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ORIGINAL ARTICLE

The burden of atherosclerosis in Portugal

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Aims This article sought to estimate the burden of disease attributable to atherosclerosis in mainland Portugal in 2016.

Methods and results The burden of atherosclerosis was measured in disability-adjusted life years following the latest 2010 Global Burden of Disease (GBD) methodology. Disability-adjusted life years were estimated as the sum of years of life lost (YLL) with years lived with disability (YLD). The following clinical manifestations of atherosclerosis were included: ischaemic heart disease (IHD) (including acute myocardial infarction, stable angina, and ischaemic heart failure), ischaemic cerebrovascular disease (ICVD), and peripheral arterial disease (PAD). Years of life lost were estimated based on all-cause mortality data for the Portuguese population and mortality due to IHD, ICVD, and PAD for the year 2016 sourced from national statistics. Standard life expectancy was sourced from the GBD study. Years lived with disability corresponded to the product of the number of prevalent cases by an average disability weight for all possible combinations of disease. Prevalence data for the different clinical manifestations of atherosclerosis were sourced from epidemiological studies. Disability weights were sourced from the published literature. In 2016, 15 123 deaths were attributable to atherosclerosis, which corresponded to 14.3% of overall mortality in mainland Portugal. Disability-adjusted life years totalled 260 943, 75% due to premature death (196 438 YLL) and 25% due to disability (64 505 YLD).

Conclusion Atherosclerosis entails a high disease burden to society. A large part of this burden would be avoidable if evidence-based effective and cost-effective interventions targeting known risk factors, from prevention to treatment, were implemented.

Keywords Atherosclerosis • Burden of disease • DALYs • Morbidity • Mortality • Portugal

Introduction

Atherosclerosis is a chronic and progressive arterial disease and the most common pathophysiologic process underlying cardiovascular disease. Its major clinical manifestations include ischaemic heart disease (IHD), ischaemic cerebrovascular disease (ICVD), and peripheral arterial disease (PAD).[1] Although the landscape of cardiovascular disease has changed over the last decades, with high-

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and middle-income countries reporting declines in incidence and mortality from IHD and ischaemic stroke,[2] cardiovascular disease remains the leading cause of death worldwide,[3] particularly in Europe.[4] Changes in health behaviours and use of treatments for modifiable risk factors, such as smoking, hypertension, and dyslipidaemia, are, at least partially, responsible for the decline in cardiovascular mortality seen in high- and middle-income countries.[5,6] In Portugal, cardiovascular disease-related mortality represented 29.4% of total mortality in 2017.[7]

Therefore, atherosclerosis is expected to have a significant burden amongst the Portuguese population. This study estimated the burden of disease attributable to atherosclerosis in mainland Portugal in 2016, which is the most recent year for which data were available at the time of the study.

Methods

Study setting

In 2016, mainland Portugal had 9 809 414 inhabitants with 53% women and 21.4% men aged over 65 years.[8] Life expectancy at birth is 80.8 years, with a substantial gap between men and women. In 2016–2018, men could expect to live (77.8 years) on average 6 years less than women (83.4 years).[9]

The Portuguese health system is characterized by three overlapping systems. The National Health Service is universal, comprehensive and almost free, financed mainly through taxation. All residents are covered, irrespective of their socioeconomic, employment, or legal status. In addition, special health insurance schemes cover particular professions or sectors and can be either public (e.g. for civil servants) or private (e.g. banking sector). Private Voluntary Health Insurance is supplementary and speeds up access to elective hospital treatment and ambulatory consultations; it also increases the choice of provider.

Overview of methodology used

The current study estimated the burden of atherosclerosis based on the most recent Global Burden of Disease (GBD) 2010 methodology[10] and considered the following clinical presentations of atherosclerosis: IHD, ICVD, and PAD, along with death.

A scoping review of grey literature was conducted to identify relevant national sources of epidemiological data on the parameters of interest. The search was conducted using both international [Medline via OVID; combining the terms atherosclerosis, IHD, acute myocardial infarction (AMI), ischaemic heart failure (IHF), stable angina, ICVD, and PAD] and national databases (Portuguese Health Directorate, Statistics Portugal, and Index RMP—an index of Portuguese biomedical research and clinical sciences journal articles and monographs). A summary of the sources of information used is outlined in *Table 1*.

The overall burden of disease attributed to atherosclerosis was measured in DALYs (disability-adjusted life years), which is a metric of population health adopted by the World Health Organization and developed for the GBD studies. A DALY is equivalent to 1 year of healthy life lost and enables the measure of the burden of disease given as a gap between current health and an ideal situation where the whole population lives up to the age of standard life expectancy in perfect health, without disease or disability.[11]The DALY combines estimates of years of life lost (YLL) and years lived with disability (YLD) into a single measure, being the most widely used measure of disease burden, and can be applied across cultures.[12]

Table 1 Parameters and information sources used to estimate the burden of disease attributable to atherosclerosis in mainland Portugal, 2016

Parameter	Source
Population	Statistics Portugal 2016
All-cause mortality	Statistics Portugal 2016
Case fatality ICVD and PAD	Portuguese Health Directorate
Case fatality IHD	Statistics Portugal
Standard life expectancy	Life tables GBD 2016
DWs	GBD 2015[a]
Prevalence IHD	Hospital Morbidity Database 2016
Prevalence stable angina	National Health Survey 2014
Prevalence of angina by severity level	AVANCE registry (Borrás *et al.*, 2012)
Prevalence for NYHA Classes II–IV of IHF	EPICA study (Ceia *et al.*, 2002)
Prevalence of stroke	National Health Survey 2014
Incidence and case fatality of stroke	Hospital Morbidity Database 2016
Prevalence of PAD	Menezes *et al.* (2009)

[a]Some disability weights (DW) were weighted by the distribution of clinical diseases across levels of severity to get final estimates.
DW, disability weight; GBD, Global Burden of Disease; ICVD, ischaemic cerebrovascular disease; IHD, ischaemic heart disease; IHF, ischaemic heart failure; NYHA, New York Heart Association Classes; PAD, peripheral arterial disease.

Global Burden of Disease studies prior to 2010 utilized a discount rate of 3% to estimate the net present value of YLL and age weighting, where according to the theory of human capital, years lived as a young adult were valued more highly than years lived as a young child or an older adult, given these being years of peak productivity.[13] The current methodology does not apply discounting nor age weighting. Additionally, the current methodology used to estimate YLD is based on prevalence estimates rather than incidence cases and duration of disease.[10]

In this study, the burden of disease expressed as DALYs was estimated for mainland Portugal for the year 2016, and presented by sex and age groups. To calculate DALYs for the Portuguese population, YLL due to premature mortality from atherosclerosis were added to the number of YLD from prevalent cases related to the different clinical presentations of atherosclerosis according to the formula:

$$\mathrm{DALY}\ (c,\ s,\ a,\ t) = \mathrm{YLL}\ (c,\ s,\ a,\ t) + \mathrm{YLD}\ (c,\ s,\ a,\ t),$$

where c is the cause, s is sex, a is age, and t is time.

Years of life lost due to premature mortality

Years of life lost corresponded to the product of the number of deaths by the standard life expectancy at the age which death occurs. Mortality data were collected for International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes I20–I25 (IHD), I63–I66, I67.2, I67.8, I69.3, and I69.4 (ICVD), I70.2 and I74.3 (PAD), and I70 and I74 (atherosclerosis/arterial embolism and thrombosis, hereafter referred to as *other*). Despite IHF being one of the possible clinical presentations of IHD, deaths due to IHF were not considered because (i) the direct cause of death may not be attributable to IHF, rather to an underlying disease such as, for instance, myocardial infarction, which means that some deaths may already have been included amongst deaths due to IHD[14], and (ii) atherosclerosis is solely one amongst other causes of IHF,

Table 2 Mortality and years of life lost due to atherosclerosis, relative to mortality and years of life lost due to all other causes in mainland Portugal, 2016

	Deaths		YLL	
	N	% total[a]	*n*	% total[a]
IHD	6887	6.5%	106 905	6.7%
ICVD	7592	7.2%	83 916	5.2%
PAD	25	0.02%	204	0.01%
Other forms of atherosclerosis[b]	619	0.6%	5412	0.3%
Total	15 123	14.3%	196 438	12.2%

[a]All-cause mortality. A total of 105 542 deaths and 1.6 million YLL due to premature overall mortality in mainland Portugal, 2016.
[b]Atherosclerosis/arterial embolism and thrombosis.
ICVD, ischaemic cerebrovascular disease; IHD, ischaemic heart disease; PAD, peripheral arterial disease; YLL, years of life lost.

and hereby there was no available data on deaths specifically due to heart failure (HF) attributable to atherosclerosis.

All-cause mortality for the Portuguese population and mortality due to IHD for the year 2016 were sourced from Statistics Portugal.[15] Mortality data due to ICVD and PAD were sourced from the Portuguese Health Directorate. Standard life expectancy was defined as the maximum attainable life expectancy, based on a standard life table developed for the GBD 2016 study.[16] The total number of deaths and total YLL due to atherosclerosis were compared to the total overall mortality and total YLL due to overall premature mortality in the Portuguese population (estimated by the authors).

Years lived with disability

Years lived with disability due to atherosclerosis corresponded to the product of the number of prevalent cases by corresponding disability weights (DWs) for all clinical manifestations of disease. A DW is a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead). It quantifies societal preferences for different health states in relation to the societal ideal of good health. Disability weights were sourced from the most recent GBD 2015 study.[3] Data for the Portuguese population were used, when available, for the year 2016. When no Portuguese data were available, the next best available evidence was considered from population studies conducted in Spain given the similarities in patterns of cardiovascular disease between countries.[17]

Prevalence and disability weights of ischaemic heart disease

Three clinical presentations of IHD were included and considered separately: AMI, stable angina, and IHF. Given the different DW associated with each disease (related to severity and consequences), a weighted average DW was estimated based on the distribution of prevalent cases of disease by severity level.

Acute myocardial infarction

The prevalence of AMI was assumed to correspond to its incidence as the disability due to AMI is often associated with the acute phase of the disease, which corresponds to the first 28 days. Incidence was retrieved from the Portuguese Hospital Morbidity Database 2016, centrally held by the Central Administration of the Health System (ACSS), and corresponded to the number of episodes identified with a main diagnosis coded as 410, according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), and I21 according to the ICD-10-CM. The DW associated with an episode of AMI, corresponding to a duration of 28 days,[3] was estimated as the average of the DW attributed to the first 2 days after the event (DW = 0.432) and the DW attributed to the remaining 26 days (DW = 0.074) weighted by the distribution of incident cases across the two, and transformed into an annual weight (DW = 0.01).

Stable angina

Prevalence data by gender and age group were sourced from the National Health Survey[18] for the year 2014. Prevalence estimates were adjusted to mainland population statistics for the year 2016. Three levels of severity were considered for stable angina (mild, moderate, and severe), each attributed a different DW. Due to lack of relevant national data, the distribution of cases of angina according to severity levels were obtained from the AVANCE registry, a Spanish observational study including 2039 individuals with angina.[19] This source was chosen given the similarities and patterns of population characteristics and cardiovascular disease between countries. According to Borrás *et al.*, 40% of the cases of stable angina were mild, 45% moderate, and 15% severe, resulting in a weighted average DW of 0.07.

Ischaemic heart failure

Three DW corresponding to the levels of severity mild, moderate, and severe were considered for IHF and sourced from the GBD. These DW were considered as *proxy* to the New York Heart Association (NYHA) Classes II–IV. It was assumed that patients with NYHA Class I have no disability, hence YLD were estimated for patients with HF NYHA Classes II–IV only. Prevalence data for the NYHA Classes II–IV of IHF in mainland Portugal were sourced from data from the EPICA study,[20] a Portuguese community-based epidemiological survey of HF prevalence conducted in 1998–2000 including 5434 adult individuals aged >25 years attending primary care centres. Prevalence rates by age and sex from the study were extracted and applied to the Portuguese population in 2016 (by age and sex).

The proportion of individuals with IHF corresponded to 36% of the prevalence of HF estimated by Ceia *et al.*, of which, 41% with NYHA II, 42% NYHA III, and 7% NYHA IV. A DW of 0.06 was considered for IHF.

Prevalence and disability weights of ischaemic cerebrovascular disease

The prevalence of stroke was sourced from the latest available National Health Survey conducted in 2014,[18] a nationwide survey of the Portuguese population aged 15 and older. The survey aims to characterize the current health status, health resource use, and lifestyle-related determinants of health in a sample of the population in the last 12 months, based on self-report. The INS 2014 is harmonized and regulated at EU level [Commission Regulation (EU) No 141/2013], enabling an international comparison of the results. According to the survey, 164 829 patients were estimated to have had any kind of stroke or chronic sequelae. Prevalence rates by age and sex were extracted and applied to the Portuguese population in 2016 (by age and sex).

Using incidence and case fatality estimates retrieved from the Hospital Morbidity Database for the year 2016, we were able to estimate the corresponding number of patients with ICVD at 83% (136 725 patients). This estimate considered an incidence of 17 113 patients with stroke, and assumed that a majority of prevalent cases of ICVD were related to chronic sequelae due to stroke. The Hospital Morbidity Database is a national registry of all public hospital-related care, both inpatient and

Table 3 Mortality and years of life lost due to individual clinical manifestations of atherosclerosis in mainland Portugal, 2016

	IHD		ICVD		PAD		Other forms of atherosclerosis[a]		Atherosclerosis	
	Deaths	YLL	Deaths	YLL	Deaths	YLL	Deaths	YLL	Deaths	YLL
Men	3880	71 790	3065	39 207	10	107	191	2196	7146	113 300
Women	3007	35 115	4527	44 709	15	97	428	3216	7977	83 138
Total	6887	106 905	7592	83 916	25	204	619	5412	15 123	196 438

[a]Atherosclerosis/arterial embolism and thrombosis.
ICVD, ischaemic cerebrovascular disease; IHD, ischaemic heart disease; PAD, peripheral arterial disease; YLL, years of life lost.

ambulatory care. Around 70% of all inpatient hospital admissions occur in public hospitals.[21]

Five DWs for ICVD were retrieved from the most recent GBD 2015 study,[22] along with the distribution of prevalent cases across the five levels of disability. The former was used to estimate Portuguese prevalence estimates of ICVD across the different levels of disability. Adjustments were made to account for estimates specifying acute or chronic stroke. Disability due to acute stroke was considered to last for 28 days, and for chronic stroke from the 29th day until death. For incident cases, a DW of 0.22 was considered for the first 28 days, and a DW of 0.17 for the following days, given that according to the GBD, 24% of patients with chronic stroke present with no sequelae.[3] For patients who developed a stroke in previous years, a DW for chronic stroke of 0.22 was considered, and all patients were assumed to developed sequelae.

Prevalence and disability weights of peripheral arterial disease

The prevalence of PAD and the proportion of symptomatic individuals (individuals presenting with leg pain or discomfort when walking) were sourced from Menezes *et al.*,[23] a Portuguese observational study on the epidemiology of PAD including 5985 individuals above the age of 50 across the country. Prevalence rates by age and sex from the study were extracted and applied to the Portuguese population in 2016 (by age and sex). A DW of 0.01 was used.

Adjustments for comorbidity

YLDs for each clinical presentation of atherosclerosis corresponded to the product of the number of prevalent cases of each disease by an average DW. However, total YLDs for atherosclerosis did not correspond to the sum of YLDs for all clinical presentations, as two or more disease conditions can occur simultaneously, either dependently or independently of each other, and, importantly, this can lead to a DW of more than one. Contrary to the GBD study where DWs were estimated for different conditions independently, and no attempt was made to estimate weights for comorbid conditions, in the present study, weights were adjusted to account for comorbidities.

According to the GBD methodology,[3] prevalence estimates of pairwise comorbid combinations of disease are usually estimated based on the assumption that conditions are independent. This assumption has its limitations given that it does not account for correlation between different conditions. In fact, when considering atherosclerosis, it is not possible to assume independence between its different clinical presentations. In the present study, the overlap between the different clinical presentations of atherosclerosis was estimated using data from the primary health care database from the Lisbon and Tagus Valley Regional Health Administration (SIARS—Sistema de Informação da Administração Regional de Saúde), and later adjusted to national estimates following a two-step process. First, the prevalence of each overlapping pair was retrieved from SIARS, which was used to estimate a correction ratio between the observed prevalence and the estimated prevalence, based on the assumption that conditions are independent. Later, the correction ratio from SIARS was applied to national prevalence estimates for each condition, obtained from a National Health Survey,[18] assuming the principle of independence, to obtain national prevalence estimates for each overlapping pair (i.e. ICVD and PAD; ICVD and IHF; PAD and IHF; ICVD, PAD and IHF, etc.).

Two clinical presentations were, nevertheless, treated differently, namely stable angina and AMI. First, given the short duration of 28 days assumed for the DW for AMI, this condition was not included in the adjustment exercise for comorbidities, rather was added to the total YLDs. Furthermore, the prevalence of stable angina registered in SIARS was considerably lower than the national mainland prevalence, hence it was added to the total YLDs, assuming independence from the remaining conditions, i.e. IHF, ICVD, and/or PAD.

A multiplicative model was used to estimate weights for pairwise combinations of comorbid conditions according to the methodology described in the GBD[24], given as:

$$DW_{1+2} = 1 - (1 - DW_1) \times (1 - DW_2),$$

where DW_1 is the disability weight for condition 1, DW_2 is the disability weight for condition 2, and DW_{1+2} is the combined disability weight for both conditions.

Uncertainty around the DWs and the YLDs for both individual and pairwise clinical manifestation of atherosclerosis is presented in sensitivity analyses in the Supplementary material online, *Tables S1 and S2*.

Results

Years of life lost due to premature mortality

Table 2 shows the total number of deaths and YLL attributable to atherosclerosis relative to total mortality and YLL due to all other causes in mainland Portugal. The total number of deaths attributable to atherosclerosis totalled 15 123, which corresponded to 14.3% of overall mortality in mainland Portugal. A total of 196 438 YLL attributable to atherosclerosis was estimated based on the total number of deaths and standard life expectancy, corresponding to 12.2% of total YLL due to overall premature mortality (1.6 million YLL). The largest contributor to total YLL was IHD (6887 deaths and 106 905 YLL), followed by ICVD (7592 deaths and 83 916 YLL), and PAD and other

forms of atherosclerosis (644 deaths and 5616 YLL). Although ICVD contributed the largest mortality, IHD corresponded to the largest YLL. Each death due to atherosclerosis corresponded to an average of 13 YLL (compared to an average of 15.2 YLL for each death due to overall mortality).

Table 3 shows the number of deaths and YLL due to atherosclerosis for men and women. Amongst men, IHD was the largest contributor to years lost to mortality due to atherosclerosis, whereas amongst women ICVD contributed the largest number of deaths and YLL. Although women had larger number of deaths compared to men, total YLL were larger for men.

Figure 1A shows the number of YLL per 100 000 inhabitants due to atherosclerosis for both men and women. Men registered higher values than women in all age groups but the age group 95+, with a total of 2439 YLL for men, 1609 for women, and 2002 per 100 000 inhabitants for both sexes. Years of life lost values increased steadily with age, with individuals in older age cohorts registering the largest total YLL and YLL per 100 000 inhabitants. Total YLL per 100 000 inhabitants were also estimated for the different clinical manifestations of atherosclerosis: 1090 due to IHD, 855 due to ICVD, 2 due to PAD, and 55 due to other forms of atherosclerosis. *Figure 1B–E* shows the demographic patterns of each clinical disease, which follow similar directions to the overall YLL due to atherosclerosis. Peripheral arterial disease and other forms of atherosclerosis register, however, larger YLL for women above the age of 85 years old.

Years lived with disability

National estimates indicate that the different clinical manifestations of atherosclerosis affect ~674 000 adults in mainland Portugal (9% of the adult population). In 2016, a total of 64 505 YLD were attributable to atherosclerosis.

Table 4 shows the prevalence, DW, and YLD for each single clinical manifestation included. Stable angina was the most prevalent clinical disease, however, it was ischaemic stroke with the second largest prevalence that contributed the largest YLD (29 137 YLD). This is due to the large DW that reflects the disability and long-term consequences associated with this disease. Although relatively prevalent, AMI yielded few YLD, as the DW was attributed solely to the first 28 days after the episode has occurred.

The sensitivity analyses show the uncertainty around the YLDs for the individual and pairwise clinical manifestation of atherosclerosis. Total YLDs varied between 42 302 and 90 380 (results available in the Supplementary material online).

Prevalence, DW, and YLD for pairwise clinical manifestations are available in Supplementary material online, *Table S2*.

Total disease burden (DALYs)

The overall burden of atherosclerosis corresponding to the sum of YLL and YLD was 260 943 DALY, in mainland Portugal in 2016. Total YLL represented 75% of total DALY (196 438 YLL) (see *Figure 2*).

Discussion

Summary of results

The current study estimated the burden of disease attributable to atherosclerosis in mainland Portugal in 2016, using the 2010 GBD methodology and the DALY as the measure of disease burden.

In 2016, atherosclerosis was responsible for 14.3% of all deaths and 12.2% of overall YLL in mainland Portugal. The relative weight of atherosclerosis on total YLL was slightly lower than the weight on overall mortality, which could be explained by the fact that, on average, deaths from atherosclerosis occur amongst individuals in older age cohorts compared to deaths from all other causes. Ischaemic cerebrovascular disease contributed the largest mortality, however, IHD corresponded to the largest YLL. Although there is no direct translation of mortality into YLL, and deaths of each clinical disease occur at different ages, there is evidence that deaths by IHD occur at younger ages, which in its turn results into greater YLL. These results highlight the different relative burden of each clinical manifestation of atherosclerosis.

Total mortality was larger for women than men; however, total YLL was larger for men. This suggests that despite atherosclerosis leads to more deaths amongst women, these have longer life expectancy than men, thus contributing less to YLL. Additionally, ICVD was the largest contributor to mortality and YLL amongst women, whereas IHD was the largest contributor amongst men. These results also highlight sex-specific differences in the epidemiology of atherosclerotic disease.

Most of the overall atherosclerosis burden was attributed to YLL due to premature death, with YLD contributing 25%. The total value of 260 943 DALY estimated in our study corresponds to a loss of 10 days per adult or 128 days per symptomatic patient.

Comparison with other studies

To the authors' knowledge, this study is the first of its kind to estimate the burden attributable to atherosclerosis following the GBD methodology. Other studies have, however, estimated the burden associated with individual clinical manifestations of atherosclerosis, and the burden of CVD on a broader spectrum. Roth *et al.*[17] estimated the global, regional, and national burden of cardiovascular diseases for 10 causes between 1990 and 2015, as part of the GBD Collaborative Research project. The authors estimated 15.6 million YLL in 2015 due to CVD in Western Europe, with 57% in men, and ~1983 YLL per 100 000 inhabitants. The proportion of YLL in men and the number of YLL per 100 000 inhabitants compare favourably with the proportion of YLL in men due to atherosclerosis (57%) and the YLL per 100 000 inhabitants found in the present study (total 2002 YLL per 100 000 inhabitants in mainland Portugal in 2016). Roth *et al.* estimated the following YLL per 100 000 inhabitants in Western Europe; 1058 YLL due to IHD, 1058 due to ischaemic stroke, and 21 due to PAD. In the present study, the estimated YLL per 100 000 inhabitants for these conditions were 103%, 81%, and 10% of these values, respectively.

Another study by Henriques *et al.*[25] estimated the burden attributed to IHD in mainland Portugal, which amounted to half of that of atherosclerosis. Similar patterns were reported, with YLLs being the

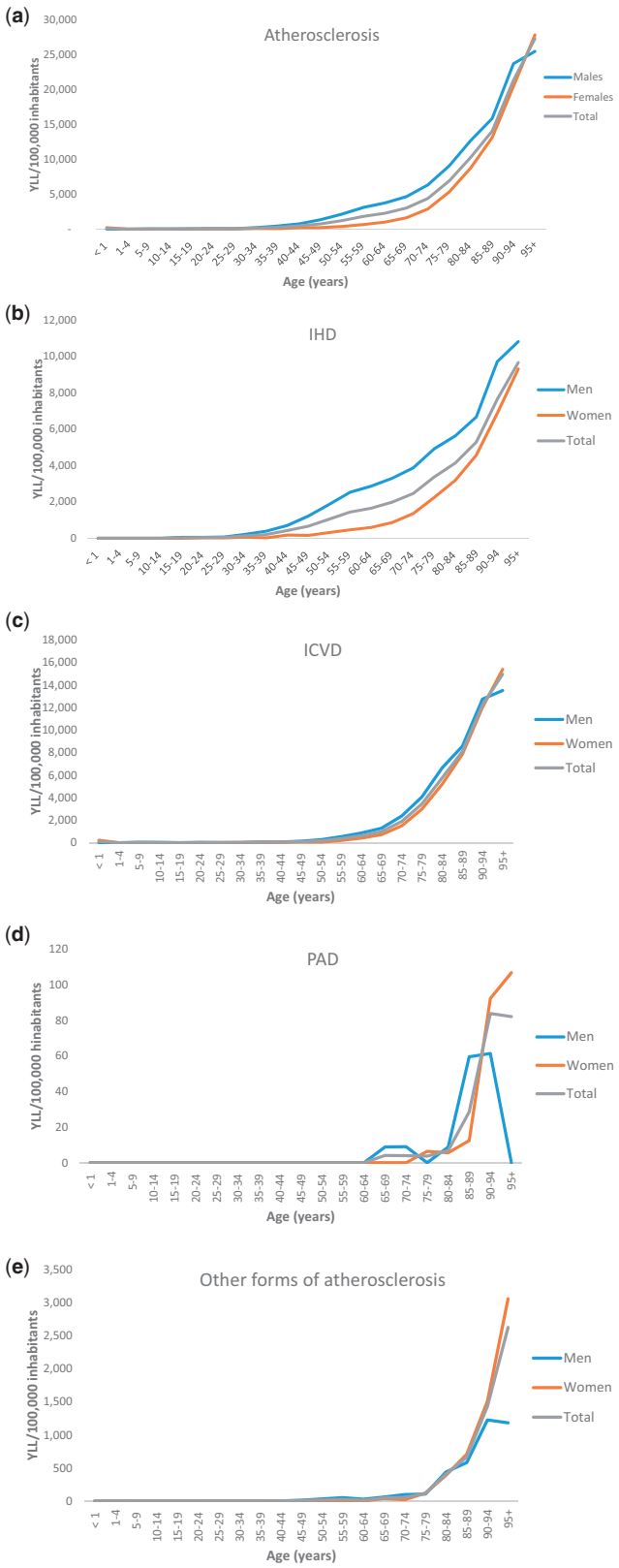

Figure 1 (*A–E*) Years of life lost due to atherosclerosis and its clinical manifestations per 100 000. ICVD, ischaemic cerebrovascular disease; IHD, ischaemic heart disease; PAD, peripheral arterial disease; YLL, years of life lost.

Table 4 Years lived with disability for individual clinical manifestations of atherosclerosis in mainland Portugal, 2016

	Prevalence	Average DW	YLD
AMI	12 671	0.01	97
Stable angina	375 278	0.07	27 864
IHF NYHA II–IV	91 046	0.06	5828
Ischaemic stroke	136 725	0.21	29 137
Symptomatic PAD	153 570	0.01	2150
Total	674 309[a]		64 505[a]

[a]Total prevalence does not correspond to the sum of all individual prevalence estimates due to account for comorbidities. Please see Supplementary material online, *Table S2* for prevalence estimates taking into account comorbidities.
AMI, acute myocardial infarction; DW, disability weight; IHF, ischaemic heart failure; NYHA, New York Heart Association Classes; PAD, peripheral arterial disease; YLD, years lived with disability.

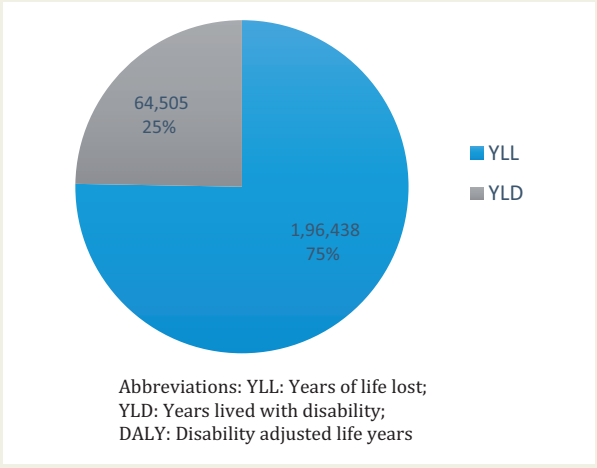

Figure 2 Total years of life lost, years lived with disability, and disability-adjusted life years attributable to atherosclerosis in mainland Portugal, 2016. YLD, years lived with disability; YLL, years of life lost.

main contributors to total DALYs, and the burden being largest amongst men and in older age cohorts.

The authors of the present study have previously estimated the burden of other cardiovascular diseases and risk factors in Portugal, such as the burden of HF[26] and hypercholesterolaemia.[27] In comparison to findings from those studies, atherosclerosis is responsible for nearly four times more deaths and YLL than HF and nine times more deaths than hypercholesterolaemia; and the total burden attributed to atherosclerosis is nine times larger than the burden of HF and 16 times that of hypercholesterolaemia.[26,27] However, these studies used the previous GBD methodology and included age weighting and discounting in their estimates, therefore, comparisons should be made with caution.

Limitations

This study has several limitations. According to the latest GBD methodology,[3] prevalence estimates of pairwise comorbid disease conditions are usually estimated based on the assumption that conditions are independent. Assuming the principle of independence when studying the burden of atherosclerosis is not reasonable as clinical manifestations of atherosclerosis often overlap, hence the authors had to adjust the prevalence of the disease to this pattern. Although assuming independence between conditions does not truly reflect reality, the principle of independence was upheld when estimating the prevalence of angina, and the authors are aware of its limitations regarding the final prevalence estimates.

Sources of estimates differed, and when no Portuguese data were available, the next best available evidence was considered, such as in the case of the distribution of angina by severity level sourced from a Spanish population study. Although this is a limitation, there are similarities between the two countries in geographical location, population characteristics, and patterns of cardiovascular disease.

Another example was the source of information for the prevalence of IHF according to level of severity, sourced from the EPICA study, which dated back to 1998–2000. As the best and most recent available evidence albeit dated, the authors are aware that therapies for IHD and HF have changed over the last decades, which may have undoubtedly altered the prevalence of IHF, as well as disease severity.

Estimates for ICVD included only ischaemic strokes and not transient ischaemic attack. However, it should be recognized that not all ischaemic strokes, such as lacunar strokes, are due to atherosclerosis. In fact, we acknowledge the possible contribution of atrial fibrillation to the stroke episodes included in our work. Nevertheless, as previously acknowledged by other authors, the interplay between the key players in stroke (atrial fibrillation, age, HF, atherosclerosis) makes it difficult to disentangle their potential individual effects. In fact, some studies suggest a biological plausibility for a causal association between atherosclerosis and atrial fibrillation.[28] Mortality attributed to IHF was not considered in total YLLs due to lack of data on deaths specifically due to HF attributable to atherosclerosis. However, given that the direct cause of death may not be attributable to IHF, rather to an underlying disease such as AMI, some deaths may have already been included amongst deaths due to IHD.[14]

Nonetheless, the mortality and YLL due to atherosclerosis have probably been underestimated because other forms of cardiovascular death, including unexplained sudden death, thromboembolic diseases, aortic pathology, and haemorrhagic stroke were not considered.

Implications for policy and practice

For the last 100 years, major causes of death and disability have shifted from communicable diseases and nutritional deficiencies to non-communicable diseases such as cancer, diabetes, and cardiovascular diseases,[29] with urbanization, economic development, and sedentary behaviour contributing to this paradigm shift. Contrarily, over the last two decades, patterns of CVD have changed, with major declines in rates of CVD being observed in high- and middle-income countries.

In Portugal, stroke and cardiovascular diseases are addressed by a priority health programme launched by the Portuguese Directorate General of Health in 2012. The adoption of preventive strategic measures and improved diagnostics and therapeutics in these areas

have contributed to a reduction in the number of deaths from cardiovascular diseases between 2011 and 2015, particularly due to ischaemic stroke before the age of 70 (39% reduction).[30] This is probably due to a set of factors, namely the introduction of new therapeutic agents and the activity of multiple stroke units.[30] Many modifiable cardiovascular risk factors have been identified through large longitudinal studies, including, but not limited to, smoking, hypertension, hypercholesterolaemia, and diabetes.[31–34]

Systemic approaches to these risk factors are needed. Preventive drug therapies can contribute to risk factor control and reduce the relative risk of cardiovascular events in high-risk patients.[35] However, when risk factor modification starts later in adulthood, the burden of atherosclerotic CVD remains high. Drug therapies targeting risk factor control in younger and early midlife adults could have the potential to regress earlier stages of atherosclerosis, thus reducing the risk of developing clinical atherosclerotic CVD events later in life.

Context relevant strategies spanning the broad spectrum of prevention, including both population-based interventions and interventions targeting high-risk individuals, are called for to reduce the prevalence of these risk factors, particularly smoking and the emerging obesity epidemic, and to mitigate the burden associated with their consequences. Several strategies are currently available with strong evidence of effectiveness and cost-effectiveness. For instance, interventions targeting increase in excise tax,[36] reduction in access to tobacco,[37] and counselling and educational programmes for smokers[38,39] are cost-effective examples targeting the reduction in smoking rates.

Other studies have demonstrated the cost-effectiveness of strategies to improve physical activity and promote healthy diets.[40] For instance, bike lanes[41] and exercise prescriptions[42] are cost-effective strategies targeting low physical activity. Sugar and salt taxes,[43] as well as policies influencing price or availability of fruits and vegetables[44] are cost-effective strategies in improving dietary habits.

Many of these cost-effective strategies are included in the existing National Program for the Promotion of Healthy Eating, the National Program for the Prevention and Control of Smoking, and the National Program for the Promotion of Physical Activity, already in place in Portugal.[45] Portugal has come a long way, but there is still a long road ahead. If societies want to combat the growing burden of atherosclerotic cardiovascular diseases, a focus needs to be routed towards systemic, multilevel, and multidisciplinary strategies targeting population health literacy, behaviours, infrastructure and, importantly, the availability and provision of adequate health strategies from prevention to treatment[46] for improving population health and reducing health sector spending in the long term.

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* online.

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Conflict of interest

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Data availability

The data underlying this article will be shared on reasonable request by the corresponding author.

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