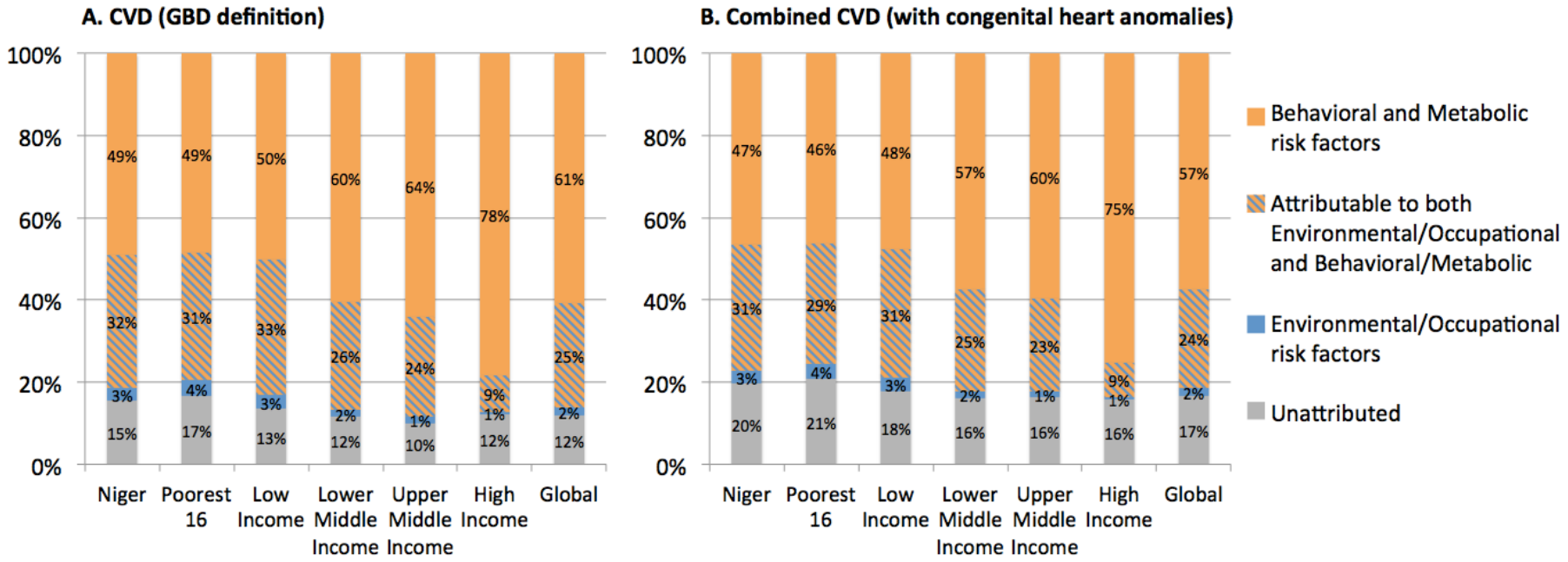


Figure S3. DALYs per 100,000 population attributable to risk factor categories for (A) congenital heart anomalies, (B) CVD (as defined in the GBD study), and (C) all CVD including congenital heart anomalies, age-standardized, by World Bank income category, the GBD study. In the GBD study, congenital heart anomalies are not included within the CVD cause of death category.

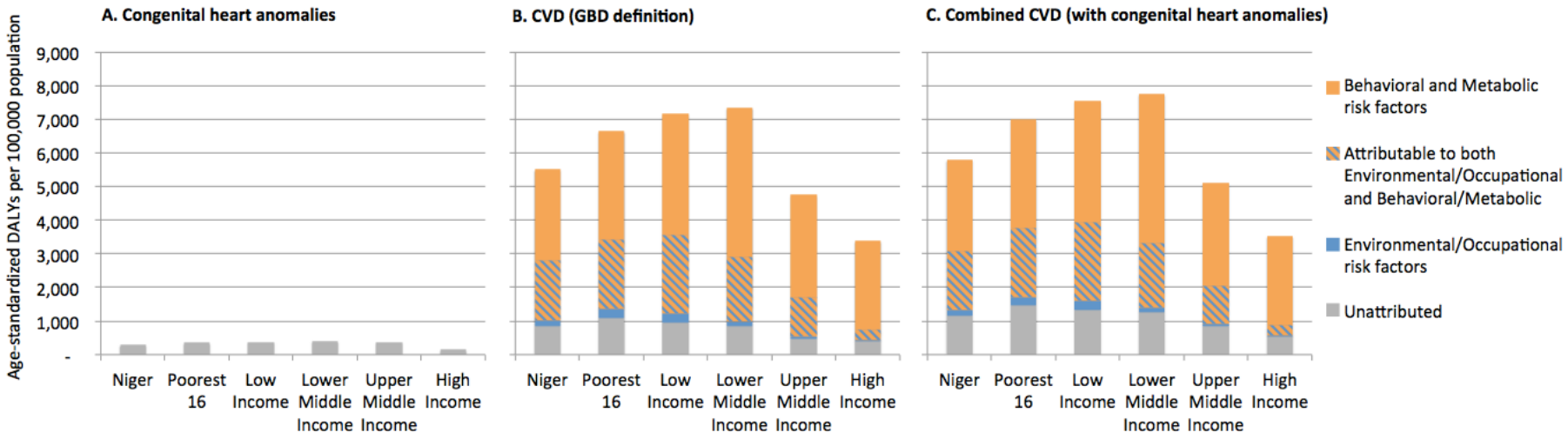


Table S1. Proportion of the worldwide poorest people by region.

	Multidimensional poverty*			
World Bank Region†	**by country**	**by sub-national region**	**by individual**	**by income[#]**
South Asia	59.8%	53.8%	54.4%	36.9%
Sub-Saharan Africa	40.1%	45.0%	38.3%	40.7%
East Asia & Pacific[§]	0.1%	0.3%	5.3%	17.6%
Latin America & Caribbean	0%	0.3%	0.9%	3.6%
Middle East & North Africa	0%	0.6%	1.2%	-
Europe & Central Asia	0%	0%	0.1%	1.2%
Total number of the poorest people (billion)	**1.129**	**1.001**	**1.062**	**1.047**

* The cut-point to define the poorest people varies by level of disaggregation: by country (MPI > 0.283), by sub-national region (MPI >0.247); by individual (weighted deprivation score ≥ 44.4%). [49]

† Sudan and Somalia are included in Sub-Saharan Africa using the World Bank Definition

§ Notably, the multidimensional poverty analysis lacks sub-national data for Western China.

2012 data. Income cut-point of <$2.05/day adjusted for 2011 purchasing power parity, except Bangladesh, Cabo Verde, Cambodia, Laos, and Jordan which use $/day in 2005 PPP. Survey coverage for the Middle East and North Africa region is too low to report the results. The survey data does not include about 4.5% of the population in developing countries and is likely a slight underestimate. Source: The World Bank.[50]

Table S2. Multidimensional poverty by individual.[49]

Rank	Country	World Bank Region *	MPI data source		Multidimensional poverty			Total population		Poorest billion	
			Survey†	Year	Multidimensional Poverty Index (MPI = H*A)	Headcount ratio: Population in multidimensional poverty (H)#	Intensity of deprivation among the poor (A)	Population 2011	Number of MPI poor people identified as the poorest billion in 2011	Proportion of the poorest billion living in the country	Proportion of the population identified as the poorest billion (k≥44))
					Range 0 to 1	% Population	Average % of weighted deprivations	Thousands	Thousands	%	%
1	Niger	SSA	DHS	2012	0.605	89.27	67.7	16,511	13,576	1.28%	82.22%
2	Ethiopia	SSA	DHS	2011	0.564	87.33	64.6	89,393	70,838	6.66%	79.24%
3	South Sudan	SSA	MICS	2010	0.557	91.09	61.2	10,381	8,521	0.80%	82.09%
4	Chad	SSA	MICS	2010	0.554	87.22	63.5	12,080	9,402	0.88%	77.83%
5	Burkina Faso	SSA	DHS	2010	0.535	84.00	63.7	15,995	11,417	1.07%	71.38%
6	Somalia	SSA	MICS	2006	0.514	81.16	63.3	9,908	7,124	0.67%	71.91%
7	Sierra Leone	SSA	DHS	2013	0.464	81.00	57.3	5,865	3,813	0.36%	65.00%
8	Guinea-Bissau	SSA	MICS	2006	0.462	77.54	59.6	1,624	1,045	0.10%	64.31%
9	Guinea	SSA	DHS-MICS	2012	0.459	75.12	61.1	11,162	6,843	0.64%	61.31%
10	Mali	SSA	DHS	2013	0.457	77.66	58.9	14,417	9,161	0.86%	63.54%
11	Burundi	SSA	DHS	2010	0.454	80.78	56.2	9,540	6,211	0.58%	65.10%
12	Central African Republic	SSA	MICS	2010	0.430	77.57	55.5	4,436	2,805	0.26%	63.23%
13	Congo, Democratic Republic of the	SSA	DHS	2014	0.401	75.09	53.4	63,932	37,128	3.49%	58.07%
14	Mozambique	SSA	DHS	2011	0.389	69.60	55.9	24,581	13,891	1.31%	56.51%
15	Liberia	SSA	DHS	2013	0.374	71.23	52.5	4,080	2,095	0.20%	51.35%
16	Uganda	SSA	DHS	2011	0.367	69.92	52.5	35,148	18,267	1.72%	51.97%
17	Timor-Leste	EAP	DHS	2010	0.360	68.07	52.9	1,096	545	0.05%	49.67%
18	Madagascar	SSA	DHS	2009	0.357	66.88	53.3	21,679	11,568	1.09%	53.36%
19	Afghanistan	SAR	MICS	2011	0.353	66.16	53.4	29,105	13,812	1.30%	47.45%
20	Rwanda	SSA	DHS	2010	0.350	68.95	50.8	11,144	5,334	0.50%	47.87%
21	Tanzania	SSA	DHS	2010	0.332	65.56	50.7	46,355	22,374	2.10%	48.27%
22	Gambia	SSA	DHS	2013	0.323	60.35	53.4	1,735	783	0.07%	45.13%
23	Sudan	SSA	MICS	2010	0.321	57.80	55.6	36,431	16,337	1.54%	44.84%

Rank	Country	World Bank Region *	MPI data source		Multidimensional poverty			Total population		Poorest billion	
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					Range 0 to 1	% Population	Average % of weighted deprivations	Thousands	Thousands	%	%
24	Cote d'Ivoire	SSA	DHS	2012	0.310	58.75	52.8	19,390	8,278	0.78%	42.69%
25	Senegal	SSA	DHS Cont.	2014	0.309	56.90	54.3	13,331	5,434	0.51%	40.76%
26	Benin	SSA	DHS	2012	0.307	62.22	49.3	9,780	3,908	0.37%	39.96%
27	Nigeria	SSA	DHS	2013	0.303	53.25	56.8	164,193	65,478	6.16%	39.88%
28	Mauritania	SSA	MICS	2011	0.285	52.18	54.6	3,703	1,476	0.14%	39.85%
29	India	SAR	DHS	2006	0.283	53.75	52.7	1,221,156	457,334	43.03%	37.45%
30	Zambia	SSA	DHS	2014	0.281	56.56	49.8	13,634	5,268	0.50%	38.64%
31	Malawi	SSA	DHS	2010	0.265	56.01	47.4	15,458	7,202	0.68%	46.60%
32	Togo	SSA	DHS	2014	0.252	50.10	50.4	6,472	2,060	0.19%	31.83%
33	Haiti	LAC	DHS	2012	0.248	49.40	50.3	10,033	3,329	0.31%	33.18%
34	Cameroon	SSA	DHS	2011	0.248	46.02	53.8	21,156	6,797	0.64%	32.13%
35	Yemen	MNA	MICS	2006	0.236	45.87	51.4	23,304	8,420	0.79%	36.13%
36	Pakistan	SAR	DHS	2013	0.230	44.17	52.1	176,166	49,988	4.70%	28.38%
37	Kenya	SSA	DHS	2009	0.229	47.81	48.0	42,028	12,624	1.19%	30.04%
38	Nepal	SAR	DHS	2011	0.217	44.20	49.0	27,156	7,503	0.71%	27.63%
39	Namibia	SSA	DHS	2013	0.193	41.96	46.0	2,218	525	0.05%	23.66%
40	Congo	SSA	DHS	2012	0.181	39.71	45.7	4,225	948	0.09%	22.45%
41	Lao	EAP	MICS/DHS	2012	0.174	34.12	50.9	6,521	1,429	0.13%	21.91%
42	Bangladesh	SAR	DHS	2011	0.174	37.28	46.6	152,862	48,970	4.61%	32.04%
43	Comoros	SSA	DHS-MICS	2012	0.173	36.04	47.9	700	150	0.01%	21.39%
44	Ghana	SSA	MICS	2011	0.156	33.68	46.2	24,821	3,741	0.35%	15.07%
45	Lesotho	SSA	DHS	2009	0.156	35.27	44.1	2,030	389	0.04%	19.19%
46	Sao Tome	SSA	DHS	2009	0.154	34.47	44.7	183	28	0.00%	15.55%
47	Cambodia	EAP	DHS	2010	0.146	33.02	44.3	14,606	3,291	0.31%	22.53%
48	Djibouti	MNA	MICS	2006	0.139	29.32	47.3	847	134	0.01%	15.85%

Rank	Country	World Bank Region *	MPI data source		Multidimensional poverty			Total population		Poorest billion	
			Survey†	Year	Multidimensional Poverty Index (MPI = H*A)	Headcount ratio: Population in multidimensional poverty (H) #	Intensity of deprivation among the poor (A)	Population 2011	Number of MPI poor people identified as the poorest billion in 2011	Proportion of the poorest billion living in the country	Proportion of the population identified as the poorest billion (k≥44))
					Range 0 to 1	% Population	Average % of weighted deprivations	Thousands	Thousands	%	%
49	Vanatu	EAP	MICS	2007	0.129	30.12	42.7	242	28	0.00%	11.64%
50	Zimbabwe	SSA	MICS	2014	0.127	29.71	42.7	13,359	1,839	0.17%	13.77%
51	Bhutan	SAR	MICS	2010	0.119	27.15	43.9	729	88	0.01%	12.10%
52	Bolivia	LAC	DHS	2008	0.089	20.45	43.7	10,324	1,040	0.10%	10.08%
53	Swaziland	SSA	MICS	2010	0.086	20.44	41.9	1,212	101	0.01%	8.32%
54	Honduras	LAC	DHS	2012	0.072	15.84	45.7	7,777	491	0.05%	6.32%
55	Nicaragua	LAC	DHS	2012	0.072	16.09	45.0	5,905	499	0.05%	8.45%
56	Gabon	SSA	DHS	2012	0.070	16.49	42.5	1,594	111	0.01%	6.98%
57	Morocco	MNA	PAPFAM	2011	0.067	15.43	43.7	32,059	2,237	0.21%	6.98%
58	Indonesia	EAP	DHS	2012	0.066	15.47	42.9	243,802	16,411	1.54%	6.73%
59	Tajikistan	ECA	DHS	2012	0.054	13.21	40.8	7,815	361	0.03%	4.62%
60	Philippines	EAP	DHS	2013	0.052	11.01	47.3	95,053	6,701	0.63%	7.05%
61	Iraq	MNA	MICS	2011	0.045	11.64	38.5	31,837	828	0.08%	2.60%
62	South Africa	SSA	NIDS	2012	0.044	11.10	39.5	51,949	1,681	0.16%	3.24%
63	Peru	LAC	DHS-Cont	2012	0.043	10.50	41.0	29,615	1,215	0.11%	4.10%
64	Mongolia	EAP	MICS	2010	0.037	9.17	40.7	2,754	99	0.01%	3.59%
65	Guyana	LAC	DHS	2009	0.030	7.70	39.2	791	17	0.00%	2.13%
66	Suriname	LAC	MICS	2010	0.024	5.88	40.8	530	10	0.00%	1.94%
67	China	EAP	CFPS	2012	0.023	5.24	43.2	1,368,440	26,526	2.50%	1.94%
68	Colombia	LAC	DHS	2010	0.022	5.38	40.9	47,079	844	0.08%	1.79%
69	Azerbaijan	ECA	DHS	2006	0.021	5.32	39.4	9,202	138	0.01%	1.50%
70	Dominican Republic	LAC	DHS	2013	0.020	5.11	39.0	10,148	132	0.01%	1.30%
71	Trinidad&Tobago	LAC	MICS	2006	0.020	5.62	35.1	1,333	5.0	0.00%	0.37%
72	Maldives	SAR	DHS	2009	0.018	5.16	35.6	332	1.1	0.00%	0.34%
73	Belize	LAC	MICS	2011	0.018	4.62	39.6	316	4.3	0.00%	1.36%

Rank	Country	World Bank Region *	MPI data source		Multidimensional poverty			Total population		Poorest billion	
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					Range 0 to 1	% Population	Average % of weighted deprivations	Thousands	Thousands	%	%
74	Viet Nam	EAP	MICS	2011	0.017	4.23	39.5	89,914	1,095	0.10%	1.22%
75	Syrian Arab Republic	MNA	PAPFAM	2009	0.016	4.39	37.4	21,804	156	0.01%	0.71%
76	Egypt	MNA	DHS	2014	0.014	3.56	38.1	79,392	457	0.04%	0.58%
77	Ecuador	LAC	ECV	2014	0.013	3.47	38.5	15,246	118	0.01%	0.77%
78	Mexico	LAC	ENSANUT	2012	0.011	2.80	38.8	119,361	875	0.08%	0.73%
79	Argentina	LAC	ENNyS	2005	0.011	2.86	37.6	40,729	127	0.01%	0.31%
80	Brazil	LAC	PNDS	2006	0.011	2.69	39.3	196,935	709	0.07%	0.36%
81	Uzbekistan	ECA	MICS	2006	0.008	2.32	36.2	28,152	81	0.01%	0.29%
82	Jamaica	LAC	JSLC	2010	0.008	2.01	39.4	2,755	14	0.00%	0.50%
83	Kyrgyzstan	ECA	DHS	2012	0.007	2.03	36.4	5,403	13	0.00%	0.24%
84	Thailand	EAP	MICS	2006	0.006	1.65	38.5	66,576	200	0.02%	0.30%
85	Jordan	MNA	DHS	2012	0.006	1.69	35.0	6,731	10	0.00%	0.15%
86	Palestine, State of	MNA	MICS	2010	0.006	1.54	38.3	4,114	9.1	0.00%	0.22%
87	Libya	MNA	PAPFAM	2007	0.006	1.51	37.0	6,103	11	0.00%	0.18%
88	Albania	ECA	DHS	2009	0.005	1.37	37.7	3,154	7.8	0.00%	0.25%
89	Tunisia	MNA	MICS	2012	0.004	1.16	38.5	10,753	31	0.00%	0.28%
90	Ukraine	ECA	MICS	2012	0.004	1.22	34.8	45,803	5.4	0.00%	0.01%
91	Georgia	ECA	MICS	2005	0.003	0.80	35.2	4,374	3.5	0.00%	0.08%
92	Moldova	ECA	MICS	2012	0.003	0.76	35.9	3,543	3.0	0.00%	0.08%
93	Macedonia	ECA	MICS	2011	0.002	0.68	35.7	2,104	0.8	0.00%	0.04%
94	Bosnia and Herzegovina	ECA	MICS	2012	0.002	0.51	37.3	3,839	0.2	0.00%	0.01%
95	Montenegro	ECA	MICS	2013	0.001	0.27	46.4	621	0.9	0.00%	0.15%
96	Armenia	ECA	DHS	2010	0.001	0.29	35.2	2,964	1.4	0.00%	0.05%
97	Serbia	ECA	MICS	2014	0.001	0.24	40.5	9,597	8.0	0.00%	0.08%
98	Kazakhstan	ECA	MICS	2011	0.001	0.18	36.2	16,098	2.9	0.00%	0.02%

*EAP, East Asia and Pacific Region; ECA, Europe and Central Asia Region; LAC, Latin America and Caribbean Region; MNA, Middle East and North Africa (Arab States) Region; SAR, South Asia Region; SSA, sub-Saharan Africa Region.
†Data sources: CFPS, China Family Panel Studies; DHS, Demographic and Health Survey; ECV, Living Standards Survey (Ecuador); ENNyS, National Nutrition and Health Survey (Argentina); ENSANUT, National Health and Nutrition Survey (Mexico); JSLC, Jamaica Survey of Living Conditions; MICS, Multiple Indicator Cluster Survey; NIDS, National Income Dynamics Survey; PAPFAM, Pan Arab Project for Family Health; PNDS, National Demographic and Health Survey (Brazil)
[#] Weighted deprivation score ≥33.3%.

Table S3. Cause-specific adult mortality rates per 1000 person-years for acute and other cardiac diseases by verbal autopsy for people age < 65 years at demographic and health surveillance sites, by site, and sex, 2006-2012.[51] Red shades indicate sites with more acute (ischemic) than other cardiac deaths. Green shades indicate sites with less acute (ischemic) than other cardiac deaths.

		Males			Females		
Country	**Site**	Acute (ischemic) cardiac	Other cardiac	% Acute (ischemic) cardiac	Acute (ischemic) cardiac	Other cardiac	% Acute (ischemic) cardiac
Bangladesh	Matlab	0.30	0.27	53%	0.05	0.10	33%
Bangladesh	Bandarban	0.35	0.06	85%	-	0.13	-
Bangladesh	Chakaria	0.06	0.10	38%	0.03	0.10	23%
Bangladesh	AMK	0.40	0.35	53%	0.06	0.22	21%
Burkina Faso	Nouna	-	-	-	0.01	-	-
Burkina Faso	Ouagadougou	0.15	0.06	71%	0.05	0.06	45%
Cote d'Ivoire	Taabo	0.02	0.07	22%	0.03	0.11	21%
Ethiopia	Kilite Awlaelo	0.03	0.07	30%	0.01	0.06	14%
The Gambia	Farafenni	0.14	0.06	70%	0.02	0.05	29%
Ghana	Navrongo	0.37	0.16	70%	0.09	0.14	39%
Ghana	Dodowa	0.24	0.06	80%	0.17	0.09	65%
India	Ballabgarh	0.22	0.12	65%	0.20	0.07	74%
India	Vadu	0.08	0.07	53%	0.08	0.15	35%
Kenya	Kilifi	0.03	0.15	17%	0.02	0.14	13%
Kenya	Kisumu	0.05	0.39	11%	0.03	0.38	7%
Kenya	Nairobi	1.16	5.61	17%	1.58	6.25	20%
Malawi	Karonga	0.08	0.04	67%	-	0.04	-
Senegal	Niakhar	0.60	0.14	81%	0.38	0.20	66%
South Africa	Agincourt	0.07	0.17	29%	0.04	0.19	17%
South Africa	Africa Centre	0.12	0.33	27%	0.06	0.47	11%
Vietnam	Filabavi	0.06	0.32	16%	0.02	0.14	13%

Table S4. Age-Standardized, DALYs per 100,000, the GBD study, 2013

	Poorest 16 countries	Lower Income	Lower Middle Income	Upper Middle Income	High Income	World
Ischemic Heart Disease (IHD)	1,752.6	2,292.1	3,711.7	1,960.1	1,697.5	2,371.7
Cardiovascular Disease (CVD)	6,644.4	7,165.3	7,349.5	4,747.8	3,380.5	5,197.2
Congenital Heart Anomalies	356.2	377.5	406.0	364.7	142.2	356.4
Noncommunicable Disease (NCD)	24,455.5	25,282.0	25,301.4	19,793.2	18,446.9	21,420.2
All Cause	62,869.3	53,403.7	44,327.1	26,840.0	22,563.9	35,478.6

Table S5. Age-standardized DALYs per 100,000 population (%) by risk factor category, GBD study 2013

Risk Factor Category*	Niger†		Poorest 16 countries		Low income		Lower middle income		Upper middle income		High income		Global	
Congenital Heart Anomalies														
Behavioral and Metabolic risk factors	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Environmental/Occupational risk factors	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unattributed	291	(100)	356	(100)	378	(100)	406	(100)	365	(100)	142	(100)	1,290	(100)
Total	291		356		378		406		365		142		1,290	
Cardiovascular Diseases (CVD)														
Behavioral and Metabolic risk factors	4,474	(81)	5,284	(80)	5,955	(83)	6,374	(87)	4,199	(88)	2,950	(87)	19,477	(86)
Environmental/Occupational risk factors	1,956	(36)	2,316	(35)	2,605	(36)	2,059	(28)	1,223	(26)	320	(9)	6,207	(27)
Unattributed	850	(15)	1,101	(17)	966	(13)	848	(12)	478	(10)	412	(12)	2,704	(12)
Total	5,506		6,643		7,165		7,349		4,748		3,381		22,642	
Combined CVD and congenital heart anomalies														
Behavioral and Metabolic risk factors	4,474	(77)	5,284	(75)	5,955	(79)	6,374	(82)	4,199	(82)	2,950	(84)	19,477	(81)
Environmental/Occupational risk factors	1,956	(34)	2,316	(33)	2,605	(35)	2,059	(27)	1,223	(24)	320	(9)	6,207	(26)
Unattributed	1,141	(20)	1,457	(21)	1,343	(18)	1,254	(16)	842	(16)	554	(16)	3,994	(17)
Total	5,797		7,000		7,542		7,755		5,112		3,523		23,933	

* The behavioral and metabolic category includes any overlap with environmental/occupational. The environmental/occupational category includes any overlap with behavioral and metabolic. Because of multicausality and the resulting overlap, the sum of the DALY rates in a given column will be greater than the total and greater that 100).

† Niger is the country with the largest proportion of its population (82%) within the world's poorest billion people.

Table S6. Distribution of crude DALYs (%) for CVD and congenital heart anomalies by age and World Bank income group, all ages, GBD study 2013.

Age group	Poorest 16 Countries		Low-Income		Lower-Middle Income		Upper-Middle Income		High Income		Global	
Congenital Heart Anomalies												
0-29 years	2,395,271	(98.9)	4,964,197	(97.8)	11,183,501	(91.9)	7,118,714	(93.8)	1,012,806	(74.6)	24,301,292	(92.7)
30-69 years	25,612	(1.1)	101,713	(2.0)	872,633	(7.2)	448,232	(5.9)	306,518	(22.6)	1,730,849	(6.6)
≥70 years	2,029	(0.1)	10,694	(0.2)	111,970	(0.9)	25,786	(0.3)	38,324	(2.8)	187,073	(0.7)
CVD												
0-29 years	1,766,114	(17.7)	3,696,796	(12.0)	11,134,350	(8.9)	4,710,824	(4.4)	1,016,318	(1.5)	20,588,227	(6.2)
30-69 years	5,868,860	(58.7)	18,974,225	(61.8)	79,575,147	(63.6)	60,706,852	(56.5)	30,159,577	(45.7)	189,722,092	(57.5)
≥70 years	2,364,707	(23.6)	8,013,319	(26.1)	34,324,703	(27.5)	42,054,014	(39.1)	34,787,323	(52.7)	119,395,307	(36.2)
CVD + Congenital Heart Anomalies												
0-29 years	4,161,385	(33.5)	8,660,994	(24.2)	22,317,851	(16.3)	11,829,538	(10.3)	2,029,124	(3.0)	44,889,520	(12.6)
30-69 years	5,894,472	(47.4)	19,075,938	(53.3)	80,447,780	(58.6)	61,155,084	(53.1)	30,466,095	(45.3)	191,452,941	(53.8)
≥70 years	2,366,736	(19.1)	8,024,013	(22.4)	34,436,673	(25.1)	42,079,800	(36.6)	34,825,648	(51.7)	119,582,380	(33.6)

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