THE CHANGING FACE OF CARDIOVASCULAR DISEASE 2000 – 2012: AN ANALYSIS OF THE WORLD HEALTH ORGANISATION GLOBAL HEALTH ESTIMATES DATA

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OVERVIEW

The pattern and global burden of disease has evolved considerably over the last two decades, from primarily communicable, maternal, and perinatal causes to non-communicable disease (NCD). Cardiovascular disease (CVD) has become the single most important and largest cause of NCD deaths worldwide at over 50%. The World Health Organization (WHO) estimates that 17.6 million people died of CVD worldwide in 2012. Proportionally, this accounts for an estimated 31.43% of global mortality, with ischaemic heart disease (IHD) accounting for approximately 7.4 million deaths, 13.2% of the total. IHD was also the greatest single cause of death in 2000, accounting for an estimated 6.0 million deaths. The global burden of CVD falls, principally, on the low and middle-income (LMI) countries, accounting for over 80% of CVD deaths. Individual populations face differing challenges and each population has unique health burdens, however, CVD remains one of the greatest health challenges both nationally and worldwide.

Introduction

Global disease burden has changed considerably over the last two decades. The worldwide health burden has shifted from communicable, maternal and perinatal causes to non-communicable diseases (NCD)[1, 2] with cardiovascular diseases (CVD) being the largest single contributor worldwide.[1, 3] This tendency is explained by the concept of the 'epidemiological transition', whereby the socio-economic development of a region causes a general shift from communicable to non-communicable disease. The WHO estimates 17.6million people died of CVD globally in 2012, representing a substantial increase from 2000.[4] The burden of CVD is also considerably contributing to life years lost to disability.[5] The nature of the CVD burden is not distributed equally across the world and represents different challenges dependent on factors such as culture, risk factor prevalence, ethnicity, economics and geography.[6]
Understanding the global impact of CVD burden and causative factors allow international health groups and governments to plan public health strategies and interventions to combat the growing global burden. The aim of this review is to assess and analyse the changes in CVD health burden over the last twelve years using the global health estimates data from the WHO and World Bank [5,7,8] and to examine the risk factor prevalence and possible associations.

Methodology

This is a secondary data analysis of the 2000 and 2012 global health estimates published by the WHO and World Bank. Only aggregate data of absolute numbers, rates and percentages of subjects falling into categories were made available and thus analysed. Wald confidence intervals are presented for proportions and comparisons of the proportion of deaths attributed to diseases are made using Wald tests or Pearson's

Chi-squared tests and logistics regression for factors with more than two categories such as region. For ordinal variables the Cochran-Armitage trend test is used. The statistical analysis was conducted using SAS v9.4 TS1M2.

Metrics of CVD Health Burden and Limitations of the WHO data

To evaluate the extent of the CVD global burden a standard set of definitions and metrics must be rigorously applied. All WHO member states use the International Classification of Diseases Tenth edition (ICD-10), translated into 43 different languages.[9] The ICD-10 is used to code all health diagnoses and most member states use it to define primary mortality.[9] Despite its widespread use, ICD-10 is not used by every member state and only 60 countries meet the inclusion criteria to admit statistics to the WHO mortality database.[10] Furthermore, not all mortality statistics admitted to WHO are coded to the same standard.[10] **Table 1** demonstrates all subset diagnoses that contribute to CVD total as per ICD-10 coding, except '*congenital heart anomalies'* which is of the '*congenital anomalies'* ICD-10 category.[9] Throughout this review *'congenital heart anomalies'* will be discussed with CVD burden, but not contribute to the total metrics presented.

The highest standard of submitted data is from WHO member states that utilise a national vital registration system for mortality, allowing real-time health statistics to be produced. However, even the highest standard systems suffer from data that is partially inaccurate.[11] Studies have demonstrated disparity between diagnosis on death certificate and actual cause of death in national vital registration systems. [12] Several WHO member states lack the infrastructure to provide usable/reliable real-time mortality statistics[11] making accurate data on global health challenging. Sample

vital registration systems have been utilised to overcome this problem.[11] These systems have been designed to represent a random subset of the population over a period of time to infer population based health statistics.[11] China and India use sample vital registration systems.[13] In China the Disease Surveillance Point system is used, which represents 1% of the population and India uses a nationally representative household survey that monitors for cause of death in a population of over 14 million.[13] However, not all WHO member states have a real-time sampling system in place.[11] In situations where no previous data is available, other small sources like verbal autopsies, disease surveillance systems and analyses from WHO technical programs are used.[10, 11] Where data is absent or unusable then interpolation and extrapolation is used.[10] This data can then be used to inform reasonably robust prediction models.[11]

Measurement of disease burden uses several variables. Mortality rate, whilst a critically important measure of health status and disease burden, assigns the same value to each death regardless of age.[14] Disability Adjusted Life Years (DALY) accounts for years of life lost as well as the years of healthy life lost due to a condition.[14] Lost DALYs represent condition specific fatal and non-fatal disease burden, representing the full impact of any given condition. One DALY equates to one year of healthy life lost making it a powerful metric in assessing global disease burden.[14] Both measurements will be utilised in this review to measure CVD burden.

Global Cardiovascular Disease Burden: Mortality

The percentage of CVD as a proportion of global mortality has increased significantly from 28.2% in 2000 to 31.4% in 2012 ($p<0.001$, **table 1**).[4] Ischaemic heart disease

(IHD) and stroke represent the top two causes of mortality. Moreover, the gap between these and the next leading cause is widening (**table 2**) with the difference estimated to be 4.11% (95% CI [4.10 – 4.12]) in 2000 and 6.39% (95% CI 6.37 – 6.40). Three CVD categories are in the top 10 causes of global mortality for 2012: IHD, stoke and hypertensive heart disease (**table 2**). CVD mortality is not distributed equally across the globe ($p<0.001$ test of equality of proportions for 2000 and 2012, respectively). **Figure 1** demonstrates this geographical variation in CVD mortality from 2000-2012. Europe is still the frontrunner in CVD mortality despite a decrease since 2000. Comparatively, Europe's mortality rate at 47.9% is higher than the 2012 global mortality rate.[8] Europe, on the WHO global health estimated dataset, is classified as including Western Europe and Russian Federation. In 2012, CVD mortalities accounted for 59.6% of the total for the Russian Federation, compared to 30.5% of mortalities in the United Kingdom.[8] Such intra-regional differences are also apparent in the Americas. A population wide comparative observational study in Brazil for IHD mortality demonstrated regional variations in death rates depending on economic status over a ten-year period. [15] Comparatively poorer North and Northeast regions demonstrated increasing mortality rates compared to a decrease in the South and Southeast regions.[15] Economic status of a particular country has an important impact upon cardiovascular disease mortality rates. [7] The WHO/World Bank classify countries by economic status in comparison of health metrics to control this significant variable.[7] **Figure 2** compares mortality rates for NCD and CVD based on further sub-classification of World Bank Economic regions into HI and low-middle income (LMI) countries for 2000 and 2012.[7] All LMI regions assessed demonstrated a statistically significant increase in both CVD and NCD mortality during this period

whilst the proportion of deaths due to CVD in high income countries was falling significantly in the same period by 5.50% [5.46 – 5.54]) .

Variation amongst population occurs between regions and within regions. **Figure 3a** demonstrates, males carry the higher burden overall as they age (p<0001); this is until females pass the menopause when CVD mortality burden accelerates more rapidly for females.[4] There is variation of mortality rates within each gender based on age and region (**figure 3b and 3c**). However, what is consistent across all regions and genders is that there is rapid increase in CVD mortality once >60years old (p<0.001 for difference in rates between <60 and ≥60 years for all regions expect Africa where p=0.012). Of these CVD mortality for the African region is the lowest for males and females in older age and reflects an alternative health burden. The CVD burden tends to occur at younger ages in Africa.[16] The acceleration in mortality rate starts earlier in the South Asian region for males at >30years compared with others. No such pattern affects South Asian females. Significantly, the rate of tobacco smoking in South Asia is much higher in males than females and likely significant contributory factor for the discrepancy.[1]

Global Cardiovascular Disease Burden: DALYs

CVD accounted 393.8 million (14.4%) of total global DALYs lost in 2012. This is a significant increase in the proportion from 12.3% (352.8 million) in 2000.[5] **Table 3** compares DALYS lost for 2000 and 2012 for NCD, total CVD and specific cardiovascular subset categories.[5] The WHO global health data suggests an overall decrease in total lost DALYs between 2000-2012; the contribution of NCD, however, has increased driven primarily by CVD. The fatal and non-fatal health burden of

specific conditions has changed between 2000 and 2012.[2] Table 4 represents the top 10 specific causes of loss of DALYs for 2000 and 2012.[2] Importantly, the top ten for both years includes chronic medical conditions and mental health problems.[2] Specifically the global disease burden of IHD and stroke has increased between 2000 and 2012.[5] Lower Respiratory Tract Infection (LRTI) in 2000 was the single largest cause of loss of DALYs. This had reduced by 2012 where LRTI was the second commonest cause of loss of DALYS.[2] Interestingly, other CVD conditions like atrial fibrillation (AF) and peripheral vascular disease (PVD) have significantly increased between 1990 and 2010.[2] The change in rankings demonstrates the increasing contribution of CVD to fatal and non-fatal health burden worldwide.[5]

The economic status of the WHO member states impacts on the fatal and non-fatal NCD including CVD burden. **Figure 4** compares rates of lost DALYs for NCD and CVD World Banking region in 2000 and 2012. In all LMI regions the number of DALYs attributable to NCD and CVD increased from 2000-2012. The LMI regions South Asia with East Asia and the Pacific have the greatest increase of DALYs lost due to NCD. HI countries had >80% of their DALYs attributed to NCD in 2000 and 2012.[17] DALYs attributable to CVD decrease between 2000-2012. This pattern mimics that of NCD and CVD mortality rates (**figure 2**).

Figure 5a outlines lost DALYs globally classified by gender/age. Overall, males and females have respectively lost 216.1 million (14.5%) and 177.7 million (14.1%) DALYs attributable to CVD.[5] The leading cause of loss of DALYs in males is IHD and stroke for females.[5] Overall, both genders behave in a similar way, with all

regions losing more DALYs with increasing age (**figures 5b and 5c**). This is more pronounced in earlier life for males than females. European females have a more rapid loss of DALYs in later years, in contrast to males who have a greater loss of DALYs in earlier and middle life.[5] South East Asian males have a rapid loss of DALYs in earlier life than females.[5] The Western Pacific region has the greatest loss of DALYs with age in both genders.[5] The African region demonstrated lowest overall loss of DALYs due to CVD. Increased loss of DALY's with increasing age, per gender, is demonstrated but the overall rate of loss is significantly lower than all other WHO regions and World Banking regions.[5] This suggests alternative reasons for loss of DALYS in this region.[5]

Total health burden has decreased across the world, but the burden of NCD and specifically CVD has increased. The World Banking global health estimates report suggests HI countries have turned the corner on lost DALYs due to CVD.[17] The focus of CVD burden is now on LMI countries with all regions increasing from 2000-2012.[17] The African region represents the biggest potential expansion in the future, given the projected epidemiological transition and current low contribution to loss of DALY's. This estimate of fatal and non-fatal CVD burden and projection is one of the critical factors for world authorities to plan public health strategies to target and tackle this problem.

Global Risk Factors and Health Conditions Impacting on CVD

The majority of CVD burden can be attributed to a few specific factors. The distribution of these specific risk factors and health conditions vary across the world and is associated with the prevalence of CVD. These risk factors include, but are not restricted to, hypertension, diabetes mellitus, tobacco smoking, dyslipidaemia and alcohol consumption.[18] The presence of particular lifestyle risk factors varies between countries and explains how ethnic constructs influence CVD burden worldwide. Each risk factor is discussed with reference to its global prevalence.

Hypertension

Worldwide hypertension contributes 7.5million deaths (12.8%) and 5.7million lost DALYs (3.7%).[1, 19] It is a known risk factor for numerous CVDs and the number with uncontrolled hypertension increased from 600million in 1980 to approximately 1billion in 2008,[1, 19] and projected to rise to 1.56billion by 2025 [20] with 67.5% of patients residing in LMI countries.[20]

Diabetes Mellitus

Diabetes Mellitus (DM) is one of the great future health burdens with ever increasing numbers being affected. In 2000, approximately 171 million were affected and projected to increase by 2030 to an estimated 366 million with the biggest burden in the Middle East, Sub-Saharan Africa and India.[21] In 2012 DM was responsible for approximately 1.5 million deaths worldwide with a third of this in South Asia.[7] DM accounted for 2.2% of total lost DALYs in 2012.[4] Crucially almost 60% of deaths from DM are due to CVD.[1]

Tobacco

Globally 9% of all NCD mortalities are attributable to tobacco. Smoking poses one of the greatest risks for development of CVD.[19] Europe has the highest prevalence of smokers (31%), the lowest is Africa (10%).[22] The WHO global atlas of CVD compared rates of smoking in both genders across the world for 2011.[1] Overall the prevalence of smoking is the same in Eastern Europe and the Russian Federation for both genders.[1] A higher proportion of males smoke in South-East Asia than females.[1] In Europe and South-America the trend is reversed.[1] In 1965, 41.7% of USA adults smoked, compared with 19.3% in 2010.[3] In Eastern Europe and South-East Asia, smoking is the third largest risk for CVD. [2]

Dyslipidaemia

Hypercholesterolaemia increases risk of IHD and stroke[23] and is associated with a third of all IHD deaths and is estimated to be the cause of 2.6million (4.5%) deaths and 29.7million (2.0%) lost DALYs.[1,24] In 2008, the global rate of raised total cholesterol was 39.0% (male 37.0%/females 40.0%).[1] Over 50% of the population of HI countries have elevated total cholesterol. There has been no change in mean total cholesterol between 1980-2008, with <0.1mmol/L fall per decade.[1] The prevalence is highest in Europe at 54.0% (both genders), followed by the Americas at 48.0% (both genders).[1] The lowest prevalence was found in Africa at 23.0% and South-East Asia at 30.0% (both genders).[19]

Physical Activity

Insufficient physical activity is defined as less than 30 minutes of moderate activity per week. Lack of exercise is a leading cause of CVD, especially IHD.[3, 25] The impact of physical inactivity on the global health burden is 3.2million deaths (5.5%) and

32.1million lost DALYs (2.1%).[24] Individuals who have insufficient activity have 20-30% increased risk of all-cause mortality.[1] Participation in exercise reduces the risk of IHD and stroke in a dose dependent fashion.[26] The WHO region with greatest prevalence of inactivity is the Americas.[1] The prevalence of inactivity in HI countries is over double that of LMI countries in both men and women.[1] Approximately 41.0% men and 48.0% of women are inactive in HI countries. In contrast, 18.0% of men and 21.0% of women are inactive in lower income countries.[19] There is little variation in inactivity rates between the genders in individual countries.[1]

Alcohol

Alcohol consumption is associated with development of CVD.[25] Dangerous consumption of alcohol was responsible for 2.5million deaths (3.6%) in 2004, over half due to CVD, liver cirrhosis and cancer.[1, 24] In all regions of the world it contributes to prevalence of CVD, with more significant contribution in LMI countries.[1] Eastern Europe has high alcohol consumption and is the fifth largest contributor to CVD.[27] Interestingly, in other regions alcohol is not as high a contributor to CVD burden.[2] Traditionally, alcohol was thought to be cardio-protective, a view immortalised by the 1996 WHO/World Bank report on global burden of disease that "alcohol is cardio-protective at all levels of consumption".[28] A large meta-analysis was performed to reconcile the conflict between the cardio-protective role of alcohol outlined in the West and association between consumption and CVD in Eastern Europe.[29] The study demonstrated that problematic drinking was the key risk factor.[29] The analysis demonstrated a strong association between excess alcohol consumption, arrhythmias and sudden cardiac death.[29] A case-control study from Moscow demonstrated higher rate of sudden cardiac deaths at weekends,

coinciding with higher rates of alcohol consumption.[30] Alcohol consumption patterns are causative for CVD and in particular sudden cardiac death. [30] Traditionally, Eastern Europe and the Russian Federation drink alcohol in a pattern of heavy binges, partly explaining the level of impact of alcohol consumption in their regions.

Ethnicity & Region Populations

European

European populations are diverse as are their experiences of CVD mortality and burden. Eastern Europe has higher fatal and non-fatal CVD burden, for both genders, compared with other European populations.[31] The Russian Federation has a six-fold higher CVD mortality than France.[31] This stark difference is largely attributable to lifestyle risk profiles with higher rates of CVD burden in Eastern Europe linked to higher rates of smoking, alcohol consumption, diets high in saturated fats and poor social circumstances.[31] Interestingly, the relatively low IHD incidence in Southern European countries is hypothesised to be due to the consumption of mono-unsaturated fats, such as olive oil.[32] Paradoxically, the higher consumption of wine has been linked to lower incidence of IHD in France.[32] Many Western European countries have experienced a reduction in CVD over recent decades, attributed largely to better primary and secondary prevention, coupled with improved medical and surgical intervention.[31]

Chinese

Compared to Western Europe, China suffers 50% higher mortality from CVD.[31] The Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) study identified haemorrhagic strokes were 2-3 times higher in Chinese compared with

white Caucasian populations.[33] Tobacco smoking is high amongst Chinese males and contributes to high CVD burden.[33] There may be genetic components that predispose Chinese populations to CVD, evidenced by the direct correlation of cholesterol to IHD mortality despite lower serum cholesterol in the Chinese.[34]

South Asian

This region includes people originating from India, Sri Lanka, Bangladesh, Nepal and Pakistan.[31] Though accurate record keeping is challenging, especially in India[31], the WHO/World Bank epidemiological modelling estimates India to have the second highest CVD mortality worldwide, at >2.5million per year.[35] Furthermore, the burden of CVD in India is set to increase, with DM expected to increase from 2000-2030 by 40%.[31] Various studies have demonstrated migrant South Asian populations experience increased risk of CVD compared to the native populace despite similar levels of exposure to risk factors as the indigenous populations.[36]

Hispanic

This includes Americans of Cuban, Mexican and Puerto Rican descent. They account for 16.3% of the USA population.[37] Globally, CVD accounts for 28% of male and 34% of female Hispanic mortality.[31] The USA Hispanic population have a higher prevalence of classic risk factors in both genders, such as hypertension, smoking, elevated cholesterol, DM and obesity.[31] The USA Hispanic population has a higher incidence of acute myocardial infarction than non-Hispanic americans.[31] This risk is significantly higher for those <60years.[31]

African

The Sub-Saharan Africa population varies significantly to other groups of black people of African origin. Atherosclerosis only causes half of all CVD burden here which is lower than all other regions.[16] The leading cause of death is stroke, 38.8% in 2010,[16] but despite this Sub-Saharan Africa has the lowest mortality rate due to CVD globally at only 10.0%, as recorded in 2012.[7] Sub-Saharan Africa also has the lowest number of years of life lost to CVD[6], accounting for only 3.5% of total lost DALYs in this region.[17] As a region undergoes socio-demographic development the epidemiological profile and burden of disease changes[38], there is a tendency from communicable to NCD as countries grow economically.[38] The unusual profile for Sub-Saharan Africa may be explained by it being at an earlier stage of epidemiological transition with lower average life expectancy (58years for both genders).[39] As a result CVD burden has a different pattern and occurs at younger ages[16], and traditional IHD risk factor burden is lower.[40] It must be acknowledged that much of this information is based on epidemiological modelling to account for data depletion or absence, some caution in its interpretation is therefore warranted.[6] CVD is of particular concern future of African populations as they progress through stages of epidemiological transition and the process of urbanisation accelerates. With increasing urbanisation comes increased exposure to risk factors such as hypertension and hypercholesterolaemia, which has already been attested within the black population of South Africa.[31] Urbanisation rates are projected to increase globally and with this CVD burden will follow. The concept of the epidemiological transition is useful for describing the paradigm change in disease burden but does not supplant country-specific lost DALYs profile as a means of informing health policy decisions.[38]

CVD Global Burden of Individual Conditions

Ischaemic Heart Disease

IHD was the single greatest cause of fatal and non-fatal global disease burden in 2012 with an estimated 165million lost DALYs, which accounts for 6.0% of the total.[5] The burden of IHD has increased from 2000, when the largest single cause of lost DALYs was LRTIs accounting for 7.3% of the total.[5] Globally, there are large variations in total burden of IHD. When the WHO regions are stratified by the world banking organisation income status classification, the highest proportion of lost DALYs attributed to IHD in 2012 was in the LMI South-East Asia region at 26.0%.[17] The LMI Africa and America regions had the lowest proportion of lost DALYs attributable to IHD, both 6%.[17] **Figures 6a and 6b** show the WHO/World Bank regions contribution to the worldwide IHD DALYs lost in 2000 and 2012 respectively.[17] The reduction in DALYs lost in HI countries reflects improvements in healthcare and primary prevention. The significant increases in the LMI South-East Asia and Western Pacific regions reflect an aging population, increasing exposure to lifestyle risk factors and more effective treatment of other health conditions. During 2012, the LMI South-East Asia region had a much larger proportion of men than women affected by IHD.[17] The significant gender difference in South-East Asia is likely to be associated with a significant disparity in tobacco smoking.[1]

Atrial Fibrillation

Atrial fibrillation (AF) is the commonest cardiac arrhythmia worldwide.[41] The global burden of AF is very difficult to estimate as statistics are based on epidemiological studies from North America and Europe[42] with the populations recruited being mainly white Caucasians. In the UK, the West Birmingham-AF project demonstrated a prevalence of 2.4% in white Caucasians and 0.6% among Indo-Asians.[43] Furthermore other studies suggest the proportion of AF in black populations is lower.[41] Lip et al. performed a systematic review to identify and collate the current evidence.[41] The estimated prevalence of AF ranged from 0.1% in India to 4% in Australia.[41] The prevalence in Japan was fairly consistent between 0.6-1.6%. [41] The Chinese and Thai community cohorts were more variable, ranging from 0.8%-2.8% and 0.4%-2.2%, respectively.[41] Lip et al, demonstrated the majority of studies associate increasing age in all populations with AF prevalence.[41] It is for this reason that Rahman et al predicted AF prevalence to double in rapidly developing countries such as India, Brazil, Indonesia, China and Bangladesh.[44]

Heart Failure

Heart failure (HF) is a heterogeneous condition and can be the result of various CVDs. IHD is the predominant cause of CVD in high income nations and non-ischaemic cardiomyopathy and rheumatic heart disease are more common in developing countries.[45] Specific consideration must be given to Chagas disease in Latin America as it is the commonest cause of non-ischaemic cardiomyopathy in the region. [46] There are 6-7 million cases of Chagas disease, with an estimated 25-41% of patients developing HF.[46, 47]

The challenge in estimating HF's specific global burden is partly due to lack of uniformity in making the diagnosis. ICD-10 does not clearly define HF as a separate diagnosis and as such HF is not examined in the GBD study.[9, 14] HF affects approximately 26 million people worldwide[48] and has an estimated 30-40% mortality within the first year of diagnosis.[49] However, 6-month mortality rate decreased from 26% in 1995 to 14% in 2005.[50] The hospitalisation rate for HF patients is high. In Europe and USA, HF is a leading cause of hospitalisation.[50] This accounts for >1million hospital admissions representing 1-2% of all hospitalisations.[52] It is estimated that hospital admissions due to heart failure will rise by 50% over the next 25 years[52] meaning, irrespective of the issues in classification, the condition is one that cannot be ignored in the future of CVD burden.

Congenital Heart Disease

Congenital Heart Disease (CHD) is defined as a clinically significant structural heart disease present at birth.[53] It is a major cause of morbidity and mortality worldwide. In 2012, an estimated 230,000 deaths were attributable to CHD.[4] In 2000, the number of estimated deaths was higher at 234,000, but both years the proportion remained the same at 0.4%.[4] CHD in 2012 was the cause of an estimated 19.8million lost DALYs, which was a reduction from 2000 figures that totalled 20.3million.[5] Proportionally this remained the same in both years at 0.7%.[5] The incidence of CHD has increased, due to the ability to diagnose milder forms of disease that do not cause long-term problems.[53] The current incidence is estimated at 10-12 per 1000 live births.[53] These figures do not appear congruent with the decline in absolute numbers of mortality and loss of DALYs globally. Between 1990-2010 there has been a reduction in loss of

DALYs.[2] Globally, these numbers reflect a greater rate of diagnosis, reflecting better screening and assessment methods.

Conclusion

The patterns of CVD are likely to change, particularly in developing countries. Africa is likely to follow the trends seen in the Indian subcontinent with increasing urbanisation influencing physical activity and diet, as well as improvement in management of communicable diseases leading to more coronary events. Whilst not true for all regions, there is a tendency toward increased CVD burden as the lower income nations progress through the epidemiological transition and the prevalence of key risk factors in these populations increases. The impending worldwide epidemic of DM and AF will have significant roles to play, impacting heavily on global burden of coronary disease and HF. CVD currently represents a leading NCD and is set to remain the most significant global health burden for decades to come.

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Table 1: Global CVD Mortality: 2000 and 2012.

Source: World Health Organization. Comparison of Specific CVD conditions[4]

	2000 Deaths (%)	**2000 95% CI(%)**	**2012 Deaths (%)**	**2012 95% CI(%)**
All Cause	**52,806,000 (100.0%)**		**55,859,000 (100.0%)**	
Communicable, Perinatal, Maternal and Nutritional	16,310,000 (30.89%)	[30.87 - 30.90]	12,822,000 (22.95%)	**[22.94 – 22.97]**
NCD	31,470,000 (59.60%)	[59.58 - 59.61]	37,892,000 (67.84%)	**[67.82 – 67.85]**
CVD	**14,881,500 (28.18%)**	[28.17 – 28.19]	**17,519,300 (31.36%)**	**[31.35 – 31.38]**
Rheumatic heart disease	*371,900 (0.70%)*	[0.70 – 0.71]	*337,300 (0.60%)*	**[0.60 – 0.61]**
Hypertensive heart disease	*849,000 (1.61%)*	[1.60 – 1.61]	*1,141,200 (2.04%)*	**[2.04 – 2.05]**
Ischaemic heart disease	*5,974,100 (11.31%)*	[11.30 – 11.32]	*7,356,100 (1317.%)*	**[13.16 – 13.18]**
Stroke	*5,661,500 (10.72%)*	[10.71 – 10.73]	*6,670,900 (11.94%)*	**[11.93 – 11.95]**
Cardiomyopathy, myocarditis, endocarditis	*401,500 (0.76%)*	[0.76 – 0.76]	*472,300 (0.85%)*	**[0.84 – 0.85]**
Congenital heart anomalies	*234,000 (0.44%)*	[0.44 – 0.44]	*230,000 (0.41%)*	**[0.41 – 0.41]**
*Other circulatory diseases**	*1,623,500 (3.07)*	[3.07 – 3.08]	*1,541,500 (2.76%)*	*[2.76 – 2.76]*

All percentages represent a proportion of total all cause mortality for that respective year

*** =** Not categorised as a 'cardiovascular disease' in the Global Health Estimates report

Table 2: Top 10 Global Causes of Morality in 2000 and 2012.

2000			
Rank	**Cause**	**Deaths (%) [CI]**	**Deaths/100,000 population**
0	**All Causes**	**52,806,020 (100.0%)**	**862.3**
1	Ischaemic heart disease	5,974,060 (11.3%) [11.30 – 11.32]	97.6
2	Stroke	5,661,550 (10.7%) [10.71 – 10.73]	92.5
3	Lower respiratory infections	3,490,570 (6.61%) [6.60 – 6.62]	57.0
4	Chronic obstructive pulmonary disease	3,059,320 (5.79%) [5.79 – 5.80]	50.0
5	Diarrhoeal diseases	2,171,250 (4.11%) [4.11 – 4.12]	35.5
6	HIV/AIDS	1,678,220 (3.18%) [3.17 – 3.18]	27.4
7	Tuberculosis	1,343,080 (2.54%) [2.54 – 2.55]	21.9
8	Preterm birth complications	1,316,100 (2.49%) [2.49 – 2.50]	21.5
9	Trachea, bronchus, lung cancers	1,164,430 (2.21%) [2.20 – 2.21]	19.1
10	Diabetes mellitus	1,045,760 (198.%) [1.98 – 1.98]	17.1
2012			
Rank	**Cause**	**Deaths (%)**	**Deaths/100,000 population**
0	**All Causes**	**55,858,720 (100.0%) [CI]**	**789.5**
1	Ischaemic heart disease	7356060 (13.17%) [13.16 – 13.18]	104.0
2	Stroke	6,670,930 (11.94%) [11.93 – 11.95]	94.3
3	Chronic obstructive pulmonary disease	3,104,330 (5.56%) [5.55 – 5.56]	43.9
4	Lower respiratory infections	3,051,990 (5.46%) [5.46 – 5.47]	43.1
5	Trachea, bronchus, lung cancers	1,599,560 (2.86%) [2.86 – 2.87]	22.6
6	HIV/AIDS	1,533,760 (2.75%) [2.74 – 2.75]	21.7
7	Diarrhoeal diseases	1,497,720 (2.68%) [2.68 – 2.69]	21.2
8	Diabetes mellitus	1,497,370 (2.68%) [2.68 – 2.68]	21.2
9	Road injury	1,254,530 (2.25%) [2.24 – 2.25]	17.7
10	Hypertensive heart disease	1,141,210 (2.041%) [2.04 – 2.05]	16.1

Source: World Health Organization. Comparison of rates between regions 2014[4]

Table 3: Global CVD DALY's Lost: 2000 and 2012.

Source: World Health Organization. Global Health Estimates[5]

	2000 DALYS (%)	**2012** DALYS (%)
All Cause	**2,872,910,085 (100.0%)**	**2,743,857,491 (100.0%)**
Communicable, maternal, perinatal and nutritional conditions	1,243,421,591 (43.3%)	925,727,921 (33.7%)
NCD	1,315,770,489 (45.8%)	1,512,577,728 (55.1%)
CVD	**352,854,272 (12.3%)**	**393,804,862 (14.4%)**
Rheumatic heart disease	*14,312,769 (0.5%)*	*11,953,850 (0.4%)*
Hypertensive heart disease	*19,246,058 (0.7%)*	*23,408,695 (0.9%)*
Ischaemic heart disease	*142,225,562 (5.0%)*	*165,717,210 (6.0%)*
Stroke	*125,127,132 (4.4%)*	*141,348,082 (5.2%)*
Cardiomyopathy, myocarditis, endocarditis	*13,537,411 (0.5%)*	*14,603,113 (0.5%)*
Other circulatory diseases	*38,405,340 (1.3%)*	*36,773,908 (1.3%)*
Congenital heart anomalies	*20,291,404 (0.7%)*	*19,784,491 (1.3%)*

Table 4: Top 10 causes of DALYs between 2000 and 2012

	2000		
Rank	**Cause**	**% DALYs**	**DALYs per 100,000 population**
0	All Causes	100	46913.5
1	Lower respiratory infections	7.3	3402.0
2	Diarrhoeal diseases	5.6	2624.5
3	Ischaemic heart disease	5.0	2322.5
4	Stroke	4.4	2043.3
5	Preterm birth complications	4.3	2015.9
6	Birth asphyxia and birth trauma	3.6	1666.1
7	HIV/AIDS	3.5	1659.8
8	Chronic obstructive pulmonary disease	3.1	1460.2
9	Malaria	2.7	1277.7
10	Road injury	2.4	1129.0
	2012		
Rank	**Cause**	**% DALYs**	**DALYs per 100,000 population**
0	All Causes	100	38779.9
1	Ischaemic heart disease	6.0	2342.1
2	Lower respiratory infections	5.4	2075.7
3	Stroke	5.2	1997.7
4	Preterm birth complications	3.9	1515.2
5	Diarrhoeal diseases	3.6	1409.5
6	Chronic obstructive pulmonary disease	3.4	1305.6
7	HIV/AIDS	3.4	1299.0
8	Road injury	2.9	1112.6
9	Unipolar depressive disorders	2.8	1081.2
10	Birth asphyxia and birth trauma	2.7	1054.3

Source: World Health Organisation. [2]

Figure titles

Figure 1: CVD Mortality in 2000 and 2012 by WHO region.

Figure 2: CVD and NCD mortality in 2000 and 2012 by World Bank Economic Regions.

All LMI regions demonstrate a statistically significant increase (p value <0.001).

Figure 3a: Mortality by Sex and Age in 2012.

Figure 3b: CVD mortality in Males by Age and WHO region in 2012.

Figure 3c: CVD Mortality in Females by Age and WHO region in 2012.

Figure 4: DALYs lost to CVD and NCD in 2000 and 2012 by World Bank Economic Regions

Figure 5a: DALYs lost to CVD by Sex and Age in 2012.

Figure 5b: DALYs lost to CVD in Males by Age and WHO region in 2012.

Figure 5c: DALYs lost to CVD in Females by Age and WHO region in 2012.

Figure 6a: WHO/World Bank Regions contribution to IHD DALYs lost in 2000.

Figure 6b: WHO/World Bank regions contribution to IHD DALYs lost in 2012.