

ORIGINAL ARTICLE

Cardiovascular disease burden:
Italian and global perspectivesAndrea SAGLIETTO^{1,2*}, Roberto MANFREDI^{1,2}, Edoardo ELIA^{1,2}, Fabrizio D'ASCENZO^{1,2},
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ABSTRACT

BACKGROUND: Cardiovascular disease (CVD) is still the leading cause of death worldwide, responsible for an estimated 17.8 million deaths globally in 2017, accounting for 31.8% of all deaths. In this review, we aim to provide an updated overview of CVD burden from an Italian and a global perspective.**METHODS:** Crude and age-standardized incidence and prevalence, as well as age-standardized mortality rate and morbidity rate (expressed as disability-adjusted life years – DALYs), of different cardiovascular conditions, derived from the Global Burden of Disease Injuries, and Risk Factors Study (GBD) 2017, were reported and compared between Italy and the world.**RESULTS:** Crude prevalence of CVD in Italy is nearly twofold higher than global prevalence (12.9% vs. 6.6%), while age-standardized estimates are similar (6.2% vs. 6.3%). Mortality and morbidity from CVD are reduced in Italy, as compared to worldwide estimates (age-standardized mortality rate 113/100,000 vs. 233/100,000; age-standardized rate of DALYs lost 1764/100,000 vs. 4598/100,000). Of the evaluated cardiovascular conditions, the most important CVD burden is due to ischemic heart disease, which show a crude prevalence of 3.6% in Italy (age-standardized: 1.7%), doubling the corresponding crude global estimate (1.7%; age-standardized: 1.6%).**CONCLUSIONS:** This latest update on the epidemiology of CVD within Italy and the world summarizes the burden of major cardiovascular conditions. CVD, especially ischemic heart disease, is still an important cause of mortality and morbidity. The impact of increasing life-expectancy is a key determinant of CVD epidemiology in Italy, if compared to worldwide data, since older age is one of the major risk factors for CVD.*(Cite this article as: Sgalletto A, Manfredi R, Elia E, D'Ascenzo F, De Ferrari GM, Biondi-Zoccai G, et al. Cardiovascular disease burden: Italian and global perspectives. Minerva Cardiol Angiol 2021;69:231-40. DOI: 10.23736/S2724-5683.21.05538-9)***KEY WORDS:** Cardiovascular diseases; Epidemiology; Italy.

Cardiovascular disease (CVD) is still the leading cause of death worldwide, responsible for an estimated 17.8 million deaths globally in 2017, of which more than three quarter in low- and middle-income countries.¹ It accounted for 31.8% of all deaths, nearly twice that caused by cancer (17.1%). Even though the age-standardized CVD mortality rate is decreasing, the absolute number of deaths for CVD is still rising, due

to population aging (being age itself a risk factor for CVD).^{2, 3} This dramatic impact on mortality highlights the importance of a continuous epidemiological update.

In this review, we aim to provide an updated overview of CVD burden from an Italian and a global perspective, reporting the most recent data regarding incidence, prevalence, mortality and morbidity of different cardiovascular conditions.

For this purpose, we used epidemiological estimates derived from the Global Burden of Disease Injuries, and Risk Factors Study (GBD)^{1, 4-11} 2017.

Materials and methods

Global Burden of Disease Injuries, and Risk Factors Study (GBD) 2017

The Global Burden of Disease Study (GBD) is a comprehensive regional and global research program of disease burden assessing mortality and disability from major diseases, injuries, and risk factors. Since 2010, GBD has produced disease burden estimates by country. Each update includes new data sources and methodological advancements, together with a re-analysis of the entire time-series of results. In GBD 2017, 282 causes of death, 359 diseases and injuries, and 84 risk factors for 195 countries and territories by sex, age, and year were included in the estimation. A detailed description of measures and methods employed in the GBD study may be found elsewhere.^{1, 4-11}

Briefly, basing on several data sources, point estimates of incidence, prevalence, excess mortality, and remission were calculated in DisMod-MR 2.1, a Bayesian meta-regression tool,¹² together with uncertainty intervals of the point estimates reflecting uncertainty from model specification, stochastic variation, and measurement bias.

Italian and global GBD data

For the present analysis, data were obtained from the freely accessible GBD Results Tool,¹³ while graphs and pictures were downloaded from GBD VizHub Tool.¹⁴ Location-specific estimates were presented for Italy, as well as global estimates. The evaluated cardiovascular conditions were: cardiovascular disease, ischemic heart disease, hypertensive heart disease, stroke, cardiomyopathies and myocarditis, non-rheumatic valvular heart disease, rheumatic heart disease, atrial fibrillation and flutter, infective endocarditis, congenital heart disease. The list of the corresponding International Classification of Diseases (ICD) codes may be found on the GBD website

(<http://ghdx.healthdata.org/record/ihme-data/gbd-2017-cause-icd-code-mappings>). The evaluated metrics related to the abovementioned conditions were:

- incidence: the number of new cases diagnosed (for 100,000 people); ‘age-standardized’ and ‘all ages’ estimates were reported;
- prevalence: the proportion of people in a population who are a case of a disease (for 100,000 people); ‘age-standardized’ and ‘all-ages’ (crude) estimates were reported;
- mortality rate: number of deaths occurring in a population (for 100,000 people); ‘age-standardized’ estimates was reported, together with the percentage impact of the cause-specific mortality rate on the overall mortality rate;
- disability-adjusted life years (DALYs): the sum of years lost due to premature death and years lived with disability (per 100,000 people); ‘age-standardized’ estimates was reported, together with the percentage impact of the cause-specific DALYs on the overall DALYs.

In order to provide an easier way to read and compare data, we only reported point estimates for the evaluated metrics. Uncertainty intervals can be found at GBD Results Tool (<https://gbd2017.healthdata.org/gbd-search>). Data stratified by sex were also reported in Supplementary Appendix. In addition, we also evaluated historical trends of a subgroup of the analyzed metrics (based on data from previous GBD studies), in order to provide a picture of the epidemiological trajectories throughout the past few decades (from 1990 to 2017).

Results

Detailed data regarding incidence and prevalence are reported in Table I. Supplementary Tables I and II (Supplementary Digital Material 1) provide incidence and prevalence data stratified by sex. Similarly, Table II provides detailed data regarding mortality and morbidity (DALYs), while Supplementary Tables III and IV (Supplementary Digital Material 2) show sex-stratified estimates. Figure 1 reports a global map displaying age-standardized prevalence of CVD, while Figure 2 shows a global map reporting age-standardized CVD mortality rate.

TABLE I.—Crude and age-standardized incidence and prevalence of different cardiovascular conditions estimated by GBD 2017.

Disease	Italy				Global			
	Incidence		Prevalence		Incidence		Prevalence	
	Crude	Age-standardized	Crude	Age-standardized	Crude	Age-standardized	Crude	Age-standardized
Cardiovascular disease	0.576%	0.232%	12.874%	6.154%	0.189%	0.181%	6.589%	6.324%
Ischemic heart disease	0.079%	0.030%	3.613%	1.654%	0.027%	0.026%	1.715%	1.646%
Hypertensive heart disease	nr	nr	0.720%	0.285%	nr	nr	0.231%	0.226%
Stroke	0.042%	0.016%	1.291%	0.617%	0.031%	0.029%	1.413%	1.352%
Cardiomyopathies and myocarditis	0.012%	0.007%	0.539%	0.233%	0.007%	0.007%	0.073%	0.071%
Non-rheumatic valvular heart disease	0.359%	0.141%	1.716%	0.753%	0.079%	0.076%	0.403%	0.394%
Rheumatic heart disease	0.001%	0.0004%	0.011%	0.007%	0.003%	0.003%	0.533%	0.520%
Atrial fibrillation and flutter	0.021%	0.009%	1.457%	0.597%	0.007%	0.007%	0.509%	0.500%
Infective endocarditis	0.004%	0.001%	0.033%	0.015%	0.003%	0.004%	0.008%	0.008%
Congenital heart disease	0.001%	0.004%	0.107%	0.179%	0.006%	0.007%	0.162%	0.177%

nr., not reported.

TABLE II.—Age-standardized mortality rate and rate of DALYs lost, with respective percentage on total deaths and total DALYs lost, for different cardiovascular conditions estimated by GBD 2017.

Disease	Italy				Global			
	Deaths		DALYs		Deaths		DALYs	
	Age-standardized rate (per 10 ⁵ individuals)	Percentage on total deaths	Age-standardized rate (per 10 ⁵ individuals)	Percentage on total deaths	Age-standardized rate (per 10 ⁵ individuals)	Percentage on total DALYs	Age-standardized rate (per 10 ⁵ individuals)	Percentage on total DALYs
Cardiovascular disease	113.15	34.814%	1763.826	16.038%	233.07	31.800%	4597.928	14.662%
Ischemic heart disease	51.392	15.505%	748.851	6.757%	116.949	15.962%	2132.124	6.826%
Hypertensive heart disease	10.611	3.536%	126.755	1.326%	12.283	1.654%	209.419	0.662%
Stroke	30.417	9.541%	458.373	4.263%	80.453	11.023%	1657.227	5.291%
Cardiomyopathies and myocarditis	4.09	1.253%	76.778	0.641%	4.797	0.658%	130.296	0.410%
Non-Rheumatic valvular heart disease	2.862	0.870%	44.885	0.426%	1.97	0.258%	32.736	0.101%
Rheumatic heart disease	1.593	0.448%	25.976	0.211%	3.676	0.510%	118.724	0.376%
Atrial fibrillation and flutter	4.817	1.594%	90.44	0.918%	4	0.513%	77.969	0.238%
Infective endocarditis	1.08	0.298%	20.043	0.151%	1.192	0.149%	29.045	0.089%
Congenital heart disease	0.958	0.049%	83.332	0.146%	3.856	0.466%	330.047	0.891%

Prevalence

Crude prevalence of CVD in Italy is nearly two-fold higher than global prevalence (12.874% vs. 6.589%), while age-standardized estimates show similar results (6.154% vs. 6.324%). The most important CVD burden is due to ischemic heart disease and stroke, which show a crude prevalence of 3.613% and 1.291% in Italy (age-standardized estimates: 1.654% and 0.617%), with a corresponding global estimates of 1.715% and 1.413% (age-standardized estimates: 1.646% and 1.352%). Crude prevalence of hypertensive heart disease is 0.720% in Italy (age-standardized estimate: 0.285%), while it settles at 0.231% global-

ly (age-standardized estimate: 0.226%). Among valvular heart disease, non-rheumatic etiology is more frequent in Italy (crude estimate: 1.716%; age-standardized estimate: 0.753%) than globally (crude estimate: 0.403%; age-standardized estimate: 0.394%), while rheumatic etiology is by far more prevalent globally as compared to Italy (Italy: crude estimate 0.007%, age-standardized estimate 0.011%; worldwide: crude estimate 0.533%, age-standardized estimate 0.520%). Crude prevalence of cardiomyopathies and myocarditis, infective endocarditis and congenital heart disease in Italy is, respectively, 0.539%, 0.033% and 0.107% (age-standardized

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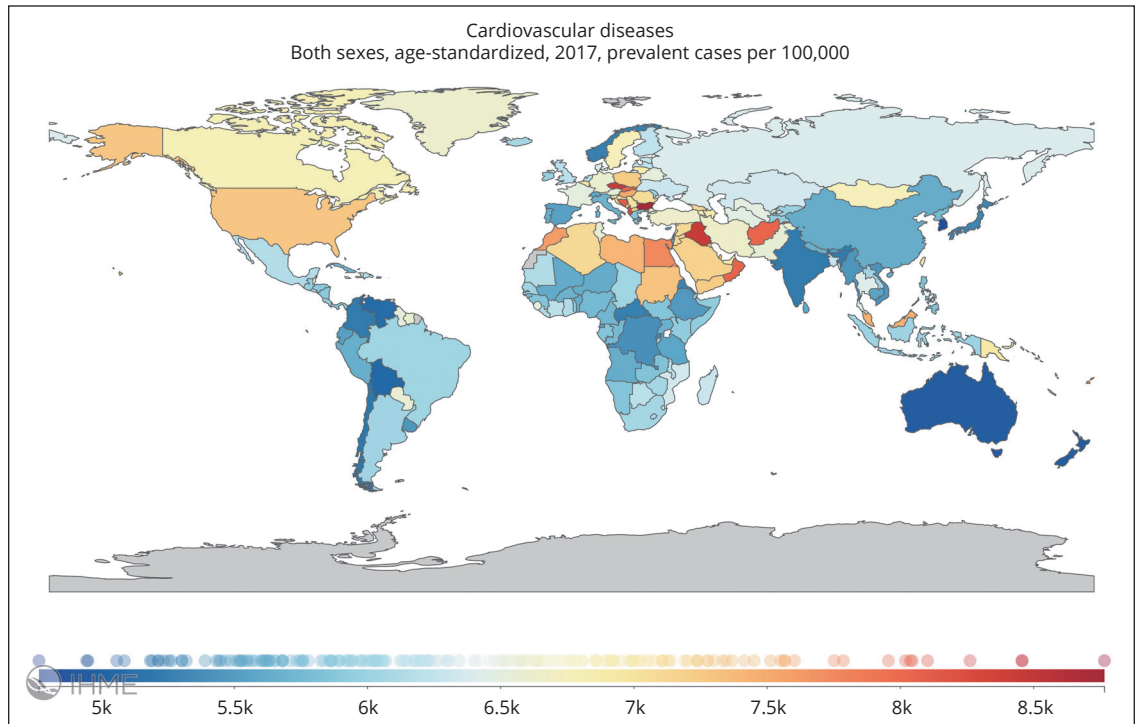


Figure 1.—Global age-standardized prevalence of CVD in 2017 (graph obtained using Viz Hub).¹⁴

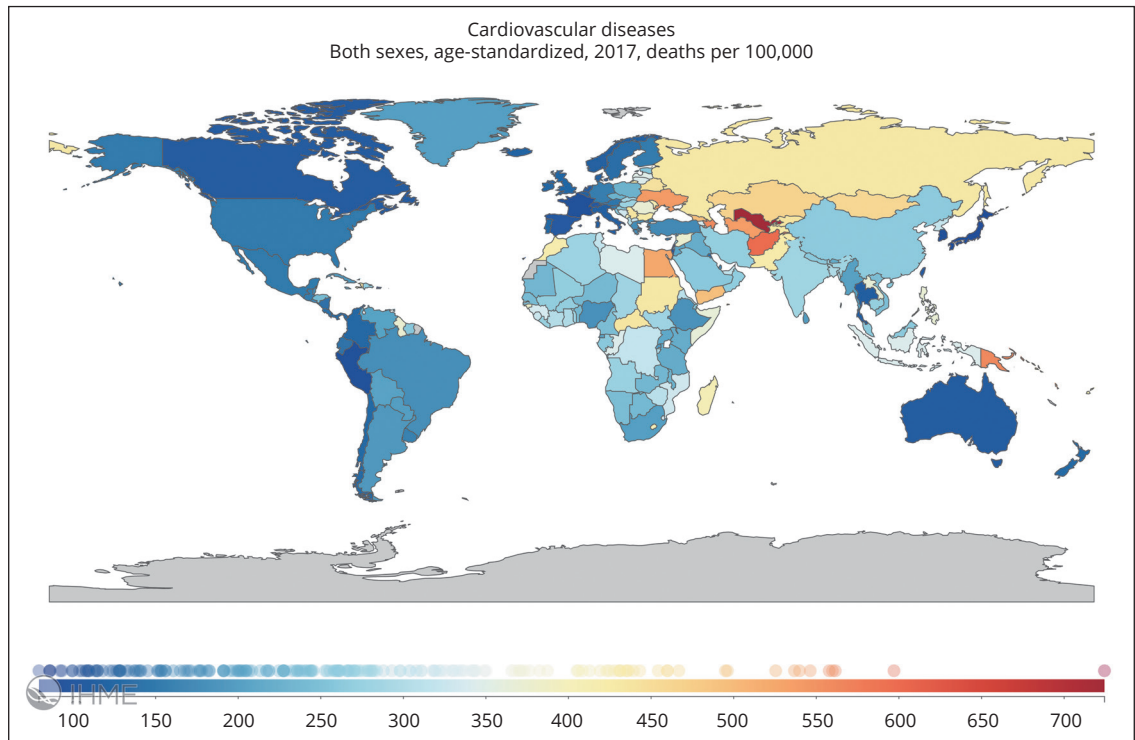


Figure 2.—Global age-standardized CVD deaths in 2017 (graph obtained using Viz Hub).¹⁴

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estimates: 0.233%, 0.015% and 0.179%), while it settles at 0.073%, 0.008% and 0.162% (age-standardized estimates: 0.071%, 0.008% and 0.177%) globally. Finally, estimated prevalence of atrial fibrillation/flutter in Italy is 1.457% (age-standardized estimate: 0.597%), which is nearly threefold than global prevalence, settled at 0.509% (age-standardized estimate: 0.500%).

Incidence

Crude incidence of CVD in Italy is higher than global incidence (0.576% vs. 0.189%), while age-standardized estimates are similar (0.232% vs. 0.181%). In Italy, ischemic heart disease and stroke show crude incidence estimates of 0.079% (age-standardized estimate: 0.030%) and 0.042% (age standardized-estimate: 0.016%), while the corresponding global estimates are 0.027% (age-standardized estimate: 0.026%) and 0.031% (age-standardized estimate: 0.029%). Incidence of non-rheumatic and rheumatic valvular heart disease in Italy is, respectively 0.359% (age-standardized estimate: 0.141%) and 0.001% (age-standardized estimate: 0.0004%), differently from the corresponding global estimates which are settled at 0.079% (age-standardized: 0.076%) and 0.003% (age-standardized: 0.003%). Concerning cardiomyopathies and myocarditis, infective endocarditis and atrial fibrillation/flutter estimated incidence in Italy are 0.012% (age-standardized: 0.007%), 0.004% (age-standardized: 0.001%) and 0.021% (age-standardized: 0.009%), while globally estimated values are settled at 0.007% (age-standardized: 0.007%), 0.003% (age-standardized: 0.004%) and 0.007% (age-standardized: 0.007%) respectively. Finally, the incidence of congenital heart disease in Italy is 0.001% (age-standardized estimate: 0.004%), which is lower than its global counterpart (crude estimate: 0.005%; age-standardized estimate: 0.006%).

Mortality

CVD accounts for 34.81% of deaths in Italy, with an age-standardized mortality rate of 113/100,000; similarly CVD accounts for 31.80% of deaths globally, showing an higher age-standardized mortality rate (233.01/100,000). Focusing on ischemic heart disease and stroke,

they cause 15.51% (age-standardized mortality rate: 51.39/100,000) and 9.54% (age-standardized mortality rate: 30.41/100,000) of deaths in Italy, while accounting for 15.96% (116.94/100,000 deaths age standardized) and 11.02% (80.45/100,000 deaths age standardized) of worldwide mortality burden. Hypertensive heart disease, non-rheumatic heart disease and rheumatic heart disease account for, respectively, 3.53% (age-standardized mortality rate: 10.61/100,000), 0.87% (age-standardized mortality rate: 2.86/100,000) and 0.45% (age-standardized mortality rate: 1.59/100,000) of deaths in Italy, with their corresponding worldwide estimates settled at 1.65% (age-standardized mortality rate: 12.28/100,000), 0.26% (age-standardized mortality rate: 1.97/100,000) and 0.51% (age-standardized mortality rate: 3.68/100,000). Cardiomyopathies and myocarditis, infective endocarditis and atrial fibrillation/flutter in Italy contributes to 1.25% (age-standardized mortality rate: 4.09/100,000), 0.30% (age-standardized mortality rate: 1.08/100,000) and 1.59% (age-standardized mortality rate: 4.8/100,000) of total deaths, while they contribute for 0.66% (4.80/100,000 deaths age standardized), 0.15% (1.9/100,000 deaths age standardized) and 0.51% (4.0/100,000 deaths age standardized) of global deaths, respectively. Lastly, congenital heart disease is responsible for 0.05% of deaths in Italy (age-standardized mortality rate: 0.96/100,000), while it accounts for 0.47% of deaths worldwide (age-standardized mortality rate: 3.86/100,000).

Morbidity

CVD accounts for 16.038% of total DALYs lost in Italy (age-standardized rate of DALYs lost: 1763.826/100,000 age standardized), with a corresponding worldwide estimate of 14.662% (age-standardized rate of DALYs lost: 4597.928/100,000). The impact of ischemic heart disease and stroke on morbidity is, respectively, 6.757% and 4.263% in Italy (age-standardized rate of DALYs lost: 748.851/100,000 and 458.373/100,000), while they account for 6.826% and 5.291% of total DALYs lost globally (age-standardized rate of DALYs lost: 2132.124/100,000 and 1657.227/100,000). DALYs lost for hypertensive heart disease account for

1.326% (age-standardized rate of DALYs lost: 126.755/100,000) of the total amount in Italy, while settling at 0.662% globally (age-standardized rate of DALYs lost: 209.419/100,000). Among valvular heart disease, DALYs lost due to non-rheumatic etiology are 0.426% (age-standardized rate of DALYs lost: 44.885/100,000) in Italy, as compared to a global estimate of 0.101% (age-standardized rate of DALYs lost: 32.736/100,000), while DALYs lost due to rheumatic etiology are 0.211% (age-standardized rate of DALYs lost: 25.976/100,000 age standardized) of total DALYs in Italy, with a global estimate settled at 0.376% (age-standardized rate of DALYs lost: 118.724/100,000).

Cardiomyopathies and myocarditis, infective endocarditis and congenital heart disease contribute, respectively, for 0.641%, 0.151% and 0.146% (age-standardized rate of DALYs lost: 76.778/100,000, 20.043/100,000, 83.332/100,000) of total DALYs lost in Italy, and for 0.410%, 0.089% and 0.891% (age-standardized rate of DALYs lost: 130.296/100,000, 29.045/100,000, 330.047/100,000) globally.

Finally, atrial fibrillation/flutter burden on total DALYs in Italy is 0.918% (age-standardized rate of DALYs lost: 90.440/100,000 age standardized), as compared to 0.238% (age-standardized rate of DALYs lost: 77.969/100,000 age standardized) globally.

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Discussion

Despite CVD mortality has shown a decreasing trend since 1990 (Figure 3), it is still one the main cause of death worldwide and in Italy, accounting for 31.80% and 34.81% of total deaths, respectively.^{15, 16} In particular, CVD is still the leading cause of death globally, while in Italy during the last 10 years neoplasms have passed CVD as the leading cause of death (Figure 4 illustrates the rankings of cause of mortality, both globally and in Italy, for 2007 and 2017). In this regard, considering that cancer is expected to overtake CVD becoming the leading mortality cause globally for the 21st century, Italy is probably ahead of time as concerns this trend inversion, due to some peculiar features, in particular older mean age, environmental characteristics, Mediterranean diet and healthier lifestyle.^{17, 18}

Focusing on incidence and prevalence, the crude impact of CVD is more evident in Italy, with a nearly threefold incidence and twofold prevalence compared to the global estimates. Age-standardized data, which correct the bias induced by the older population in Italy (where

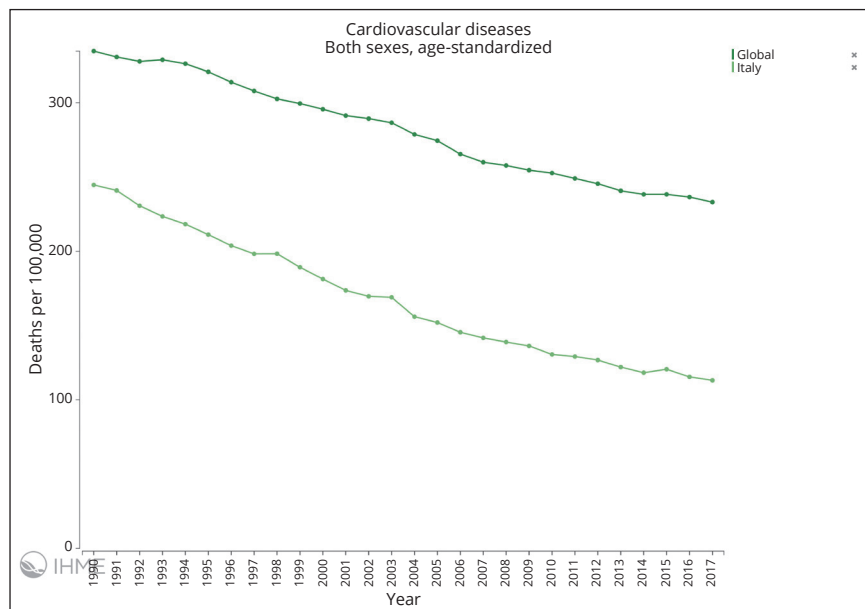


Figure 3.—CVD mortality rate from 1990 (graph obtained using Viz Hub).¹⁴

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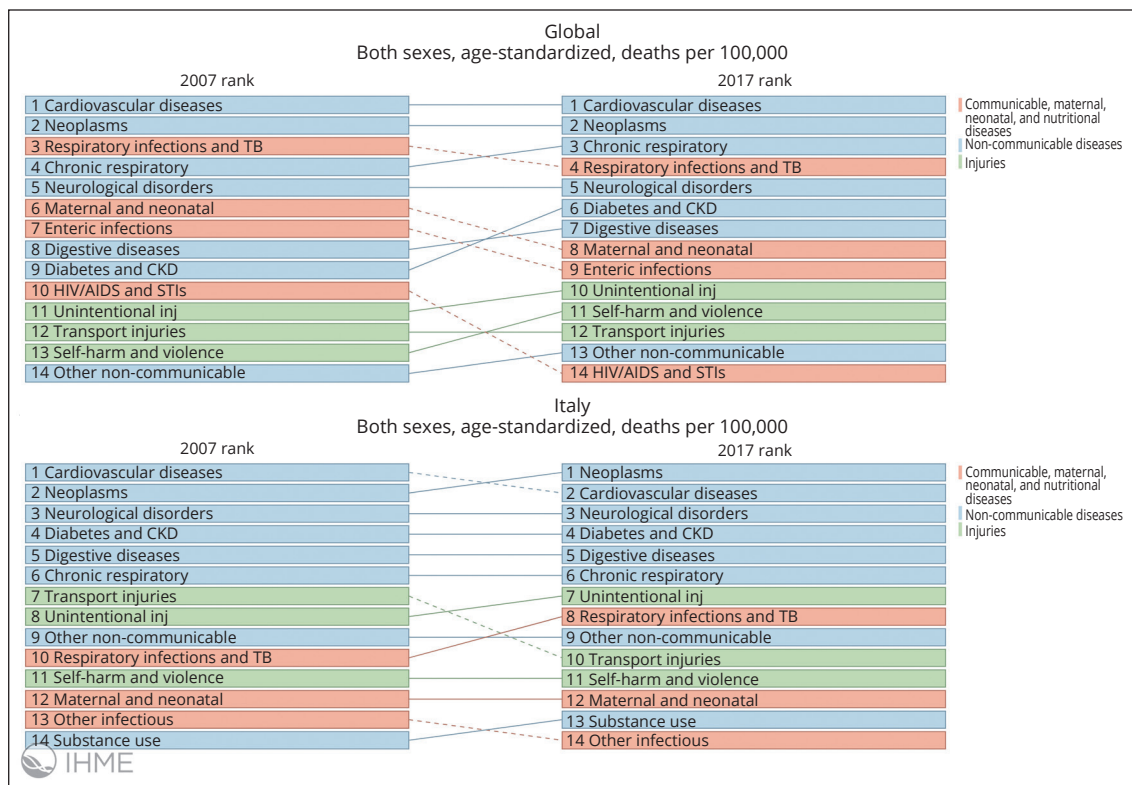


Figure 4.—2007 and 2017 ranks for age-standardized mortality rate in Italy and globally (graph obtained using Viz Hub).¹⁴

median age was 45.5 years in 2017, ranked 5th in the world; global median age was 30 years),¹⁹ shows a similar prevalence, with a slightly higher incidence of CVD in Italy, indicating that older population age is the most poignant confounder when comparing crude CVD epidemiological measures, being strongly correlated with CVD and CVD risk factors, such as hypertension. Comparing Italian data with some peer-countries (major European countries, the USA, Japan) some differences in prevalence can be seen, with the highest values in the USA, followed by Northern European countries, intermediate values in Mediterranean countries (Italy, Spain), and lower values in Japan, which may be explained by several factors, such race, lifestyle and dietary factors (Supplementary Digital Material 3: Supplementary Table IV). What is noteworthy is the fact that age-standardized mortality rate from CVD is twofold higher globally, suggesting high-quality standard of care of Italian National Health System (NHS) and a more

difficult access to healthcare facilities in low- and middle-income countries. In addition, also environmental factors, Mediterranean diet and a healthier Italian lifestyle may partly explain this finding.^{20, 21} Morbidity data show a similar trend, with nearly threefold rate of DALYs lost per 100,000 individuals globally, as compared to Italy. If we compare Italian data with some peer-countries (major European countries, the USA, Japan) some differences in cardiovascular disease burden can be seen, with the highest values found in the USA and Northern European countries, intermediate values in Mediterranean countries, and lower values in Japan (Supplementary Table IV).

Ischemic heart disease is responsible for the main component of CVD burden both in Italy and globally. Italy shows a higher crude prevalence and incidence of ischemic heart disease, but age-standardized estimates of these quantities are similar, underlining the importance of the age-population structure when deal-

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ing with epidemiological data. If we consider mortality and morbidity data, age-standardized estimates of ischemic heart disease mortality rate and rate of DALYs lost due to this condition are one third of the corresponding global estimates, thus highlighting the importance of the high-quality treatment provided by Italian NHS and possibly suggesting a lower age at diagnosis worldwide as compared to Italy.^{22, 23} Since ischemic heart disease and cerebrovascular diseases share a comparable pathophysiological background, stroke data are similar to ischemic heart disease data, with the only difference that age-standardized prevalence seems to be lower in Italy as compared to the global estimate, most likely due to more premature cerebrovascular events, especially in low- and middle-income countries.²⁴

Hypertension and hypertensive heart disease are strictly related to age, as crude prevalence estimate indicates that they are more common in Italy with respect to the rest of the world. It is important to notice that age-standardized data show greater mortality rate worldwide, but a higher morbidity burden in Italy, hinting that an early diagnosis and treatment slow the progression of the disease, ultimately leading to lower mortality, at the cost of higher DALYs lost.²⁵

Regarding valvular heart disease, as expected, Italy shows higher incidence, prevalence, mortality and DALYs lost for non-rheumatic valvular heart disease compared to the world, which, on the other hand, presents with higher incidence, prevalence, mortality and DALYs lost for rheumatic valvular heart disease. This divergency is mainly due to the different pathophysiology of these diseases, since the lack of antibiotics availability in some of the non-western countries implies an increased burden of rheumatic heart disease, while older age and the consequent higher prevalence of cardiovascular risk factors in Italy pave the way for the development of non-rheumatic valvular heart disease.^{6, 26}

Epidemiological data regarding the prevalence of congenital heart disease in Italy and worldwide are similar, while a lower incidence can be seen in Italy as compared to global estimate, probably due to an easier access to prenatal diagnosis. The diffusion of prenatal diagnosis

also led to better treatment, which could explain the divergence of age-standardized mortality rate and rate of DALYs lost between Italy and the world, resulting in a more favorable prognosis in Italy.²⁷

Atrial fibrillation/flutter is characterized by a higher crude incidence and prevalence in Italy compared to worldwide data, most likely due to an older population and the superimposition of other risk factors for atrial arrhythmias in the elderly, even though non-Caucasian ethnicity seems to be associated with greater risk.²⁸ In support of this claim, age-standardized prevalence and incidence do not differ too much (they are slightly higher in Italy), thus highlighting the key role played by age-population structure in this context, with literature data reporting an atrial fibrillation/flutter prevalence ranging from 3% in 65-69 years old to 16.1% in >85 years old age groups, and mortality increasing steeply with age, being above 1% among people aged 85 or more.^{29, 30} Concerning mortality and morbidity, the percentual impact of atrial fibrillation/flutter on total deaths and DALYs lost is more than three-fold higher in Italy as compared to worldwide estimate, with similar age-standardized estimates, suggesting that in a western country the percentual impact of atrial arrhythmias on overall mortality and morbidity may be higher than in a non-western country. Moreover, comparing Italy with other similar countries, disease burden is comparable, with the only exception of Japan (Supplementary Digital Material 4: Supplementary Table VI).

Cardiomyopathies and myocarditis have a similar incidence in Italy and worldwide, with higher prevalence in Italy, probably due to the older population and to easier access to diagnostic tools.^{31, 32} It should be remembered that cardiomyopathy etiology and prognosis are heterogeneous, since various phenotypes may underlie genetic, environmental and individual factors.^{33, 34} Concerning mortality and morbidity, higher age-standardized mortality rate and rate of DALYs lost are seen worldwide, again supporting the claim that Italian NHS has high-quality standards in terms of therapeutic achievements.

Infective endocarditis is quite uncommon between the investigated diseases and has a

similar crude incidence in Italy and globally, while age-standardized incidence globally is about four times higher than in Italy. Crude prevalence in Italy is about four times higher than the global one, while age-standardized prevalence is nearly twofold. These data may be explained by different factors, such as the higher prevalence of predisposing conditions like older age in developed countries like Italy (which is associated to native valve degenerative disease), while strong risk factors for infective endocarditis in developing countries are rheumatic heart disease and lower standards of prophylaxis during dental procedures.^{35, 36} Age-standardized mortality and morbidity data regarding infective endocarditis are higher worldwide: this observation may be explained by the fact that infective endocarditis is an insidious disease, whose etiologic agent is often nonidentified, particularly in developing countries (where also access to surgery is more difficult), thus hampering proper pharmacological and non-pharmacological therapy.³⁷

Conclusions

This latest update on the epidemiology of CVD within Italy and the world summarizes the burden of major cardiovascular conditions, described through prevalence, incidence, mortality and morbidity data. Despite the decreasing trend of CVD mortality seen both in Italy and worldwide, the burden of CVD, especially ischemic heart disease, is still an important cause of mortality and morbidity. Moreover, the impact of increasing life-expectancy is a key determinant of CVD epidemiology in Italy, if compared to worldwide data, since older age is one of the major risk factors for CVD.

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