



The burden of nonrheumatic valvular heart diseases in Iran between 1990 and 2017: Results from the global burden of disease study 2017

Jalal Arabloo^a, Negar Omidi^b, Aziz Rezapour^a, Ali Sarabi Asiabar^a, Seyyed Mojtaba Ghorashi^b, Samad Azari^{c,*}

^a Health Management and Economics Research Center, Health Management Research Institute, Iran University of Medical Sciences, Tehran, Iran

^b Cardiovascular Disease Research Institute, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran

^c Hospital Management Research Center, Health Management Research Institute, Iran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:

Cardiovascular diseases
Burden of disease
Nonrheumatic valvular heart disease
Iran

ABSTRACT

Background: Nonrheumatic valvular heart diseases (NRVDs) are some of the common and treatable cardiovascular diseases. The objective of this study was to describe the burden of NRVDs in Iran from 1990 to 2017 and to compare the findings with those from the world and in particular, the North Africa and Middle East (NAME) region.

Methods: Using publicly available estimates from the Global Burden of Disease 2017 Study (the GBD 2017 Study) for Iran and the NAME region, we reported the years of life lost (YLLs), years lived with disability (YLDs), disability-adjusted life years (DALYs), and the prevalence for NRVDs by age group and sex between 1990 and 2017.

Results: There were an estimated 174,071 cases and 957 deaths from NRVDs in Iran in 2017. In addition, 1844 YLDs, 21,661 YLLs, and 23,506 DALYs were caused by NRVDs in Iran in 2017. Between 1990 and 2017, the age-standardized prevalence rate increased in Iran by 15%, the death rate by 15.3%, and DALYs by 2%. Nevertheless, in the world and the NAME region, the age-standardized rates for DALYs and deaths decreased and the age-standardized prevalence rate increased till 2017.

Conclusions: The burden of NRVDs is on the rise in Iran. A reduction in the burden of NRVDs in Iran requires the development of appropriate plans to meet the health needs of patients, the decrease of the modifiable risk factors, the allocation of adequate resources for the early diagnosis and management of the diseases, and an improvement in access to treatment technologies.

1. Introduction

The third goal of the Sustainable Development Goals (SDGs), devised by the United Nations, states that ensuring health through the promotion of healthy lifestyles and well-being at all ages is of paramount importance to achieve sustainable human development [1]. A major barrier to sustainable development and one of the main causes of mortality are cardiovascular diseases (CVDs) [1,2]. In 2017, CVDs represented the main cause of years of life lost (YLLs) [3]. Among the most common and treatable CVDs are nonrheumatic valvular heart diseases (NRVDs) [4,5]. Aortic and mitral valve diseases affect up to 2.5% of the population of the United States [5,6].

The Global Burden of Disease 2017 Study (the GBD 2017 Study) estimated the incidence, prevalence, mortality, YLLs, years lived with

disability (YLDs), and disability-adjusted life years (DALYs) by age and sex for 354 specific diseases in 195 countries and territories across 21 regions and 7 super-regions in the period from 1990 to 2017 [7–10]. For the first time in 2018, the GBD 2017 Study estimated the burden of NRVDs, including calcific aortic valve disease, degenerative mitral valve disease, and noncongenitally diseases of the pulmonic and tricuspid valves. According to the study, 1.5 million and 1.1 million DALYs were lost due to calcific aortic and degenerative mitral valve diseases across the world, respectively, representing 0.12% of the total health lost from all diseases in 2017 [4].

In some countries such as Iran, the burden of NRVDs is almost unknown and is, thus, not considered a public health problem because previous studies have focused mostly on the burden of ischemic heart disease, heart failure, and other CVDs [2,11]. Also, studies in middle-

* Corresponding author.

E-mail addresses: rezapour.a@iums.ac.ir (A. Rezapour), azari.sa@iums.ac.ir (S. Azari).

<https://doi.org/10.1016/j.ijcha.2022.100956>

Received 28 October 2021; Received in revised form 26 December 2021; Accepted 4 January 2022

Available online 17 January 2022

2352-9067/© 2022 Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

income countries have shown a considerable increase in life expectancy in recent decades, denoting that the etiology of valvular heart diseases may be shifting to NRVDs [11–13]. To our knowledge, the current literature lacks research on the national burden of NRVDs in Iran. Based on the assumption that NRVDs are highly prevalent and represent a public-health problem in developing countries, we aimed to draw upon the publicly available GBD 2017 Study estimates to describe the burden of NRVDs in Iran from 1990 to 2017 and compare the findings with the estimates from the world and in particular, the North Africa and Middle East (NAME) region. Estimates on NRVDs are crucial to a better understanding of this group of diseases and preparation of health systems accordingly. We hope that our findings will aid policy- and decision-makers to make evidence-based decisions with a view to prioritizing and allocating resources more efficiently for NRVDs, taking into account trade-offs and opportunities.

2. Materials and methods

The present study drew upon publicly available estimates from the GBD 2017 Study to report the counts, all-age rates, age-standardized rates per 100,000 population of deaths, YLLs, YLDs, DALYs, and the prevalence for NRVDs by age group and sex for Iran and NAME countries from 1990 to 2017.

The methods applied in this study in accordance with the Declaration of Helsinki (1964).

Detailed descriptions of the methodology of the GBD 2017 Study have been described in previous publications [4,7–10]. The methodology is compliant with the recommendations of the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [14]. All estimates presented here are from the GBD 2017 Study and are publicly available online at <http://ghdx.healthdata.org>.

In the GBD 2017 Study, calcified aortic valve disease was defined as a clinical diagnosis of aortic valve stenosis or regurgitation due to the progressive calcification of the valve or the annulus leading to hemodynamically moderate or severe stenosis or regurgitation. Degenerated mitral valve disease was defined as a disorder caused by the myxomatous degeneration of the mitral valve leading to hemodynamically moderate or severe regurgitation. Other NRVDs comprised a residual category that encompassed nonrheumatic, noncongenitally valve disorders of the tricuspid and pulmonary valves. Finally, a category of total NRVD was defined as the aggregate of the 3 previously mentioned categories (i.e., calcific aortic valve disease, degenerative mitral valve disease, and other NRVDs) [5].

YLDs were computed by multiplying disease prevalence by disability weighted for that condition, reflecting the severity of different conditions as assessed by means of surveys administered to the general public [7]. YLLs were defined as the number of years lost due to premature mortality and were calculated by subtracting the age at death from the longest possible life expectancy [15]. DALYs were defined as the quantitative measurement of the overall span of years of healthy life lost due to disease [15,16]. NRVD DALYs were considered to be the sum of YLDs and YLLs for each location, year, sex, and age group.

All age-standardized rates for all the measures were calculated using the GBD 2017 Study standard population

It should be noted that the GBD 2017 Study estimated causes of death by incorporating sophisticated methods to adjust for incomplete or missing values, including vital registration and verbal autopsy data, general heterogeneity in data completeness and quality, and the redistribution of the so-called “garbage codes” (i.e., those insufficiently specific or implausible causes of death codes) [7]. Additionally, the GBD 2017 Study provided a standardized approach for estimating incidence, prevalence rates, DALYs, YLLs, and YLDs by cause, age, sex, year, and location [9]. It also utilized statistical modeling tools, including the Cause of Death Ensemble model (CODEm) for estimating the fatal outcomes and YLLs and DisMod-MR 2.1, a Bayesian meta-regression tool for estimating nonfatal health loss [10].

The GBD 2017 Study calculated a 95% uncertainty interval (95% UI) for each parameter. These 95% UIs were derived from the 2.5th and 97.5th centile values of 1000 draws for each parameter.

The data sets generated for this study can be found in the GBD 2017 Study at <http://ghdx.healthdata.org/gbd-results-tool>.

3. Results

3.1. Prevalence

Table 1 shows that there were an estimated 174,071 (95% UI: 166,524 to 181,553) cases of NRVDs in 2017 in Iran, accounting for approximately 0.6% of total cases in the world. Between 1990 and 2017, the number of prevalent cases increased by 212%, while the all-age prevalence rate of NRVDs increased by 120% from 96.44 (95% UI: 92.5 to 100.4) to 211.83 (95% UI: 202.6 to 220.9) per 100,000 population. Also, between 1990 and 2017, the age-standardized prevalence rate of NRVDs in Iran rose relatively slightly by 15%, from 215.56 (95% UI: 206.98 to 224.37) in 1990 to 248.92 (95% UI: 238.0 to 259.9) in 2017 per 100,000 population. The rate increased by 15% in males and 16% in females.

As is depicted in Fig. 1, the all-age prevalence rates and age-standardized prevalence rates for females were higher than those for males in all the years studied.

Fig. 2A demonstrates that the prevalence rate increased with age, and this increase in the population over 60 years old was severe.

A comparison of the age-standardized prevalence rate between the world and the NAME region as a whole showed an increase by 2% (4% in males and 0% in females) and 13% (12% in males and 13% in females), respectively (Fig. 3A).

3.2. Death

Table 1 shows that in Iran, NRVDs resulted in 957 (95% UI: 890 to 1076) deaths in 2017, with slightly more deaths in females than males. Between 1990 and 2017, the age-standardized death rate of NRVDs in Iran increased by 15%, from 1.30 (95% UI: 1.17 to 1.49) in 1990 to 1.50 (95% UI: 1.37 to 1.67) in 2017 per 100,000 populations. The rate increased by 10% in males and 24% in females. The all-age death rate rose by 114% in the same period; nonetheless, the increase was higher in the age group 70 or older than in others since 1990 (Fig. 2B).

In the world and the NAME region as a whole, however, the age-standardized death rate decreased by –3% (–4% in males and –2% in females) and –19% (–10% in males and –25% in females), respectively (Fig. 3B).

3.3. YLLs, YLDs, and DALYs

In 2017, NRVDs resulted in 1844 (95% UI: 1051 to 2895) YLDs, 21,661 (95% UI: 20,513 to 25,467) YLLs, and 23,506 (95% UI: 22,021 to 27,182) DALYs in Iran. While moderate increases were estimated in the NRVD prevalence and mortality from 1990 to 2017, the age-standardized rates of YLLs and YLDs due to NRVDs increased slightly over this period by 1.4% and 7%, correspondingly, resulting in a 2% increase in the age-standardized DALYs rate, from 31.54 (95% UI: 27.93 to 36.83) in 1990 to 32.12 (95% UI: 29.99 to 36.49) in 2017 per 100,000 populations in Iran (Table 1). The rate rose by 4% in males and 0.6% in females. In the same period, the all-age DALY rates increased by 64% (Fig. 2C).

In the world and the NAME region as a whole, the age-standardized DALY rate decreased by –12.5 (–13% in males and –12% in females) and –20.4% (–14% in males and –25% in females), respectively (Fig. 3C).

Table 1
The prevalence, deaths, YLDs, YLLs, and DALYs counts and rates (per 100,000) for NRVDs by sex between 1990 and 2017 in Iran.

Measure	Gender	Number [95% UI]			Rate (per 100,000) [95% UI]			Age-Standardized Rate (per 100,000) [95% UI]		
		1990	2017	% Change	1990	2017	% Change	1990	2017	% Change
Prevalence	Male	26,990 (25,739–28,311)	81,192 (77,344–85,182)	201%	91.54 (87.30–96.03)	194.82 (185.59–204.40)	113%	202.09 (193.18–211.17)	232.69 (221.33–244.13)	15%
	Female	28,819 (27,616–29,954)	92,879 (88,894–96,810)	222%	101.54 (97.30–105.53)	229.33 (219.49–239.03)	126%	229.27 (220.26–238.25)	265.15 (253.49–276.19)	16%
	Both	55,809 (53,562–58,130)	174,072 (166,524–181,553)	212%	96.44 (92.56–100.46)	211.83 (202.64–220.93)	120%	215.56 (206.98–224.37)	248.92 (238.04–259.92)	15%
Death	Male	161 (135–194)	467 (387–566)	190%	0.55 (0.46–0.66)	1.12 (0.93–1.36)	104%	1.28 (1.07–1.53)	1.41 (1.16–1.67)	10%
	Female	149 (127–177)	490 (462–534)	230%	0.52 (0.45–0.62)	1.21 (1.14–1.32)	133%	1.29 (1.14–1.49)	1.60 (1.50–1.73)	24%
	Both	310 (273–364)	957 (890–1,076)	209%	0.54 (0.47–0.63)	1.16 (1.08–1.31)	115%	1.30 (1.17–1.49)	1.50 (1.37–1.67)	15%
YLDs	Male	260.5 (146.1–419.3)	863.3 (491.6–1,363.7)	231%	0.88 (0.50–1.42)	2.07 (1.18–3.27)	135%	2.70 (1.57–4.24)	2.87 (1.66–4.47)	6%
	Female	290.9 (163.5–465.2)	981.6 (562.4–1,533.8)	237%	1.0 (0.58–1.64)	2.4 (1.3–3.7)	140%	3 (1.76–4.7)	3.27 (1.88–5.06)	9%
	Both	551.5 (314.0–883.9)	1,844.9 (1,051.4–2,895.4)	235%	0.95 (0.54–1.53)	2.25 (1.28–3.52)	137%	2.87 (1.76–4.46)	3.07 (1.77–4.77)	7%
YLLs	Male	4,999.4 (4,147.2–6,103.5)	11,474.8 (10,005.5–14,505.8)	129%	16.9 (14.0–20.7)	27.5 (24.0–34.8)	63%	28.9 (24.4–35.0)	30.1 (25.8–37.4)	4%
	Female	4,527.3 (3,751.9–5,530.8)	10,186.8 (9,574.6–11,416.4)	125%	15.9 (13.2–19.4)	25.1 (23.6–28.1)	58%	28 (23.7–33.6)	28 (26.4–31.3)	0%
	Both	9,526.8 (8,178.7–11,329.3)	21,661.6 (20,513.8–25,467.0)	127%	16.4 (14.1–19.5)	26.3 (24.9–30.9)	60%	28.6 (25.1–33.7)	29.0 (27.4–33.7)	1.4%
DALYs	Male	5,260.01 (4,379.47–6,389.91)	12,338.18 (11,073.42–15,282.5)	135%	17.84 (14.85 to 21.67)	29.61 (26.57–36.67)	66%	31.66 (26.72–38.23)	32.97 (29.28–40.10)	4%
	Female	4,818.37 (4,004.34–5,831.81)	11,168.4 (10,379.4–12,493.9)	132%	16.98 (14.11 to 20.55)	27.58 (25.63–30.85)	62%	31.12 (26.24–36.83)	31.33 (29.14–34.99)	0.7%
	Both	10,078.37 (8,711–11,942.64)	23,506.61 (22,021.52–27,182.36)	133%	17.42 (15.05 to 20.64)	28.61 (26.80 to 33.08)	64%	31.54 (27.93 to 36.83)	32.12 (29.99–36.49)	2%

DALYs: disability-adjusted life years; NRVDs: Nonrheumatic valvular heart diseases; YLDs: years lived with disability; YLLs: years of life lost.

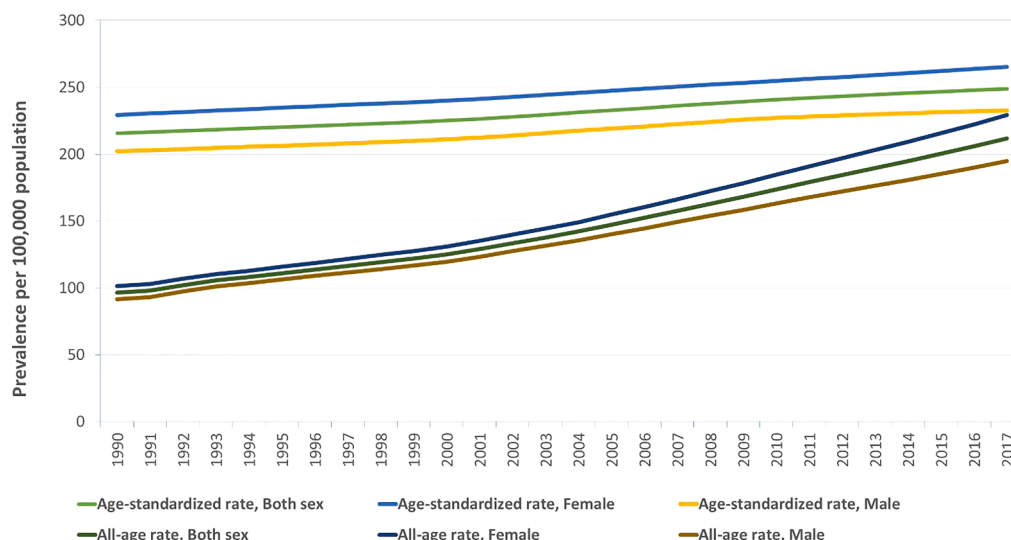


Fig. 1. Trends in age-standardized and all-age prevalence rates by sex in Iran from 1990 to 2017 are illustrated herein.

4. Discussion

The current study presents the first national estimates of NRVD burden in Iran. Such estimates of NRVD burden should enable countries to systematically monitor progress in the prevention and treatment of this group of diseases. Our study showed that the burden of NRVDs is on the rise in Iran due to population growth and aging [4,17].

The incremental trend in age-standardized prevalence rate in Iran during 1990–2017 (215.56 to 248.92 per 100,000) could be due to increased life expectancy from 63.8 years in 1990 to 76.2 in 2017 and increasing risk factors such as obesity and hypertension in Iran, about 13% of the world's adult population was obese in 2016, whereas the national prevalence rates of obesity in Iran are 22.7% (15.3% of men and 29.8% of women) [18–20]. Also, there was a significant difference between the prevalence of obesity among males and females in Iran.

Admittedly, the age-standardized prevalence rate in North America during three decades has decreased (1532 to 1438 per 100,000) while this has increased in Western Europe (471 to 640 per 100,000). On the other hand the age-standardized death rate in North America decreased (4.46 to 4.25 per 100,000) while this has increased in Western Europe (4.78 to 4.82 per 100,000). These results show that the trend of age-standardized prevalence and death rate are in the same direction.

Previous studies have shown that access to health care can affect the likelihood of identifying, diagnosing, or treating the disease. It seems that the estimated low burden of NRVD in recent years in Iran may be due to low diagnosis or lower survival of patients. Diagnosis of CAVD cases depends on the availability of echocardiography, which could lead to a lower estimation of the true burden of CAVD [4]. With improvement in availability of access to diagnostic tools, the reported incidence of CAVD will gradually increase. This may explain why countries with higher socioeconomic development had a higher age-standardized prevalence rate [21].

There are potential factors that influence NRVD mortality. For example, the prevalence of NRVD and related risk factors, access to diagnostic procedures and experience of surgical and trans-catheter interventions. The increase in the age-standardized rate of death over the study period in Iran; could probably be related to population aging or an increased chance of NRVD diagnosis with more access to diagnostic modalities. In Iran, the patients with NRVD are often elderly with a high rate of comorbidities and cardiovascular risk factors. In addition, studies showed that complications and mortality reduce with greater TAVI experiences and numbers, that it seems Iran is a slow TAVI adopter and has the lower numbers of TAVI procedures in comparison to Western

European countries. The NRVD mortality in Iran is likely to be different to that of NAME countries. This relates to the population affected (elderly vs. younger), as well as the access to resources to diagnose and treat the NRVD [22,23].

We found large geographic differences in the prevalence of NRVDs in Iran in comparison with the world. This could be due to variations in the levels of atherosclerotic risk factors such as high serum cholesterol, smoking, high body mass index, and high systolic blood pressure among countries [4,24,25]. On the other hand, we observed fewer geographic variations in the mortality rate of NRVDs, which is consistent with the previous literature showing that NRVDs may be unrelated to atherosclerotic risk factors [4]. Lower NRVD prevalence in Iran and NAME countries in comparing with globally could be due to lower access to health care service such as diagnosis and treatment intervention in developing countries, this is the most important barrier to accessing universal health coverage (UHC).

Despite a relatively trivial increase in the age-standardized rate of DALYs associated with NRVDs in the last 27 years in Iran, we observed a considerable increase in the number and rate of YLDs, demonstrating an increasing demand for health services and necessitating more efforts in the hospital sector to provide adequate services to the Iranian population.

Our study results also showed variations in the burden of NRVDs by both age and sex in Iran, which is concordant with the findings reported by other countries. Higher age-standardized and all-age mortality rates and the prevalence of NRVDs among women can be attributed, at least partially, to the high life expectancy or high survival of women to the oldest age group compared with men. The more rate prevalence, death and YLD in women in Iran could be attribute to higher life expectancy and higher risk factors like obesity. Our findings showed that prevalence and mortality increased with age, with older age groups being less likely to have had such treatments as transcatheter aortic valve replacement and transcatheter mitral valve repair for NRVDs [4].

The present study has limitations similar to those reported in previous publications in the GBD 2017 Study [7,16,24] such as wide 95% UIs around estimates due to the availability and quality of data. Another drawback of our study is that, in contrast to the GBD 2017 Study, we failed to divide NRVDs into 3 types, namely calcific aortic valve disease, degenerative mitral valve disease, and other NRVDs. It is worthy of note, however, that the GBD 2017 Study also did not differentiate between surgical and catheter-based valve interventions. In our study, it may be difficult to distinguish between cases of valve diseases from NRVDs and cases caused by other etiologies.

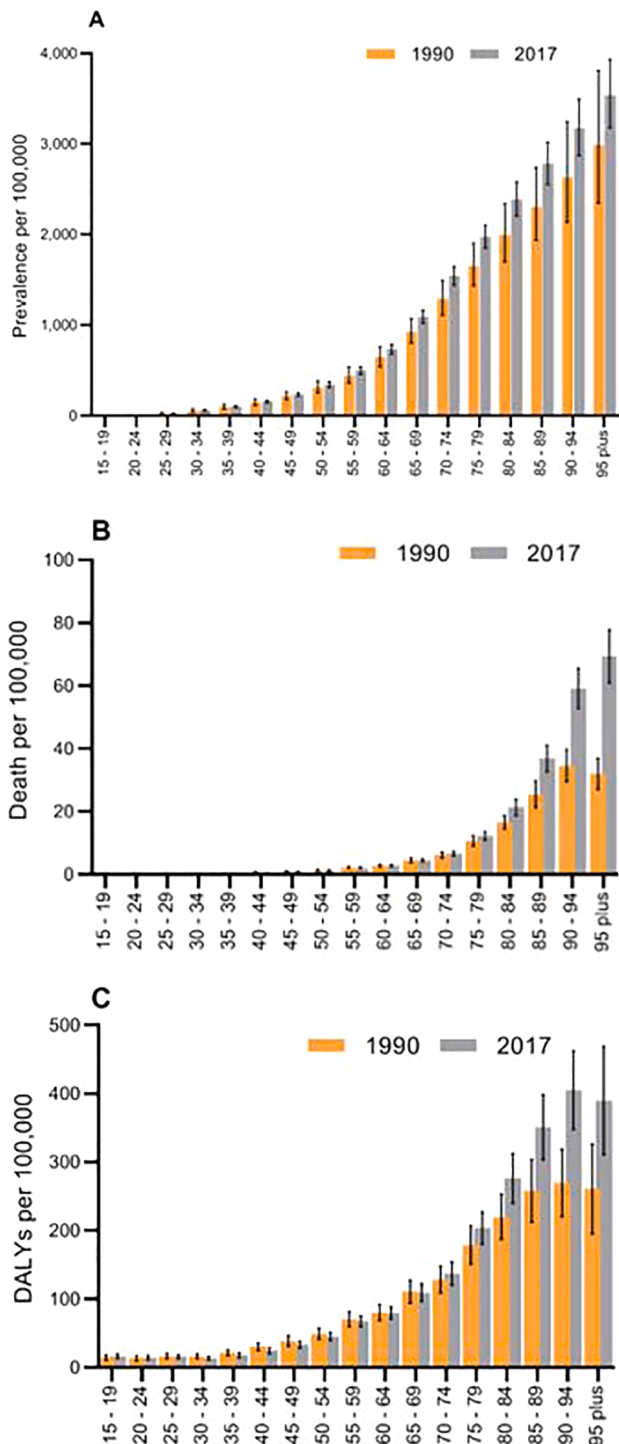


Fig. 2. Prevalence (A), deaths (B), and DALYs (C) per 100,000 for NRVDs by age groups in Iran between 1990 and 2017 are presented herein. DALYs: Disability-adjusted life years; NRVDs Nonrheumatic valvular heart diseases.

5. Conclusions

The results of the present study show that women and the elderly are at risk for NRVDs. Given the increasing burden of NRVDs in Iran, driven by population aging and increased prevalence of risk factors such as hypertension, it is essential for health policy-makers to develop appropriate plans with the aim of meeting the health needs of patients (especially the elderly), reducing modifiable risk factors, allocating adequate resources for the early diagnosis and management of this

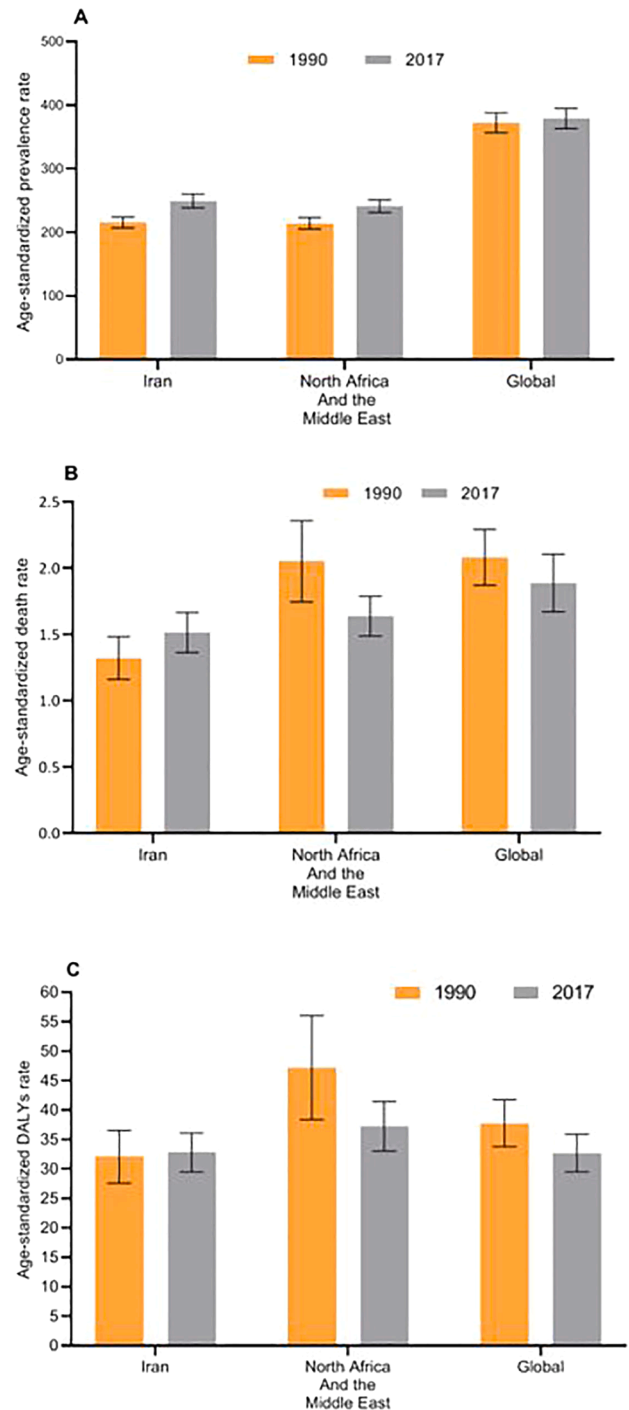


Fig. 3. Age-standardized prevalence (A), deaths (B), and DALYs (C) per 100,000 for NRVDs in Iran, the North Africa and Middle East region, and the world are illustrated herein (both sexes). DALYs: Disability-adjusted life years; NRVDs: Nonrheumatic valvular heart diseases.

group of diseases, and facilitating access to treatment technologies such as valve repair and replacement. This study provides burden estimations at the national level of Iran. It is necessary to estimate and analyze the burden of NRVDs at sub-national levels to find further details regarding the disease burden.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Permission for publishing these data was granted by Professor Christopher J. L. Murray, the director of the Institute for Health Metrics and Evaluation (IHME), to the Health Management Research Institute, Iran University of Medical Sciences.

Funding

There is no funding for this study. The Global Burden of Diseases 2017 Study was funded by the Bill and Melinda Gates Foundation. The funders had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, or final approval of the manuscript; and the decision to submit the manuscript for publication.

References

- [1] G.A. Roth, C. Johnson, A. Abajobir, F. Abd-Allah, S.F. Abera, G. Abyu, M. Ahmed, B. Aksut, T. Alam, K. Alam, Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015, *J. Am. Coll. Cardiol.* 70 (1) (2017) 1–25.
- [2] D.A. Watkins, C.O. Johnson, S.M. Colquhoun, G. Karthikeyan, A. Beaton, G. Bukhman, M.H. Forouzanfar, C.T. Longenecker, B.M. Mayosi, G.A.J.N.E.J.o.M. Mensah, Global, regional, and national burden of rheumatic heart disease, 1990–2015, *377*(8) (2017) 713–722.
- [3] P. Moraga, G.C.o.D.C.J.T. Lancet, Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016, *390*(10100) (2017) 1151–1210.
- [4] S.R. Yadgir, T. Alam, C. Johnson, M. Naghavi, G.J.C. Roth, Global burden of calcific aortic and degenerative mitral valve diseases. analysis from the global burden of disease 2017 study, 2018. *A17238 A17238*.
- [5] V.T. Nkomo, J.M. Gardin, T.N. Skelton, J.S. Gottdiener, C.G. Scott, M.J.T.L. Enriquez-Sarano, Burden of valvular heart diseases: a population-based study, *368* (9540) (2006) 1005–1011.
- [6] A.B. Goldstone, P. Chiu, M. Baiocchi, B. Lingala, W.L. Patrick, M.P. Fischbein, Y. J. Woo, Mechanical or biologic prostheses for aortic-valve and mitral-valve replacement, *New Engl. J. Med.* 377 (19) (2017) 1847–1857.
- [7] GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet* (London, England) 392(10159) (2018) 1789–1858.
- [8] GBD 2017 Mortality Collaborators, Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet* (London, England) 392(10159) (2018) 1684–1735.
- [9] GBD 2017 Causes of Death Collaborators, Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017, *The Lancet* 392(10159) (2018) 1736–1788.
- [10] GBD 2017 DALYs and HALE Collaborators, Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet* (London, England) 392(10159) (2018) 1859–1922.
- [11] J. Rwebembera, W. Manyilira, Z. Zhu, J. Nabbaale, J. Namuyonga, I. Ssinabulya, S. Lubega, P. Lwabi, J. Omagino, E. Okello, Prevalence and characteristics of primary left-sided valve disease in a cohort of 15,000 patients undergoing echocardiography studies in a tertiary hospital in Uganda, *BMC Cardiovascular Disorders* 18 (1) (2018), 82–82.
- [12] M. Essop, V. Nkomo, Rheumatic and nonrheumatic valvular heart disease: epidemiology, management, and prevention in Africa, *Circulation* 112 (23) (2005) 3584–3591.
- [13] H. Boudoulas, M. Vavuranakis, C. Wooley, Valvular heart disease: the influence of changing etiology on nosology, *J. Heart Valve Disease* 3 (5) (1994) 516–526.
- [14] G.A. Stevens, L. Alkema, R.E. Black, J.T. Boerma, G.S. Collins, M. Ezzati, J. T. Grove, D.R. Hogan, M.C. Hogan, R. Horton, Guidelines for accurate and transparent health estimates reporting: the GATHER statement, *The Lancet* 388 (10062) (2016) e19–e23.
- [15] Y. Xie, B. Bowe, A.H. Mokdad, H. Xian, Y. Yan, T. Li, G. Maddukuri, C.-Y. Tsai, T. Floyd, Z. Al-Aly, Analysis of the global burden of disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016, *Kidney Int.* 94 (3) (2018) 567–581.
- [16] GBD 2016 Causes of Death Collaborators, Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016, *The Lancet* 390(10100) (2017) 1151–1210.
- [17] X. Cheng, Y. Yang, D. Schwebel, Z. Liu, L. Li, P. Cheng, P. Ning, G. Hu, Population ageing and mortality during 1990–2017: A global decomposition analysis, *PLoS Med.* 17 (6) (2020) e1003138 e1003138.
- [18] World Health Organization(WHO). Obesity and overweight 2017 [Available from: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.
- [19] M. Blüher, Obesity: global epidemiology and pathogenesis. *Nature reviews, Endocrinology* 15 (5) (2019) 288.
- [20] S. Djalalinia, S.M. Saeedi, A. Sheidaei, N. Rezaei, S.I. Naghibi, M. Modirian, H. Zokaei, M. Yousefi, K. Gohari, A. Kousha, Patterns of obesity and overweight in the Iranian population: findings of STEPs 2016, *Front. Endocrinol.* 11 (2020), 42–42.
- [21] B. Yi, W. Zeng, L. Lv, P.J.A. Hua, Changing epidemiology of calcific aortic valve disease: 30-year trends of incidence, prevalence, and deaths across 204 countries and territories, *13*(9) (2021) 12710.
- [22] B.F. Stewart, D. Siscovick, B.K. Lind, J.M. Gardin, J.S. Gottdiener, V.E. Smith, D.W. Kitzman, C.M. Otto, C.H.S.J.J.o.t.A.C.o. Cardiology, Clinical factors associated with calcific aortic valve disease, *29*(3) (1997) 630–634.
- [23] A. Hartley, M. Hammond-Haley, D.C. Marshall, J.D. Saliccioli, I.S. Malik, R.Y. Khamis, J.J.F.i.C.M. Shalhoub, Trends in mortality from aortic stenosis in Europe: 2000–2017, *8* (2021).
- [24] GBD 2016 Risk Factors Collaborators, Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, *The Lancet* 390(10100) (2017) 1345–1422.
- [25] M. Ezzati, S.H. Vander, C. Lawes, R. Leach, W. James, A. Lopez, A. Rodgers, C. Murray, Rethinking the “diseases of affluence” paradigm: global patterns of nutritional risks in relation to economic development, *PLoS Med.* 2 (5) (2005) e133 e133.